(12) STANDARD PATENT (11) Application No. **AU 2013323360 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Azaquinazoline inhibitors of atypical protein kinase C

(51) International Patent Classification(s)
C07D 471/04 (2006.01) ***A61P 35/00*** (2006.01)
A61K 31/437 (2006.01) ***C07D 519/00*** (2006.01)

(21) Application No: **2013323360** (22) Date of Filing: **2013.09.27**

(87) WIPO No: **WO14/052699**

(30) Priority Data

(31) Number	(32) Date	(33) Country
61/707,340	**2012.09.28**	**US**
61/781,364	**2013.03.14**	**US**

(43) Publication Date: **2014.04.03**
(44) Accepted Journal Date: **2017.09.07**

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(56) Related Art
MAURICE J VAN EIS ET AL, BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, GB, vol. 21, no. 24, doi:10.1016/J.BMCL.2011.10.025, ISSN 0960-894X, (2011-10-07), pages 7367 - 7372, (2011-10-21)

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 April 2014 (03.04.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/052699 A1

(51) International Patent Classification:
C07D 471/04 (2006.01) *A61K 31/437* (2006.01)
C07D 519/00 (2006.01) *A61P 35/00* (2006.01)

(21) International Application Number:
PCT/US2013/062085

(22) International Filing Date:
27 September 2013 (27.09.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/707,340 28 September 2012 (28.09.2012) US
61/781,364 14 March 2013 (14.03.2013) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

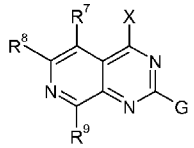
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

WO 2014/052699 A1

(54) Title: AZAQUINAZOLINE INHIBITORS OF ATYPICAL PROTEIN KINASE C



(I)

(57) Abstract: The present invention provides a compound of formula (I) or a salt thereof, wherein R^7, R^8, R^9, G, and X are as defined herein. A compound of formula (I) and its salts have a PKC inhibitory activity, and may be used to treat proliferative disorders.

AZAQUINAZOLINE INHIBITORS OF ATYPICAL PROTEIN KINASE C

BACKGROUND OF THE INVENTION

PKCι and PKCζ (accession numbers NM_002740 and NM_002744 respectively) together define the atypical sub-class of the protein kinase C (PKC) family. The aPKCs are structurally and functionally distinct from the other PKC sub-classes, classic/conventional and novel, as their catalytic activity is not dependent on diacylglycerol and calcium (Ono, Y., Fujii, T., Ogita, K., Kikkawa, U., Igarashi, K., and Nishizuka, Y. (1989). Protein kinase C zeta subspecies from rat brain: its structure, expression, and properties. Proc Natl Acad Sci U S A *86*, 3099-3103). Structurally, PKCι and PKCζ contain a C-terminal serine/threonine kinase domain (AGC class) and an N-terminal regulatory region containing a Phox Bem 1 (PB1) domain involved in mediating protein:protein interactions critical for aPKC function. At the amino acid level the aPKCs share 72% overall homology, however, the kinase domains share 84% identity and differ in the active site by just a single amino acid. This striking homology suggests an ATP-competitive ligand would not be expected to exhibit significant aPKC isoform selectivity.

The aPKCs have been implicated in a diverse number of signalling pathways, demonstrating both redundant and distinct signalling functions. Both isoforms have emerged as central players in the mechanisms that regulate the establishment and maintenance of cellular polarity in multiple cell types (reviewed in Suzuki, A., and Ohno, S. (2006). The PAR-aPKC system: lessons in polarity. J Cell Sci *119*, 979-987). Genetic dissection of their functions using knockout mice have also revealed preferential roles for PKCζ in the regulation of NF-kB signalling (Leitges, M., Sanz, L., Martin, P., Duran, A., Braun, U., Garcia, J.F., Camacho, F., Diaz-Meco, M.T., Rennert, P.D., and Moscat, J. (2001). Targeted disruption of the zetaPKC gene results in the impairment of the NF-kappaB pathway. Mol Cell *8*, 771-780), and PKCι in insulin secretion and action (Farese, R.V., Sajan, M.P., Yang, H., Li, P., Mastorides, S., Gower, W.R., Jr., Nimal, S., Choi, C.S., Kim, S., Shulman, G.I., *et al.* (2007). Muscle-specific knockout of PKC-lambda impairs glucose transport and induces metabolic and diabetic syndromes. J Clin Invest *117*, 2289-2301). In addition, both isoforms have been implicated in the pathogenesis of cancer making a strong case for the inhibition of the aPKCs as a novel therapeutic avenue.

PKCι is a known oncogene in non-small cell lung cancer (NSCLC). In one study it was shown to be overexpressed in 69% of NSCLC cases at the protein level. Consistent with this, the PKCι gene (*PRKCI* residing on chromosome 3q26) was shown to be amplified in 36.5% of NSCLC tumours examined, including 96% of the squamous cell carcinoma sub-type (Regala, R.P., Weems, C., Jamieson, L., Khoor, A., Edell, E.S., Lohse, C.M., and Fields, A.P. (2005b). Atypical protein kinase C iota is an oncogene in human non-small cell lung cancer. Cancer Res *65*, 8905-8911). Amplification of 3q26 has also been reported in 44% of ovarian cancers, including >70% of serous epithelial ovarian cancers where 3q26 amplification is translated into increased PKCι protein expression. Moreover, increased PKCι expression is associated with poor prognosis in NSCLC and ovarian cancer where it may serve as a diagnostic biomarker of aggressive disease (Eder, A.M., Sui, X., Rosen, D.G., Nolden, L.K., Cheng, K.W., Lahad, J.P., Kango-Singh, M., Lu, K.H., Warneke, C.L., Atkinson, E.N., *et al.* (2005). Atypical PKCiota contributes to poor prognosis through loss of apical-basal polarity and cyclin E overexpression in ovarian cancer. Proc Natl Acad Sci U S A *102*, 12519-12524; Zhang, L., Huang, J., Yang, N., Liang, S., Barchetti, A., Giannakakis, A., Cadungog, M.G., O'Brien-Jenkins, A., Massobrio, M., Roby, K.F., *et al.* (2006). Integrative genomic analysis of protein kinase C (PKC) family identifies PKCiota as a biomarker and potential oncogene in ovarian carcinoma. Cancer Res *66*, 4627-4635). 3q26 amplifications have been observed in many other cancers including oesophageal squamous cell carcinoma (Yang, Y.L., Chu, J.Y., Luo, M.L., Wu, Y.P., Zhang, Y., Feng, Y.B., Shi, Z.Z., Xu, X., Han, Y.L., Cai, Y., *et al.* (2008). Amplification of PRKCI, located in 3q26, is associated with lymph node metastasis in esophageal squamous cell carcinoma. Genes Chromosomes Cancer *47*, 127-136) and breast cancer (Kojima, Y., Akimoto, K., Nagashima, Y., Ishiguro, H., Shirai, S., Chishima, T., Ichikawa, Y., Ishikawa, T., Sasaki, T., Kubota, Y., *et al.* (2008). The overexpression and altered localization of the atypical protein kinase C lambda/iota in breast cancer correlates with the pathologic type of these tumors. Hum Pathol *39*, 824-831) suggesting that PKCι may also participate in the pathogenesis of these diseases.

In NSCLC the primary function of PKCι is to drive transformed growth via a Rac1 / PAK / MEK / ERK signalling axis. However, PKCι also functions in NSCLC survival, resistance to chemotherapy, and invasion via distinct pathways (reviewed in Fields, A.P., and Regala, R.P. (2007). Protein kinase C iota: human oncogene, prognostic marker and therapeutic target. Pharmacol Res *55*, 487-497). In ovarian cancer transformed growth is

correlated with deregulated epithelial cell polarity and increased cycle E expression (Eder et al., 2005) suggesting that PKCι can influence the cancer phenotype through multiple mechanisms. Compelling evidence has emerged to suggest that inhibition of PKCι may be a useful therapeutic approach to combat tumours characterised by increased PKCι expression. In transgenic models, mice with elevated PKCι activity in the colon are more susceptible to carcinogen-induced colon carcinogenesis, and expression of a kinase-dead mutant of PKCι blocks the transformation of intestinal cells by oncogenic Ras (Murray, N.R., Jamieson, L., Yu, W., Zhang, J., Gokmen-Polar, Y., Sier, D., Anastasiadis, P., Gatalica, Z., Thompson, E.A., and Fields, A.P. (2004). Protein kinase Ciota is required for Ras transformation and colon carcinogenesis in vivo. J Cell Biol *164*, 797-802). Finally, genetic or pharmacological inhibition of PKCι by a gold derivative – aurothiomalate (ATM) – blocks the growth of NSCLC cells in soft agar and significantly decreases tumour volume in xenograft models of NSCLC(Regala, R.P., Thompson, E.A., and Fields, A.P. (2008). Atypical protein kinase C iota expression and aurothiomalate sensitivity in human lung cancer cells. Cancer Res *68*, 5888-5895; Regala, R.P., Weems, C., Jamieson, L., Copland, J.A., Thompson, E.A., and Fields, A.P. (2005a). Atypical protein kinase Ciota plays a critical role in human lung cancer cell growth and tumorigenicity. J Biol Chem *280*, 31109-31115).

Despite the high degree of similarity between aPKC isoforms, the role of PKCζ in cancer is distinct from that of PKCι. PKCζ plays a role in NSCLC cell survival by phosphorylating and antagonising the pro-apoptotic effects of Bax in response to nicotine (Xin, M., Gao, F., May, W.S., Flagg, T., and Deng, X. (2007). Protein kinase Czeta abrogates the proapoptotic function of Bax through phosphorylation. J Biol Chem *282*, 21268-21277). PKCζ activity has also been linked to resistance against a wide range of cytotoxic and genotoxic agents. For instance, in human leukaemia cells, overexpression of PKCζ confers resistance against 1-β-D-arabinofuranosylcytosine (ara-C), daunorubicin, etoposide, and mitoxantrone-induced apoptosis (Filomenko, R., Poirson-Bichat, F., Billerey, C., Belon, J.P., Garrido, C., Solary, E., and Bettaieb, A. (2002). Atypical protein kinase C zeta as a target for chemosensitization of tumor cells. Cancer Res *62*, 1815-1821; Plo, I., Hernandez, H., Kohlhagen, G., Lautier, D., Pommier, Y., and Laurent, G. (2002). Overexpression of the atypical protein kinase C zeta reduces topoisomerase II catalytic activity, cleavable complexes formation, and drug-induced cytotoxicity in monocytic U937 leukemia cells. J Biol Chem *277*, 31407-31415). Furthermore, inhibition of PKCζ activity through expression

of a kinase-dead mutant sensitises leukaemia cells to the cytotoxic effects of etoposide both *in vitro* and *in vivo* (Filomenko et al., 2002). Atypical protein kinase C regulates dual pathways for degradation of the oncogenic coactivator SRC-3/AIB1. Mol Cell *29*, 465-476), and both of these proteins have been postulated to play a role in tamoxifen resistance in breast cancer (Iorns, E., Lord, C.J., and Ashworth, A. (2009). Parallel RNAi and compound screens identify the PDK1 pathway as a target for tamoxifen sensitization. Biochem J *417*, 361-370; Osborne, C.K., Bardou, V., Hopp, T.A., Chamness, G.C., Hilsenbeck, S.G., Fuqua, S.A., Wong, J., Allred, D.C., Clark, G.M., and Schiff, R. (2003). Role of the estrogen receptor coactivator AIB1 (SRC-3) and HER-2/neu in tamoxifen resistance in breast cancer. J Natl Cancer Inst *95*, 353-361). Together these studies suggest that inhibition of PKCζ activity may have beneficial therapeutic effects by acting as a chemosensitiser to a wide array of commonly used chemotoxic agents in the clinic.

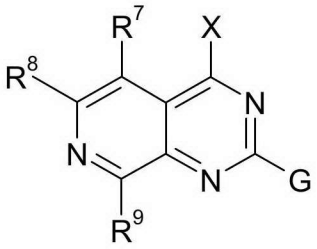
Further evidence that small molecule inhibition of PKCζ could have important therapeutic benefits has recently emerged from tumour models that link PKCζ signalling to the mTOR pathway. PKCζ is constitutively activated in follicular lymphoma and has been identified as a novel target for the anti-CD20 therapeutic antibody rituximab (Leseux, L., Laurent, G., Laurent, C., Rigo, M., Blanc, A., Olive, D., and Bezombes, C. (2008). PKC zeta mTOR pathway: a new target for rituximab therapy in follicular lymphoma. Blood *111*, 285-291). Rituximab inhibits follicular lymphoma proliferation by targeting a PKCζ-MAPK-mTOR pathway, suggesting that PKCζ is both a target of Rituximab, and a key regulator of its' anti-leukaemic effect. Regulation of the mTOR/p70S6K pathway by PKCζ has also been implicated in the transition of prostate cancer cells to an androgen-independent state (Inoue, T., Yoshida, T., Shimizu, Y., Kobayashi, T., Yamasaki, T., Toda, Y., Segawa, T., Kamoto, T., Nakamura, E., and Ogawa, O. (2006). Requirement of androgen-dependent activation of protein kinase Czeta for androgen-dependent cell proliferation in LNCaP Cells and its roles in transition to androgen-independent cells. Mol Endocrinol *20*, 3053-3069). Finally, mice containing a homozygous deletion of Par4, a negative regulator of PKCζ, exhibit greatly enhanced PKCζ activity. These mice spontaneously develop tumours of the prostate and endometrium, and potentiate Ras-induced lung carcinogenesis consistent with a role for PKCζ in lung cancer (Garcia-Cao, I., Duran, A., Collado, M., Carrascosa, M.J., Martin-Caballero, J., Flores, J.M., Diaz-Meco, M.T., Moscat, J., and Serrano, M. (2005). Tumour-suppression activity of the proapoptotic regulator Par4. EMBO Rep *6*, 577-583; Joshi, J.,

Fernandez-Marcos, P.J., Galvez, A., Amanchy, R., Linares, J.F., Duran, A., Pathrose, P., Leitges, M., Canamero, M., Collado, M., *et al.* (2008). Par-4 inhibits Akt and suppresses Ras-induced lung tumorigenesis. EMBO J *27*, 2181-2193).

A need exists for aPKC inhibitors for use as pharmaceutical agents.

SUMMARY OF THE INVENTION

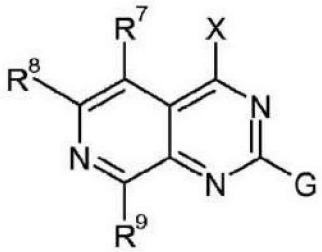
The invention provides a compound of formula (I)



(I)

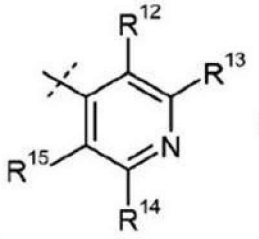
or a salt thereof, wherein R^7, R^8, R^9, G, and X are as defined herein.

According to one embodiment, there is provided a compound of formula (I)

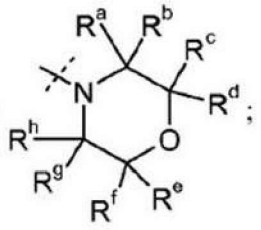


or a salt form thereof,

wherein (I)



or



;

G is a group of formula

X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-9 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally

substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{28}$, $–C(=O)OR^{28}$, $–C(=O)NR^{24}R^{28}$, $–C(O)C(=O)R^{28}$, $–NR^{24}R^{28}$, $–NR^{24}NR^{24}R^{28}$, $–N=NR^{28}$, $–NR^{24}OR^{28}$, $–NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)C(=O)R^{28}$, $–NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)OR^{28}$, $–NR^{24}C(=O)NR^{24}R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $–NR^{24}S(=O)_2R^{28}$, $–NR^{24}S(=O)_2NR^{24}R^{28}$, $–OR^{28}$, $–OC(=O)R^{28}$, $–OC(=O)NR^{24}R^{28}$, $–OC(=O)OR^{28}$, $–OS(=O)R^{28}$, $–OS(=O)_2R^{28}$, $–OS(=O)_2OR^{28}$, $–OS(=O)_2NR^{24}R^{28}$, $–S(=O)_nR^{28}$, $–S(=O)_2NR^{24}R^{28}$, and $–S(=O)NR^{24}R^{28}$;

R^7, R^8, R^9, R^{12}, R^{13}, R^{14}, R^{15}, R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(\ NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $NR^{24}P\ (=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, –

$OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$ $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})$ $(NR^{22}R^{23})$ $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$;

or any of R^7 and R^8, R^{12} and R^{13}, R^{14} and R^{15}, R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19};

R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11} aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-C(=NR^{35})R^{30}$, $-C(=NR^{35})NR^{32}R^{33}$, $-C(=NOH)NR^{32}R^{33}$, $-C(=NOR^{36})R^{30}$, $-C(=NNR^{32}R^{33})R^{30}$, $-C(=NNR^{34}C(=O)R^{31})R^{30}$, $-C(=NNR^{34}C(=O)OR^{31})R^{30}$, $-C(=S)NR^{32}R^{33}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}C(=S)R^{30}$, $-NR^{34}C(=S)OR^{30}$, $-$

$NR^{34}C(=S)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-NR^{34}P(=O)R^{78}R^{78}$, $-NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-NR^{34}P(=O)(OR^{30})(OR^{30})$, $-NR^{34}P(=O)(SR^{30})(SR^{30})$, $-OR^{30}$, =O, –OCN, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-OS(=O)R^{30}$, –OS(=O)2R^{30}, $-OS(=O)_2OR^{30}$, $-OS(=O)_2NR^{32}R^{33}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-OP(=O)(OR^{30})(OR^{30})$, $-OP(=O)(SR^{30})(SR^{30})$, $-Si(R^{34})_3$, –SCN, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-SP(=O)(OR^{30})(OR^{30})$, $-SP(=O)(SR^{30})(SR^{30})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$;

R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-6}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{28} at each occurrence is independently chosen from C_{1-10}alkyl optionally substituted by 1-13 R^{49}, C_{2-10}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59},

C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69};

R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–C(=O)C(=O)R^{70}$, $–C(=NR^{75})R^{70}$, $–C(=NR^{75})NR^{72}R^{73}$, $–C(=NOH)NR^{72}R^{73}$, $–C(=NOR^{76})R^{70}$, $–C(=NNR^{72}R^{73})R^{70}$, $–C(=NNR^{74}C(=O)R^{71})R^{70}$, $–C(=NNR^{74}C(=O)OR^{71})R^{70}$, $–C(=S)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}NR^{72}R^{73}$, $–N=NR^{74}$, $=NR^{70}$ $=NOR^{70}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)C(=O)OR^{71}$,$–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}C(=O)NR^{74}C(–O)R^{70}$, $–NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $–NR^{74}C(=NR^{75})NR^{72}R^{73}$, $–NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $–NR^{74}C(=S)R^{70}$, $–NR^{74}C(=S)OR^{70}$, $–NR^{74}C(=S)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–NR^{74}P(=O)R^{78}R^{78}$, $–NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–NR^{74}P(=O)(OR^{70})(OR^{70})$, $–NR^{74}P(=O)(SR^{70})(SR^{70})$, $–OR^{70}$, =O, –OCN, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OC(=O)OR^{70}$, $–OC(=NR^{75})NR^{72}R^{73}$, $–OS(=O)R^{70}$, $–OS(=O)_2R^{70}$, $–OS(=O)_2OR^{70}$,

–$OS(=O)_2NR^{72}R^{73}$, –$OP(=O)R^{78}R^{78}$, –$OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$OP(=O)(OR^{70})(OR^{70})$, –$OP(=O)(SR^{70})(SR^{70})$, –$Si(R^{74})_3$, –SCN, =S, –S(=O), $_nR^{70}$, –$S(=O)_2OR^{70}$, SO_3R^{77}, –$S(=O)_2NR^{72}R^{73}$, –$S(=O)NR^{72}R^{73}$, –$SP(=O)R^{78}R^{78}$, –$SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$SP(=O)(OR^{70})(OR^{70})$, –$SP(=O)(SR^{70})(SR^{70})$, –$P(=O)R^{78}R^{78}$, –$P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$P(=O)(OR^{70})(OR^{70})$, and –$P(=O)(SR^{70})(SR^{70})$;

R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkenyl optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109};

R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21

R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89};

R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{119}, C_{2-6}alkenyl optionally substituted by 1-11 R^{119} optionally substituted by 1-9 R^{119} C_{6-11}aryl optionally substituted by 1-11 R^{119}, C_{2-6}arylalkyl optionally substituted by 1-19 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{119} C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{119}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{115})R^{110}$, $–C(=NR^{115})NR^{112}R^{113}$, $–C(=NOH)NR^{112}R^{113}$, $–C(=NOR^{116})R^{110}$, $–C(=NNR^{112}R^{113})R^{110}$, $–C(=NNR^{114}C(=O)R^{111})R^{110}$, $–C(=NNR^{114}C(=O)OR^{111})R^{110}$, $–C(=S)NR^{112}R^{113}$, –NC, $–NO_2$, $–NR^{112}R^{113}$, $NR^{114}NR^{112}R^{113}$, $–N=NR^{114}$,= NR^{110}, NOR^{110}, $–NR^{114}OR^{116}$,$–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}NR^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $–NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $NR^{114}C(=NR^{115})NR^{112}R^{113}$, $–NR^{114}C(=O)C(=O)NR^{112}R^{113}$, $–NR^{114}C(=S)R^{110}$, $–NR^{114}C(=S)OR^{110}$, $–NR^{114}C(=S)NR^{114}S(=O)_2R^{111,}$ $–NR^{114}S(=O)_2NR^{112}R^{138}$,$–NR^{114}P(=O)R^{118}R^{118}$, $–NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–NR^{114}P(=O)(OR^{110})(OR^{110})$, $–NR^{114}P(=O)(SR^{110})(SR^{110})$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–OC(=NR^{115})NR^{112}R^{113}$, $–OS(=O)R^{110}$, $OS(=O)_2R^{110}$, $–OS(=O)_2OR^{110}$, $–OS(=O)_2NR^{112}R^{113}$, $–OP(=O)R^{118}R^{118}$ $–OP(=O)(NR^{112}R^{113})(NR^{112}R^{113},)$ $OP(=O)(OR^{110})(OR^{110})$, $OP(=O)(SR^{110})(SR^{110})$, –

$Si(R^{114})_3$, –SCN, =S, $–S(=O)_nR^{110}$, $–S(=O)_2OR^{110}$, $–S(=O)_2NR^{112}R^{113}$, $–S(=O)NR^{112}R^{113}$, $–SP(=O)R^{118}R^{118}$ $–SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$ $–SP(=O)(OR^{110})(OR^{110})$, $SP(=O)(SR^{110})(SR^{110})$, $–P(=O)R^{118}R^{118}$, $–P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–P(=O)(OR^{110})(OR^{110})$, and $–P(=O)(SR^{110})(SR^{110})$;

R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-1}6arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149};

R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21

membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{119} R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{159}, C_{2-6}alkenyl optionally substituted by 1-11 R^{159}, C_{2-6}alkynyl optionally substituted by 1-9 R^{159}, C_{6-11}aryl optionally substituted by 1-11 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{159}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{159}, halogen, –CN, –$C(=O)R^{150}$, –$C(=O)OR^{150}$, –$C(=O)NR^{152}R^{153}$, –$C(=O)C(=O)R^{150}$, –$C(=NR^{155})R^{150}$, –$C(=NR^{155})NR^{152}R^{153}$, –$C(=NOH)NR^{152}R^{153}$, –$C(=NOR^{156})R^{150}$, –$C(=NNR^{152}R^{153})R^{150}$, –$C(=NNR^{154}C(=O)R^{151})R^{150}$, –$C(=NNR^{154}C(=O)OR^{151})R^{150}$, –$C(=S)NR^{152}R^{153}$, –NC, –$NO_2$, –$NR^{152}R^{153}$, –$NR^{154}NR^{152}R^{153}$, –$N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, –$NR^{154}OR^{156}$, –$NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)C(=O)R^{150}$, –$NR^{154}C(=O)OR^{151}$, –$NR^{154}C(=O)C(=O)OR^{151}$, –$NR^{154}C(=O)NR^{152}R^{153}$, $NR^{154}C(=O)NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, –$NR^{154}C(=NR^{155})NR^{152}R^{153}$, –$NR^{154}C(=O)C(=O)NR^{152}R^{153}$, –$NR^{154}C(=S)R^{150}$, –$NR^{154}C(=S)OR^{150}$, –$NR^{154}C(=S)NR^{152}R^{153}$, –$NR^{154}S(=O)_2R^{151}$, –$NR^{154}S(=O)_2NR^{152}R^{153}$, –$NR^{154}P(=O)R^{158}R^{158}$, –$NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$NR^{154}P(=O)(OR^{150})(OR^{150})$, –$NR^{154}P(=O)(SR^{150})(SR^{150})$, –$OR^{150}$, =O, –OCN, –$OC(=O)R^{150}$, –$OC(=O)NR^{152}R^{153}$, –$OC(=O)OR^{150}$, –$OC(=NR^{155})NR^{152}R^{153}$, –$OS(=O)R^{150}$ –$OS(=O)_2R^{150}$, –$OS(=O)_2OR^{150}$, –$OS(=O)_2NR^{152}R^{153}$, –$OP(=O)R^{158}R^{158}$, –$OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$OP(=O)(OR^{150})(OR^{150})$, –$OP(=O)(SR^{150})(SR^{150})$, –$Si(R^{154})_3$, –SCN, =S, –$S(=O)_nR^{150}$, –$S(=O)_2OR^{150}$, –$S(=O)_2NR^{152}R^{153}$, –$S(=O)NR^{152}R^{153}$, –$SP(=O)R^{158}R^{158}$, –$SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$SP(=O)(OR^{150})(OR^{150})$, –$SP(=O)(SR^{150})(SR^{150})$,

–P(=O)$R^{158}R^{158}$, –P(=O)($NR^{152}R^{153}$)($NR^{152}R^{153}$), –P(=O)(OR^{150})(OR^{150}), and –P(=O)(SR^{150})(SR^{150});

R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179};

or any R152 and R153 may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R189 or a 5-15 membered heteroaryl optionally substituted by 1-15 R189;

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169} C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15

membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{199}, C_{2-6}alkenyl optionally substituted by 1-11 R^{199}, C_{2-6}alkynyl optionally substituted by 1-9 R^{199}, C_{6-11}aryl optionally substituted by 1-11 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{199}, halogen, –CN, –$C(=O)R^{190}$, –$C(=O)OR^{190}$, –$C(=O)NR^{192}R^{193}$, –$C(=O)C(=O)R^{190}$, –$C(=NR^{195})R^{190}$, –$C(=NR^{195})NR^{192}R^{193}$, –$C(=NOH)NR^{192}R^{193}$, –$C(=NOR^{196})R^{190}$, –$C(=NNR^{192}R^{193})R^{190}$, –$C(=NNR^{194}C(=O)R^{191})R^{190}$, –$C(=NNR^{194}C(=O)OR^{191})R^{190}$, –$C(=S)NR^{192}R^{193}$, –NC, –$NO_2$, –$NR^{192}R^{193}$, –$NR^{194}NR^{192}R^{193}$, –$N=NR^{194}$, $=NR^{190}$, $=NOR^{190}$, –$NR^{194}OR^{196}$, –$NR^{194}C(=O)R^{190}$, –$NR^{194}C(=O)C(=O)R^{190}$, –$NR^{194}C(=O)OR^{191}$, –$NR^{194}C(=O)C(=O)OR^{191}$, –$NR^{194}C(=O)NR^{192}R^{193}$, –$NR^{194}C(=O)NR^{194}C(=O)R^{190}$, –$NR^{194}C(=O)NR^{194}C(=O)OR^{190}$, –$NR^{194}C(=NR^{195})NR^{192}R^{193}$, –$NR^{194}C(=O)C(=O)NR^{192}R^{193}$, –$NR^{194}C(=S)R^{190}$, –$NR^{194}C(=S)OR^{190}$, –$NR^{194}C(=S)NR^{192}R^{193}$, –$NR^{194}S(=O)_2R^{191}$, –$NR^{194}S(=O)2NR^{192}R^{193}$, –$NR^{194}P(=O)R^{198}R^{198}$, –$NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$NR^{194}P(=O)(OR^{190})(OR^{190})$, –$NR^{194}P(=O)(SR^{190})(SR^{190})$, –$OR^{190}$, =O, –OCN, –$OC(=O)R^{190}$, $OC(=O)NR^{192}R^{193}$, –$OC(=O)OR^{190}$, –$OC(=NR^{195})NR^{192}R^{193}$, –$OS(=O)R^{190}$, –$OS(=O)_2R^{190}$, –$OS(=O)_2OR^{190}$, –$OS(=O)_2NR^{192}R^{193}$, –$OP(=O)R^{198}R^{198}$, –$OP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$OP(=O)(OR^{190})(OR^{195})$, –$OP(=O)(SR^{190})(SR^{190})$, –$Si(R^{194})_3$, –SCN, =S, –$S(=O)_nR^{190}$, –$S(=O)_2OR^{190}$, –$S(=O)_2NR^{192}R^{193}$, –$S(=O)NR^{192}R^{193}$, –$SP(=O)R^{198}R^{198}$, –$SP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$SP(=O)(OR^{190})(OR^{190})$, –$SP(=O)(SR^{190})(SR^{190})$, –$P(=O)R^{198}R^{198}$, –$P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $P(=O)(OR^{190})(OR^{190})$, and –$P(=O)(SR^{190})(SR^{190})$;

R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{219}, C_{2-6}alkenyl optionally substituted by 1-11 R^{219}, C_{2-6}alkynyl optionally substituted by 1-9 R^{219}, C_{6-11}aryl optionally substituted by 1-11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219};

or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229};

R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

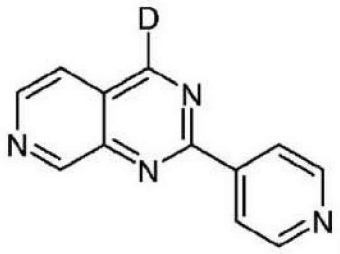
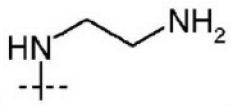
R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(–O)C(–O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}OR^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=NR^{230})NR^{230}R^{230}$, $–NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $–NR^{230}C(=S)R^{230}$, $–NR^{230}C(=S)OR^{230}$, $–NR^{230}C(=S)NR^{230}R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–NR^{230}P(=O)(SR^{230})(SR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OC(=O)OR^{230}$, $–OC(=NR^{230})NR^{230}R^{230}$, $–OS(=O)R^{230}$, $–OS(=O)_2R^{230}$, $–OS(=O)_2OR^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–OP(=O)(OR^{230})(OR^{230})$, $–OP(=O)(SR^{230})(SR^{230})$, $–Si(R^{230})_3$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2OR^{230}$, $–SO_3R^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–SP(=O)R^{231}R^{231}$, $–SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–SP(=O)(OR^{230})(OR^{230})$, $–SP(=O)(SR^{230})(SR^{230})$, $–P(=O)R^{231}R^{231}$, $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–P(=O)(OR^{230})(OR^{230})$, and $–P(=O)(SR^{230})(SR^{230})$;

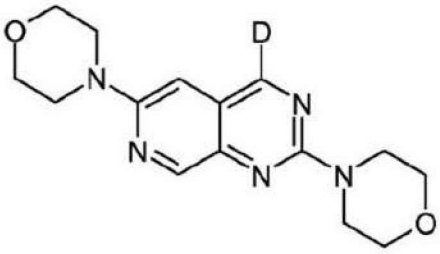
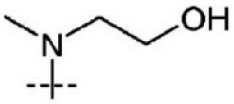
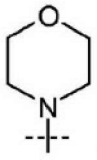
R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl;

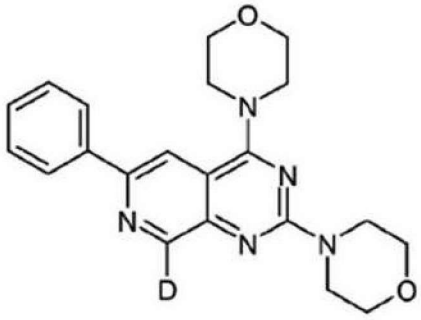
R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl; and

n at each occurrence is independently chosen from 0, 1, and 2;

with the proviso that the compound is not

(a)  in which D is H or  , or a salt form thereof;

(b)  in which D is  or  , or a salt form thereof; or

(c)  in which D is H or $-CH_3$, or a salt form thereof.

A compound of formula (I) and its salts have aPKC inhibitory activity, and may be used to treat aPKC-dependent disorders or conditions.

The present invention further provides a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with at least one pharmaceutically acceptable carrier, diluent, or excipient therefor.

In another aspect, the present invention provides a method of treating a subject suffering from an aPKC-dependent disorder or condition comprising: administering to the subject a compound of formula (I) or a pharmaceutically acceptable salt thereof.

The present invention further provides a method of treating a proliferative disorder in a subject, comprising administering to the subject a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

"About" as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass reasonable variations of the value, such as, for example, ±10% from the specified value. For example, the phrase "about 50" encompasses reasonable variations of 50, such as ±10% of the numerical value 50, or from 45 to 55.

"Alkyl" or "alkyl group" refers to a monoradical of a branched or unbranched saturated hydrocarbon chain. Examples include, but are not limited to, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, n-decyl, isopropyl, tert-butyl, isobutyl, etc. Alkyl groups typically contain 1-10 carbon atoms, such as 1-6 carbon atoms or 1-4 carbon atoms, and can be substituted or unsubstituted.

"Alkylene" or "alkylene group" refers to a diradical of a branched or unbranched saturated hydrocarbon chain. Examples include, but are not limited to, methylene ($–CH_2–$), the ethylene isomers ($–CH(CH_3)–$ and $–CH_2CH_2–$), the propylene isomers ($–CH(CH_3)CH_2–$, $–CH(CH_2CH_3)–$, $–C(CH_3)_2–$, and $–CH_2CH_2CH_2–$), etc. Alkylene groups typically contain 1-10 carbon atoms, such as 1-6 carbon atoms, and can be substituted or unsubstituted.

"Alkenyl" or "alkenyl group" refers to a monoradical of a branched or unbranched hydrocarbon chain containing at least one double bond. Examples include, but are not limited to, ethenyl, 3-buten-1-yl, 2-ethenylbutyl, and 3-hexen-1-yl. Alkenyl groups typically contain 2-10 carbon atoms, such as 2-6 carbon atoms or 2-4 carbon atoms, and can be substituted or unsubstituted.

"Alkynyl" or "alkynyl group" refers to a monoradical of a branched or unbranched hydrocarbon chain containing at least one triple bond. Examples include, but are not limited to, ethynyl, 3-butyn-1-yl, propynyl, 2-butyn-1-yl, and 3-pentyn-1-yl. Alkynyl groups typically contain 2-10 carbon atoms, such as 2-6 carbon atoms or 2-4 carbon atoms, and can be substituted or unsubstituted.

"Aryl" or "aryl group" refers to phenyl and 7-15 membered monoradical bicyclic or tricyclic hydrocarbon ring systems, including bridged, spiro, and/or fused ring systems, in which at least one of the rings is aromatic. Aryl groups can be substituted or unsubstituted. Examples include, but are not limited to, naphthyl, indanyl, 1,2,3,4-tetrahydronaphthalenyl, 6,7,8,9-tetrahydro-5H-benzocycloheptenyl, and 6,7,8,9-tetrahydro-5H-benzocycloheptenyl. An aryl group may contain 6 (i.e., phenyl) or 9 to 15 ring atoms, such as 6 (i.e., phenyl) or 9-11 ring atoms, e.g., 6 (i.e., phenyl), 9 or 10 ring atoms.

"Arylene" or "arylene group" refers to a phenylene ($–C_6H_4–$) or a 7-15 membered diradical bicyclic or tricyclic hydrocarbon ring systems, including bridged, spiro, and/or fused ring systems, in which at least one of the rings is aromatic. Arylene groups can be

substituted or unsubstituted. For example, an arylene group may contain 6 (i.e., phenylene) or 9 to 15 ring atoms; such as 6 (i.e., phenylene) or 9-11 ring atoms; e.g., 6 (i.e., phenylene), 9 or 10 ring atoms. An arylene group can also include ring systems substituted on ring carbons with one or more –OH functional groups (which may further tautomerize to give a ring C=O group).

"Arylalkyl" or "arylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by an aryl group, wherein alkyl group and aryl group are as previously defined (i.e., arylalkyl–). Arylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, benzyl ($C_6H_5CH_2$–).

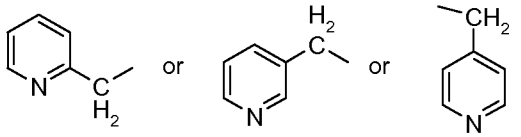
"Cycloalkyl" or "cycloalkyl group" refers to a monoradical non-aromatic carbocyclic ring system, which may be saturated or unsaturated, substituted or unsubstituted, and may be monocyclic, bicyclic, or tricyclic, and may be bridged, spiro, and/or fused. Examples include, but are not limited to, cyclopropyl, cyclopropenyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, norbornyl, norbornenyl, bicyclo[2.2.1]hexane, bicyclo[2.2.1]heptane, bicyclo[2.2.1]heptene, bicyclo[3.1.1]heptane, bicyclo[3.2.1]octane, bicyclo[2.2.2]octane, bicyclo[3.2.2]nonane, bicyclo[3.3.1]nonane, and bicyclo[3.3.2]decane. The cycloalkyl group may contain from 3 to 10 ring atoms, such as 3 to 7 ring atoms (e.g., 3 ring atoms, 5 ring atoms, 6 ring atoms, or 7 ring atoms).

"Cycloalkylalkyl" or "cycloalkylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a cycloalkyl group, wherein alkyl group and cycloalkyl group are as previously defined (i.e., cycloalkylalkyl–). Cycloalkylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, cyclohexylmethyl ($C_6H_{11}CH_2$–).

"Haloalkyl" or "haloalkyl group" refers to alkyl groups in which one or more hydrogen atoms are replaced by halogen atoms. Haloalkyl includes both saturated alkyl groups and unsaturated alkenyl and alkynyl groups, such as for example $–CF_3$, $–CHF_2$, $–CH_2F$, $–CF_2CF_3$, $–CHFCF_3$, $–CH_2CF_3$, $–CF_2CH_3$, $–CHFCH_3$, $–CF_2CF_2CF_3$, $–CF_2CH_2CH_3$, $–CF{=}CF_2$, $–CCl{=}CH_2$, $–CBr{=}CH_2$, $–CI{=}CH_2$, $–C{\equiv}C\text{-}CF_3$, $–CHFCH_2CH_3$ and $–CHFCH_2CF_3$.

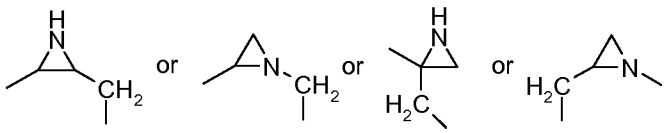
"Halogen" includes fluorine, chlorine, bromine and iodine atoms.

"Heteroaryl" or "heteroaryl group" refers to (a) 5 and 6 membered monocyclic aromatic rings, which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen or sulfur, and (b) 7-15 membered bicyclic and tricyclic rings, which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen or sulfur, and in which at least one of the rings is aromatic. Heteroaryl groups can be substituted or unsubstituted, and may be bridged, spiro, and/or fused. Examples include, but are not limited to, 2,3-dihydrobenzofuranyl, 1,2-dihydroquinolinyl, 3,4-dihydroisoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, benzoxazinyl, benzthiazinyl, chromanyl, furanyl, 2-furanyl, 3-furanyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, oxazolyl, pyridinyl, 2-, 3-, or 4-pyridinyl, pyrimidinyl, 2-, 4-, or 5-pyrimidinyl, pyrazolyl, pyrrolyl, 2- or 3-pyrrolyl, pyrazinyl, pyridazinyl, 3- or 4-pyridazinyl, 2-pyrazinyl, thienyl, 2-thienyl, 3-thienyl, tetrazolyl, thiazolyl, thiadiazolyl, triazinyl, triazolyl, pyridin-2-yl, pyridin-4-yl, pyrimidin-2-yl, pyridazin-4-yl, pyrazin-2-yl, naphthyridinyl, pteridinyl, phthalazinyl, purinyl, alloxazinyl, benzimidazolyl, benzofuranyl, benzofurazanyl, 2H-1-benzopyranyl, benzothiadiazine, benzothiazinyl, benzothiazolyl, benzothiophenyl, benzoxazolyl, cinnolinyl, furopyridinyl, indolinyl, indolizinyl, indolyl, or 2-, 3-, 4-, 5-, 6-, or 7-indolyl, 3H-indolyl, quinazolinyl, quinoxalinyl, isoindolyl, isoquinolinyl, 10-aza-tricyclo[6.3.1.$0^{2,7}$]dodeca-2(7),3,5-trienyl, 12-oxa-10-aza-tricyclo[6.3.1.$0^{2,7}$]dodeca-2(7),3,5-trienyl, 12-aza-tricyclo[7.2.1.$0^{2,7}$]dodeca-2(7),3,5-trienyl, 10-aza-tricyclo[6.3.2.$0^{2,7}$]trideca-2(7),3,5-trienyl, 2,3,4,5-tetrahydro-1H-benzo[d]azepinyl, 1,3,4,5-tetrahydro-benzo[d]azepin-2-onyl, 1,3,4,5-tetrahydro-benzo[b]azepin-2-onyl, 2,3,4,5-tetrahydro-benzo[c]azepin-1-onyl, 1,2,3,4-tetrahydro-benzo[e][1,4]diazepin-5-onyl, 2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepinyl, 5,6,8,9-tetrahydro-7-oxa-benzocycloheptenyl, 2,3,4,5-tetrahydro-1H-benzo[b]azepinyl, 1,2,4,5-tetrahydro-benzo[e][1,3]diazepin-3-onyl, 3,4-dihydro-2H-benzo[b][1,4]dioxepinyl, 3,4-dihydro-2H-benzo[f][1,4]oxazepin-5-onyl, 6,7,8,9-tetrahydro-5-thia-8-aza-benzocycloheptenyl, 5,5-dioxo-6,7,8,9-tetrahydro-5-thia-8-aza-benzocycloheptenyl, and 2,3,4,5-tetrahydro-benzo[f][1,4]oxazepinyl. For example, a heteroaryl group may contain 5, 6, or 8-15 ring atoms. As another example, a heteroaryl group may contain 5 to 10 ring atoms, such as 5, 6, 9, or 10 ring atoms.

"Heteroarylalkyl" or "heteroarylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a heteroaryl group, wherein alkyl group and heteroaryl group are as previously defined (i.e., heteroarylalkyl–). Heteroarylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, the pyridinylmethyl isomers ().

"Heterocycloalkyl" or "heterocycloalkyl group" refers to 3-15 membered monocyclic, bicyclic, and tricyclic non-aromatic rings, which may be saturated or unsaturated, can be substituted or unsubstituted, may be bridged, spiro, and/or fused, and which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen, sulfur or phosphorus. Examples include, but are not limited to, tetrahydrofuranyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indolinyl, isoindolinyl, morpholinyl, thiomorpholinyl, homomorpholinyl, homopiperidyl, homopiperazinyl, thiomorpholinyl-5-oxide, thiomorpholinyl-S,S-dioxide, pyrrolidinyl, tetrahydropyranyl, piperidinyl, tetrahydrothienyl, homopiperidinyl, homothiomorpholinyl-S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl-5-oxide, tetrahydrothienyl-S,S-dioxide, homothiomorpholinyl-5-oxide, quinuclidinyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-aza-bicyclo[3.2.1]octanyl, 3,8-diaza-bicyclo[3.2.1]octanyl, 2,5-diaza-bicyclo[2.2.1]heptanyl, 3,8-diaza-bicyclo[3.2.1]octanyl, 3,9-diaza-bicyclo[4.2.1]nonanyl, 2,6-diaza-bicyclo[3.2.2]nonanyl, [1,4]oxaphosphinanyl- 4-oxide, [1,4]azaphosphinanyl- 4-oxide, [1,2]oxaphospholanyl- 2-oxide, phosphinanyl-1-oxide, [1,3]azaphospholidinynl- 3-oxide, [1,3]oxaphospholanyl- 3-oxide and 7-oxabicyclo[2.2.1]heptanyl. A heterocycloalkyl group may contain, in addition to carbon atom(s), at least one nitrogen, oxygen, or sulfur. For example, a heterocycloalkyl group may contain, in addition to carbon atom(s), at least one nitrogen or oxygen. A heterocycloalkyl group may contain, in addition to carbon atom(s), at least one nitrogen. A heterocycloalkyl group may contain carbon atoms

and 1 or 2 nitrogen atoms. A heterocycloalkyl group may contain carbon atoms and an oxygen atom. A heterocycloalkyl group may contain carbon atoms, a nitrogen atom, and an oxygen atom. A heterocycloalkyl group may contain carbon atoms, a nitrogen atom, and a sulfur atom. A heterocycloalkyl group may contain carbon atoms and a sulfur atom. A heterocycloalkyl group may contain from 3 to 10 ring atoms. A heterocycloalkyl group may contain from 3 to 7 ring atoms. A heterocycloalkyl group may contain from 5 to 7 ring atoms, such as 5 ring atoms, 6 ring atoms, or 7 ring atoms. Unless otherwise indicated, the foregoing heterocycloalkyl groups can be C- attached or N-attached where such is possible and results in the creation of a stable structure. For example, piperidinyl can be piperidin-1-yl (N-attached) or piperidin-4-yl (C-attached).

"Heterocycloalkylene" or "heterocycloalkylene group" refers to diradical, 3-15 membered monocyclic, bicyclic, or tricyclic non-aromatic ring systems, which may be saturated or unsaturated, can be substituted or unsubstituted, may be bridged, spiro, and/or fused, and which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen, sulfur or phosphorus. Examples include, but are not limited to, the azridinylene isomers ().

The heterocycloalkylene group may contain, in addition to carbon atom(s), at least one nitrogen, oxygen, or sulfur. The heterocycloalkylene group may contain, in addition to carbon atom(s), at least one nitrogen or oxygen. The heterocycloalkylene group may contain, in addition to carbon atom(s), at least one nitrogen. For example, a heterocycloalkylene group may contain from 3 to 10 ring atoms; such as from 3 to 7 ring atoms. A heterocycloalkylene group may contain from 5 to 7 ring atoms, such as 5 ring atoms, 6 ring atoms, or 7 ring atoms. Unless otherwise indicated, the foregoing heterocycloalkylene groups can be C- attached and/or N-attached where such is possible and results in the creation of a stable structure. A heterocycloalkylene group can also include ring systems substituted on ring carbons with one or more –OH functional groups (which may further tautomerize to give a ring C=O group) and/or substituted on a ring sulfur atom by one (1) or two (2) oxygen atoms to give S=O or

SO_2 groups, respectively, and/or substituted on a ring phosphorus by an oxygen atom to give P=O.

"Heterocycloalkylalkyl" or "heterocycloalkylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a heterocycloalkyl group, wherein alkyl group and heterocycloalkyl group are as previously defined (i.e., heterocycloalkylalkyl–). Heteroycloalkylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, pyrrolidinylmethyl ($C_4H_8NCH_2$–).

"Pharmaceutically acceptable" refers to physiologically tolerable materials, which do not typically produce an allergic or other untoward reaction, such as gastric upset, dizziness and the like, when administered to a human.

"Pharmaceutical composition" refers to a composition that can be used to treat a disease, condition, or disorder in a human.

"Pseudohalogen" refers to –OCN, –SCN, $–CF_3$, and –CN.

"Stable" or "chemically stable" refers to a compound that is sufficiently robust to be isolated to a useful degree of purity from a reaction mixture. The present invention is directed solely to the preparation of stable compounds. When lists of alternative substituents include members which, owing to valency requirements, chemical stability, or other reasons, cannot be used to substitute a particular group, the list is intended to be read in context to include those members of the list that are suitable for substituting the particular group. For example, R^1 can be $C_{1\text{-}6}$alkyl optionally substituted by 1-13 R^{19}; when R^1 is methyl, the methyl group is optionally substituted by 1-3 R^{19}.

"Therapeutically effective amount" refers to an amount of a compound sufficient to inhibit, halt, or cause an improvement in a disorder or condition being treated in a particular subject or subject population. For example in a human or other mammal, a therapeutically effective amount can be determined experimentally in a laboratory or clinical setting, or may be the amount required by the guidelines of the United States Food and Drug Administration, or equivalent foreign agency, for the particular disease and subject being treated. It should be appreciated that determination of proper dosage forms, dosage amounts, and routes of administration is within the level of ordinary skill in the pharmaceutical and medical arts.

"Treatment" refers to the acute or prophylactic diminishment or alleviation of at least one symptom or characteristic associated or caused by a disorder being treated. For

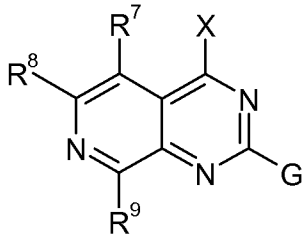
example, treatment can include diminishment of several symptoms of a disorder or complete eradication of a disorder.

II. Compounds

The compounds of the present invention are defined by the following numbered Embodiments. When a higher numbered Embodiment refers back to multiple previous lower numbered Embodiments in the alternative and contains a new limitation not present in the lower numbered Embodiments, the higher numbered Embodiment is intended to be an express description of each and every one of the alternatives. For example, if Embodiment 2 refers back to Embodiment 1 and contains a limitation not present in Embodiment 1, Embodiment 3 refers back Embodiments 1 or 2 and contains a limitation(s) not present in Embodiments 1 or 2, and Embodiment 4 refers back to any of Embodiments 1-3 and contains a limitation(s) not present in Embodiments 1, 2, or 3, then Embodiment 4 is intended to be an explicit description of a genus having the limitations of Embodiments 1 and 4, an explicit description of a genus having the limitations of Embodiments 2 and 4 (i.e., 1, 2, and 4), and an explicit description of a genus having the limitations of Embodiments 3 and 4 (i.e., 1, 3, and 4, and 1, 2, 3 and 4). By way of example, if Embodiment 1 is a compound of formula (I) defining R^7, R^8 and R^9 independently as alkyl or aryl, Embodiment 2 is a compound of Embodiment 1 defining R^7 as alkyl, Embodiment 3 is a compound of Embodiments 1 or 2 defining R^8 as alkyl, and Embodiment 4 is a compound of any of Embodiments 1-3 defininin R^9 as alkyl, then Embodiment 4 is an explicit description of a genus having the limitations of Embodiments 1 and 4 (i.e., a compound of formula (I) in which R^7 and R^8 are alkyl or aryl, and R^9 is alkyl), an explicit description of a genus having the limitations of Embodiments 2 and 4 (i.e., a compound of formula (I) in which R^8 is alkyl or aryl, and R^7 and R^9 are alkyl), an explicit description of a genus having the limitations of Embodiments 3 and 4 (i.e., a compound of formula (I) in which R^7 is alkyl or aryl, and R^8 and R^9 are alkyl; and a compound of formula (I) in which R^7, R^8 and R^9 are all alkyl). It should be noted in this regard that when a higher numbered Embodiment refers to a lower numbered Embodiment and contains limitations for a group(s) not present in the lower numbered Embodiment, the higher numbered Embodiment should be interpreted in context to ignore the missing group(s). For example, if Embodiment 1 recites a compound of formula (I) in which X is H, $C_{1\text{-}10}$alkyl, or $-C(=O)R^{28}$, Embodiment 2 recites a compound of Embodiment 1 in

which X is H or C_{1-10}alkyl, and Embodiment 3 recites a compound of Embodiments 1 or 2 in which R^{28} is alkyl, then Embodiment 3 defines a genus having the limitations of Embodiments 1 and 3 and a genus having the limitation of Embodiments 2 and 3 (i.e., 1, 2, and 3). In the genus defined by the limitations of Embodiments 2 and 3, X cannot be –C(=O)R^{28}; therefore this genus should be interpreted to ignore the Embodiment 3 definition of R^{28} = alkyl (i.e., the genus of Embodiments 2 and 3 has the same scope as the genus of Embodiment 2).

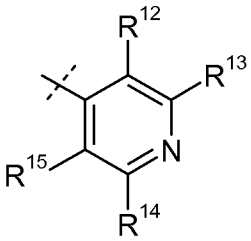
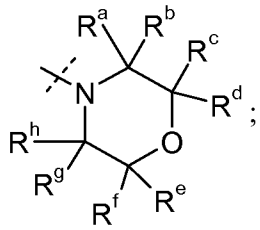
The compounds of the present invention are defined herein using structural formulas that do not specifically recite the mass numbers or the isotope ratios of the constituent atoms. It is intended that the present invention includes compounds in which the constituent atoms are present in any ratio of isotope forms. For example, carbon atoms may be present in any ratio of ^{12}C, ^{13}C, and ^{14}C; hydrogen atoms may be present in any ratio of ^{1}H, ^{2}H, and ^{3}H; etc. Preferably, the constituent atoms in the compounds of the present invention are present in their naturally occurring ratios of isotope forms.

Embodiment 1. A compound of formula (I)  or a

(I)

salt form thereof,

wherein

G is a group of formula  or  ;

X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered

heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{28}$, $–C(=O)OR^{28}$, $–C(=O)NR^{24}R^{28}$, $–C(=O)C(=O)R^{28}$, $–NR^{24}R^{28}$, $–NR^{24}NR^{24}R^{28}$, $–N=NR^{28}$, $–NR^{24}OR^{28}$, $–NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)C(=O)R^{28}$, $–NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)OR^{28}$, $–NR^{24}C(=O)NR^{24}R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $–NR^{24}S(=O)_2R^{28}$, $–NR^{24}S(=O)_2NR^{24}R^{28}$, $–OR^{28}$, $–OC(=O)R^{28}$, $–OC(=O)NR^{24}R^{28}$, $–OC(=O)OR^{28}$, $–OS(=O)R^{28}$, $–OS(=O)_2R^{28}$, $–OS(=O)_2OR^{28}$, $–OS(=O)_2NR^{24}R^{28}$, $–S(=O)_nR^{28}$, $–S(=O)_2NR^{24}R^{28}$, and $–S(=O)NR^{24}R^{28}$;

R^7, R^8, R^9, R^{12}, R^{13}, R^{14}, R^{15}, R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(=NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –

$OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$;

or any of R^7 and R^8, R^{12} and R^{13}, R^{14} and R^{15}, R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19};

R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-C(=NR^{35})R^{30}$, $-C(=NR^{35})NR^{32}R^{33}$, $-C(=NOH)NR^{32}R^{33}$, $-C(=NOR^{36})R^{30}$, $-C(=NNR^{32}R^{33})R^{30}$, $-C(=NNR^{34}C(=O)R^{31})R^{30}$, $-C(=NNR^{34}C(=O)OR^{31})R^{30}$, $-C(=S)NR^{32}R^{33}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}C(=S)R^{30}$, $-NR^{34}C(=S)OR^{30}$, $-NR^{34}C(=S)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-NR^{34}P(=O)R^{78}R^{78}$, $-NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-NR^{34}P(=O)(OR^{30})(OR^{30})$, $-NR^{34}P(=O)(SR^{30})(SR^{30})$, $-OR^{30}$, $=O$, $-OCN$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-$

$OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-OS(=O)R^{30}$, $-OS(=O)_2R^{30}$, $-OS(=O)_2OR^{30}$, $-OS(=O)_2NR^{32}R^{33}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-OP(=O)(OR^{30})(OR^{30})$, $-OP(=O)(SR^{30})(SR^{30})$, $-Si(R^{34})_3$, –SCN, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-SP(=O)(OR^{30})(OR^{30})$, $-SP(=O)(SR^{30})(SR^{30})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$;

R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-6}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{28} at each occurrence is independently chosen from C_{1-10}alkyl optionally substituted by 1-13 R^{49}, C_{2-10}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-

21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59};

or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69};

R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, $=O$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, $-SCN$, $=S$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-$

$P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$;

R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkynyl optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99};

or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109};

R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89};

R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{119}, C_{2-6}alkenyl optionally substituted by 1-11 R^{119}, C_{2-6}alkynyl optionally substituted by 1-9 R^{119}, C_{6-11}aryl optionally substituted by 1-11 R^{119}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{119}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{119}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{119}, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-C(=O)C(=O)R^{110}$, $-C(=NR^{115})R^{110}$, $-C(=NR^{115})NR^{112}R^{113}$, $-C(=NOH)NR^{112}R^{113}$, $-C(=NOR^{116})R^{110}$, $-C(=NNR^{112}R^{113})R^{110}$, $-C(=NNR^{114}C(=O)R^{111})R^{110}$, $-C(=NNR^{114}C(=O)OR^{111})R^{110}$, $-C(=S)NR^{112}R^{113}$, –NC, $-NO_2$, $-NR^{112}R^{113}$, $-NR^{114}NR^{112}R^{113}$, $-N=NR^{114}$, $=NR^{110}$, $=NOR^{110}$, $-NR^{114}OR^{116}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}C(=O)C(=O)R^{110}$, $-NR^{114}C(=O)OR^{111}$, $-NR^{114}C(=O)C(=O)OR^{111}$, $-NR^{114}C(=O)NR^{112}R^{113}$, $-NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $-NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $-NR^{114}C(=NR^{115})NR^{112}R^{113}$, $-NR^{114}C(=O)C(=O)NR^{112}R^{113}$, $-NR^{114}C(=S)R^{110}$, $-NR^{114}C(=S)OR^{110}$, $-NR^{114}C(=S)NR^{112}R^{113}$, $-NR^{114}S(=O)_2R^{111}$, $-NR^{114}S(=O)_2NR^{112}R^{113}$, $-NR^{114}P(=O)R^{118}R^{118}$, $-NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $-NR^{114}P(=O)(OR^{110})(OR^{110})$, $-NR^{114}P(=O)(SR^{110})(SR^{110})$, $-OR^{110}$, =O, –OCN, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-OC(=O)OR^{110}$, $-OC(=NR^{115})NR^{112}R^{113}$, $-OS(=O)R^{110}$, $-OS(=O)_2R^{110}$, $-OS(=O)_2OR^{110}$, $-OS(=O)_2NR^{112}R^{113}$, $-OP(=O)R^{118}R^{118}$, $-OP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $-OP(=O)(OR^{110})(OR^{110})$, $-OP(=O)(SR^{110})(SR^{110})$, $-Si(R^{114})_3$, –SCN, =S, $-S(=O)_nR^{110}$, $-S(=O)_2OR^{110}$, $-SO_3R^{1111}$, $-S(=O)_2NR^{112}R^{113}$, $-S(=O)NR^{112}R^{113}$, $-SP(=O)R^{118}R^{118}$, $-SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $-SP(=O)(OR^{110})(OR^{110})$, $-SP(=O)(SR^{110})(SR^{110})$, $-P(=O)R^{118}R^{118}$, $-P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $-P(=O)(OR^{110})(OR^{110})$, and $-P(=O)(SR^{110})(SR^{110})$;

R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139};

or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149};

R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{159}, C_{2-6}alkenyl optionally substituted by 1-11

R^{159}, C_{2-6}alkynyl optionally substituted by 1-9 R^{159}, C_{6-11}aryl optionally substituted by 1-11 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{159}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{159}, halogen, –CN, –$C(=O)R^{150}$, –$C(=O)OR^{150}$, –$C(=O)NR^{152}R^{153}$, –$C(=O)C(=O)R^{150}$, –$C(=NR^{155})R^{150}$, –$C(=NR^{155})NR^{152}R^{153}$, –$C(=NOH)NR^{152}R^{153}$, –$C(=NOR^{156})R^{150}$, –$C(=NNR^{152}R^{153})R^{150}$, –$C(=NNR^{154}C(=O)R^{151})R^{150}$, –$C(=NNR^{154}C(=O)OR^{151})R^{150}$, –$C(=S)NR^{152}R^{153}$, –NC, $–NO_2$, –$NR^{152}R^{153}$, –$NR^{154}NR^{152}R^{153}$, –$N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, –$NR^{154}OR^{156}$, –$NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)C(=O)R^{150}$, –$NR^{154}C(=O)OR^{151}$, –$NR^{154}C(=O)C(=O)OR^{151}$, –$NR^{154}C(=O)NR^{152}R^{153}$, –$NR^{154}C(=O)NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, –$NR^{154}C(=NR^{155})NR^{152}R^{153}$, –$NR^{154}C(=O)C(=O)NR^{152}R^{153}$, –$NR^{154}C(=S)R^{150}$, –$NR^{154}C(=S)OR^{150}$, –$NR^{154}C(=S)NR^{152}R^{153}$, –$NR^{154}S(=O)_2R^{151}$, –$NR^{154}S(=O)_2NR^{152}R^{153}$, –$NR^{154}P(=O)R^{158}R^{158}$, –$NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$NR^{154}P(=O)(OR^{150})(OR^{150})$, –$NR^{154}P(=O)(SR^{150})(SR^{150})$, $–OR^{150}$, =O, –OCN, –$OC(=O)R^{150}$, –$OC(=O)NR^{152}R^{153}$, –$OC(=O)OR^{150}$, –$OC(=NR^{155})NR^{152}R^{153}$, –$OS(=O)R^{150}$, –$OS(=O)_2R^{150}$, –$OS(=O)_2OR^{150}$, –$OS(=O)_2NR^{152}R^{153}$, –$OP(=O)R^{158}R^{158}$, –$OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$OP(=O)(OR^{150})(OR^{150})$, –$OP(=O)(SR^{150})(SR^{150})$, –$Si(R^{154})_3$, –SCN, =S, –$S(=O)_nR^{150}$, –$S(=O)_2OR^{150}$, –SO_3R^{1515}, –$S(=O)_2NR^{152}R^{153}$, –$S(=O)NR^{152}R^{153}$, –$SP(=O)R^{158}R^{158}$, –$SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$SP(=O)(OR^{150})(OR^{150})$, –$SP(=O)(SR^{150})(SR^{150})$, –$P(=O)R^{158}R^{158}$, –$P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$P(=O)(OR^{150})(OR^{150})$, and –$P(=O)(SR^{150})(SR^{150})$;

R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally

substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{179}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179};

or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{189};

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{199}, C_{2-6}alkenyl optionally substituted by 1-11 R^{199}, C_{2-6}alkynyl optionally substituted by 1-9 R^{199}, C_{6-11}aryl optionally substituted by 1-11 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-

40 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{199}, halogen, –CN, –$C(=O)R^{190}$, –$C(=O)OR^{190}$, –$C(=O)NR^{192}R^{193}$, –$C(=O)C(=O)R^{190}$, –$C(=NR^{195})R^{190}$, –$C(=NR^{195})NR^{192}R^{193}$, –$C(=NOH)NR^{192}R^{193}$, –$C(=NOR^{196})R^{190}$, –$C(=NNR^{192}R^{193})R^{190}$, –$C(=NNR^{194}C(=O)R^{191})R^{190}$, –$C(=NNR^{194}C(=O)OR^{191})R^{190}$, –$C(=S)NR^{192}R^{193}$, –NC, –$NO_2$, –$NR^{192}R^{193}$, –$NR^{194}NR^{192}R^{193}$, –$N=NR^{194}$, $=NR^{190}$, $=NOR^{190}$, –$NR^{194}OR^{196}$, –$NR^{194}C(=O)R^{190}$, –$NR^{194}C(=O)C(=O)R^{190}$, –$NR^{194}C(=O)OR^{191}$, –$NR^{194}C(=O)C(=O)OR^{191}$, –$NR^{194}C(=O)NR^{192}R^{193}$, –$NR^{194}C(=O)NR^{194}C(=O)R^{190}$, –$NR^{194}C(=O)NR^{194}C(=O)OR^{190}$, –$NR^{194}C(=NR^{195})NR^{192}R^{193}$, –$NR^{194}C(=O)C(=O)NR^{192}R^{193}$, –$NR^{194}C(=S)R^{190}$, –$NR^{194}C(=S)OR^{190}$, –$NR^{194}C(=S)NR^{192}R^{193}$, –$NR^{194}S(=O)_2R^{191}$, –$NR^{194}S(=O)_2NR^{192}R^{193}$, –$NR^{194}P(=O)R^{198}R^{198}$, –$NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$NR^{194}P(=O)(OR^{190})(OR^{190})$, –$NR^{194}P(=O)(SR^{190})(SR^{190})$, –$OR^{190}$, =O, –OCN, –$OC(=O)R^{190}$, –$OC(=O)NR^{192}R^{193}$, –$OC(=O)OR^{190}$, –$OC(=NR^{195})NR^{192}R^{193}$, –$OS(=O)R^{190}$, –$OS(=O)_2R^{190}$, –$OS(=O)_2OR^{190}$, –$OS(=O)_2NR^{192}R^{193}$, –$OP(=O)R^{198}R^{198}$, –$OP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$OP(=O)(OR^{190})(OR^{190})$, –$OP(=O)(SR^{190})(SR^{190})$, –$Si(R^{194})_3$, –SCN, =S, –$S(=O)_nR^{190}$, –$S(=O)_2OR^{190}$, –SO_3R^{1919}, –$S(=O)_2NR^{192}R^{193}$, –$S(=O)NR^{192}R^{193}$, –$SP(=O)R^{198}R^{198}$, –$SP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$SP(=O)(OR^{190})(OR^{190})$, –$SP(=O)(SR^{190})(SR^{190})$, –$P(=O)R^{198}R^{198}$, –$P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$P(=O)(OR^{190})(OR^{190})$, and –$P(=O)(SR^{190})(SR^{190})$;

R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{219}, C_{2-6}alkenyl optionally substituted by 1-11 R^{219}, C_{2-6}alkynyl optionally substituted by 1-9 R^{219}, C_{6-11}aryl optionally substituted by 1-11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219};

or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229};

R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(=O)C(=O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}R^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, –

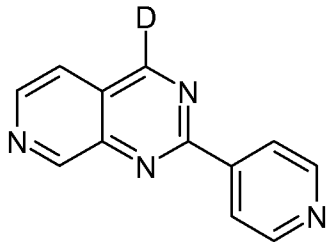
$NR^{230}C(=O)NR^{230}R^{230}$, $-NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $-NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $-NR^{230}C(=NR^{230})NR^{230}R^{230}$, $-NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $-NR^{230}C(=S)R^{230}$, $-NR^{230}C(=S)OR^{230}$, $-NR^{230}C(=S)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-NR^{230}P(=O)R^{231}R^{231}$, $-NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-NR^{230}P(=O)(OR^{230})(OR^{230})$, $-NR^{230}P(=O)(SR^{230})(SR^{230})$, $-OR^{230}$, =O, –OCN, $-OC(=O)R^{230}$, $-OC(=O)NR^{230}R^{230}$, $-OC(=O)OR^{230}$, $-OC(=NR^{230})NR^{230}R^{230}$, $-OS(=O)R^{230}$, $-OS(=O)_2R^{230}$, $-OS(=O)_2OR^{230}$, $-OS(=O)_2NR^{230}R^{230}$, $-OP(=O)R^{231}R^{231}$, $-OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-OP(=O)(OR^{230})(OR^{230})$, $-OP(=O)(SR^{230})(SR^{230})$, $-Si(R^{230})_3$, –SCN, =S, $-S(=O)_nR^{230}$, $-S(=O)_2OR^{230}$, $-SO_3R^{230}$, $-S(=O)_2NR^{230}R^{230}$, $-S(=O)NR^{230}R^{230}$, $-SP(=O)R^{231}R^{231}$, $-SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-SP(=O)(OR^{230})(OR^{230})$, $-SP(=O)(SR^{230})(SR^{230})$, $-P(=O)R^{231}R^{231}$, $-P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-P(=O)(OR^{230})(OR^{230})$, and $-P(=O)(SR^{230})(SR^{230})$;

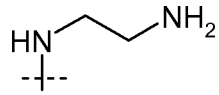
R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl;

R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl; and

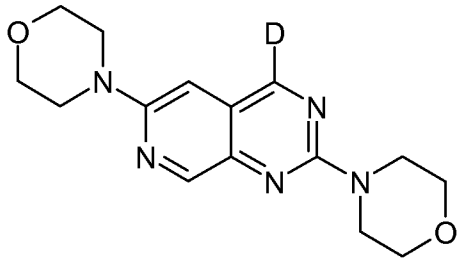
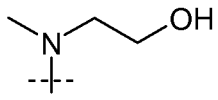
n at each occurrence is independently chosen from 0, 1, and 2;

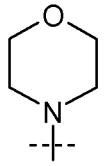
with the proviso that the compound is not

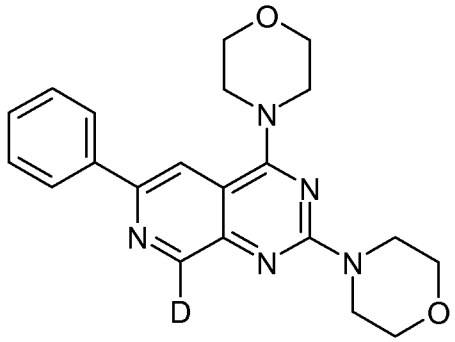
(a) 

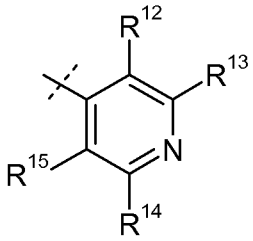
in which D is H or 

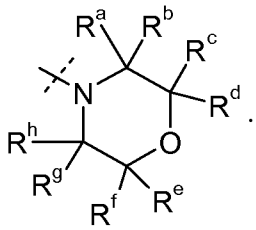
, or a salt form thereof;

(b)  in which D is  or

 , or a salt form thereof; or

(c)  in which D is H or $-CH_3$, or a salt form thereof.

Embodiment 2. The compound of Embodiment 1, wherein G is a group of formula  .

Embodiment 3. The compound of Embodiment 1, wherein G is a group of formula  .

Embodiment 4. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally

substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-C(=O)C(=O)R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}NR^{24}R^{28}$, $-N=NR^{28}$, $-NR^{24}OR^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OC(=O)OR^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2OR^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 5. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 6. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-10}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6

R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 7. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 8. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 9. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered

heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 10. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 11. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 12. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 13. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 14. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 15. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 16. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 17. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, –

$NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 18. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 19. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 20. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 21. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 22. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 23. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 24. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 25. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 26. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, $-OR^{28}$, and $-SR^{28}$.

Embodiment 27. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 28. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-9 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 29. The compound of any of Embodiments 1-3, wherein X is chosen from 3-9 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 30. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-7 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 31. The compound of any of Embodiments 1-3, wherein X is chosen from 3-7 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 32. The compound of any of Embodiments 1-3, wherein X is 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 33. The compound of any of Embodiments 1-3, wherein X is 3-9 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 34. The compound of any of Embodiments 1-3, wherein X is 3-7 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 35. The compound of any of Embodiments 1-3, wherein X is 5-6 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 36. The compound of any of Embodiments 1-3, wherein X is 6 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

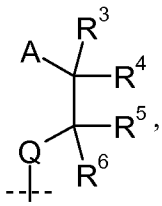
Embodiment 37. The compound of any of Embodiments 1-3, wherein X is morpholinyl, piperidinyl, or piperazinyl optionally substituted by 1-6 R^{19}.

Embodiment 38. The compound of any of Embodiments 1-3, wherein X is piperidinyl or piperazinyl optionally substituted by 1-6 R^{19}.

Embodiment 39. The compound of any of Embodiments 1-3, wherein X is piperidinyl optionally substituted by 1-6 R^{19}.

Embodiment 40. The compound of any of Embodiments 1-3, wherein X is piperazinyl optionally substituted by 1-6 R^{19}.

Embodiment 41. The compound of any of Embodiments 1-3, wherein X is $-NR^{24}R^{28}$.

Embodiment 42. The compound of any of Embodiments 1-3, wherein X is chosen from H and  , wherein

A is $-NR^1R^2$, $-CR^iR^jR^k$, $-OR^{18a}$, or $-SR^{18b}$;

Q is $-NR^{11}-$, $-CR^mR^n-$, $-O-$, or $-S-$;

R^k is H, halogen, $-CN$, $-NO_2$, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$;

R^q is H, halogen, $-CN$, $-NO_2$, $-NR^{16a}R^{17a}$ or $-OR^{18e}$;

R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, and $-OR^{70}$;

R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79},

C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, $-SCN$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$;

or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking

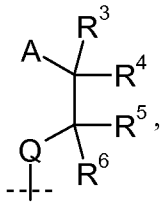
them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or R^4 and R^5 or R^n and R^5 can together form a double bond;

or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, =NR^{70}, =NOR^{70}, or =S.

Embodiment 43. The compound of any of Embodiments 1-3, wherein X is



, wherein

A is $–NR^1R^2$, $–CR^iR^jR^k$, $–OR^{18a}$, or $–SR^{18b}$;

Q is $–NR^{11}–$, $–CR^mR^n–$, –O–, or –S–;

R^k is H, halogen, –CN, $–NO_2$, $–NR^{16}R^{17}$, $–OR^{18c}$, $–SR^{18d}$, or $–CR^oR^pR^q$;

R^q is H, halogen, –CN, $–NO_2$, $–NR^{16a}R^{17a}$ or $–OR^{18e}$;

R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, and $–OR^{70}$;

R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally

substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$C(=O)C(=O)R^{70}$, –$C(=NR^{75})R^{70}$, –$C(=NR^{75})NR^{72}R^{73}$, –$C(=NOH)NR^{72}R^{73}$, –$C(=NOR^{76})R^{70}$, –$C(=NNR^{72}R^{73})R^{70}$, –$C(=NNR^{74}C(=O)R^{71})R^{70}$, –$C(=NNR^{74}C(=O)OR^{71})R^{70}$, –$C(=S)NR^{72}R^{73}$, –NC, –$NO_2$, –$NR^{72}R^{73}$, –$NR^{74}NR^{72}R^{73}$, –$N=NR^{74}$, –$NR^{74}OR^{76}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}C(=O)C(=O)R^{70}$, –$NR^{74}C(=O)OR^{71}$, –$NR^{74}C(=O)C(=O)OR^{71}$, –$NR^{74}C(=O)NR^{72}R^{73}$, –$NR^{74}C(=O)NR^{74}C(=O)R^{70}$, –$NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, –$NR^{74}C(=NR^{75})NR^{72}R^{73}$, –$NR^{74}C(=O)C(=O)NR^{72}R^{73}$, –$NR^{74}C(=S)R^{70}$, –$NR^{74}C(=S)OR^{70}$, –$NR^{74}C(=S)NR^{72}R^{73}$, –$NR^{74}S(=O)_2R^{71}$, –$NR^{74}S(=O)_2NR^{72}R^{73}$, –$NR^{74}P(=O)R^{78}R^{78}$, –$NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$NR^{74}P(=O)(OR^{70})(OR^{70})$, –$NR^{74}P(=O)(SR^{70})(SR^{70})$, –$OR^{70}$, –OCN, –$OC(=O)R^{70}$, –$OC(=O)NR^{72}R^{73}$, –$OC(=O)OR^{70}$, –$OC(=NR^{75})NR^{72}R^{73}$, –$OS(=O)R^{70}$, –$OS(=O)_2R^{70}$, –$OS(=O)_2OR^{70}$, –$OS(=O)_2NR^{72}R^{73}$, –$OP(=O)R^{78}R^{78}$, –$OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$OP(=O)(OR^{70})(OR^{70})$, –$OP(=O)(SR^{70})(SR^{70})$, –$Si(R^{74})_3$, –SCN, –$S(=O)_nR^{70}$, –$S(=O)_2OR^{70}$, –SO_3R^{77}, –$S(=O)_2NR^{72}R^{73}$, –$S(=O)NR^{72}R^{73}$, –$SP(=O)R^{78}R^{78}$, –$SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$SP(=O)(OR^{70})(OR^{70})$, –$SP(=O)(SR^{70})(SR^{70})$, –$P(=O)R^{78}R^{78}$, –$P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$P(=O)(OR^{70})(OR^{70})$, and –$P(=O)(SR^{70})(SR^{70})$;

or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and

R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or R^4 and R^5 or R^n and R^5 can together form a double bond;

or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, $=NR^{70}$, $=NOR^{70}$, or =S.

Embodiment 44. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, and $-OR^{70}$; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, –

$NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-OR^{70}$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-Si(R^{74})_3$, $-SCN$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, and $-P(=O)(OR^{70})(OR^{70})$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, $=NR^{70}$, $=NOR^{70}$, or =S.

Embodiment 45. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, and $-OR^{70}$; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by

1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–C(=O)C(=O)R^{70}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}NR^{72}R^{73}$, $–N=NR^{74}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–NR^{74}P(=O)R^{78}R^{78}$, $–NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–NR^{74}P(=O)(OR^{70})(OR^{70})$, $–OR^{70}$, –OCN, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OC(=O)OR^{70}$, $–OS(=O)R^{70}$, $–OS(=O)_2R^{70}$, $–OS(=O)_2OR^{70}$, $–OS(=O)_2NR^{72}R^{73}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–OP(=O)(OR^{70})(OR^{70})$, –SCN, $–S(=O)_nR^{70}$, $–S(=O)_2OR^{70}$, $–SO_3R^{77}$, $–S(=O)_2NR^{72}R^{73}$, $–S(=O)NR^{72}R^{73}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–SP(=O)(OR^{70})(OR^{70})$, $–SP(=O)(SR^{70})(SR^{70})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, and $–P(=O)(OR^{70})(OR^{70})$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 46. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-}

$_{11}$cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, and 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-11}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, –SCN, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, and $-S(=O)NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 47. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl

optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-11}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, and 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-11}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, –OCN, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, –SCN, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 48. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl

optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, and 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 49. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, and 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkenyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by

1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 50. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}S(=O)_2R^{71}$, $–OR^{70}$, $–OC(=O)R^{70}$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the

atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 51. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 52. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1

and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 53. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 54. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 55. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4,

R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, –CN, –C(=O)OR^{70}, –C(=O)$NR^{72}R^{73}$, –$NR^{72}R^{73}$, and –OR^{70}; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 56. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –C(=O)R^{70}, –C(=O)OR^{70}, –C(=O)$NR^{72}R^{73}$, –NC, –NO_2, –$NR^{72}R^{73}$, –$NR^{74}OR^{76}$, –NR^{74}C(=O)R^{70}, –NR^{74}C(=O)OR^{71}, –NR^{74}C(=O)$NR^{72}R^{73}$, –$NR^{74}S(=O)_2R^{71}$, –$NR^{74}S(=O)_2NR^{72}R^{73}$, –$OR^{70}$, –OC(=O)$R^{70}$, –OC(=O)$NR^{72}R^{73}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 57. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl

optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –NO_2, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 58. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6

R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 59. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 60. The compound of any of Embodiments 42-59, wherein 0-3 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 61. The compound of any of Embodiments 42-59, wherein 0-2 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d}

and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 62. The compound of any of Embodiments 42-59, wherein 1-2 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 63. The compound of any of Embodiments 42-59, wherein none of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 64. The compound of any of Embodiments 42-59, wherein one of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 65. The compound of any of Embodiments 42-59, wherein two of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 66. The compound of any of Embodiments 42-59, wherein 0-3 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17},

R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 67. The compound of any of Embodiments 42-59, wherein 0-2 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 68. The compound of any of Embodiments 42-59, wherein 1-2 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 69. The compound of any of Embodiments 42-59, wherein none of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 70. The compound of any of Embodiments 42-59, wherein one of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d}

and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 71. The compound of Embodiment 70, wherein said optionally substituted heterocarbocyclyl is a 3-7 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 72. The compound of Embodiment 70, wherein said optionally substituted heterocarbocyclyl is a 5-6 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 73. The compound of any of Embodiments 42-59, wherein two of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 74. The compound of any of Embodiments 42-73, wherein 0-2 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 75. The compound of any of Embodiments 42-73, wherein 0-1 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 76. The compound of any of Embodiments 42-73, wherein none of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 77. The compound of any of Embodiments 42-73, wherein one of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4

and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 78. The compound of any of Embodiments 42-73, wherein 0-2 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 79. The compound of any of Embodiments 42-73, wherein 0-1 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 80. The compound of any of Embodiments 42-73, wherein none of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 81. The compound of any of Embodiments 42-73, wherein one of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 82. The compound of any of Embodiments 42-73, wherein 0-2 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 83. The compound of any of Embodiments 42-73, wherein 0-1 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 84. The compound of any of Embodiments 42-73, wherein none of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 85. The compound of any of Embodiments 42-73, wherein one of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 86. The compound of Embodiment 85, wherein said optionally substituted heterocarbocyclyl is a 3-7 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 87. The compound of Embodiment 85, wherein said optionally substituted heterocarbocyclyl is a 5-6 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 88. The compound of any of Embodiments 42-87, wherein neither R^4 and R^5 nor R^n and R^5 together form a double bond.

Embodiment 89. The compound of any of Embodiments 42-88, wherein none of R^3 and R^4, R^5 and R^6, R^i and R^j, or R^m and R^n together form =O, =NR^{70}, =NOR^{70}, or =S.

Embodiment 90. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 91. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –

$NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 92. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, –CN, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, and $-OR^{70}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 93. The compound of any of Embodiments 42-89, wherein at least five of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least four of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 94. The compound of any of Embodiments 42-89, wherein at least five of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least five of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 95. The compound of any of Embodiments 42-89, wherein at least six of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least five of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 96. The compound of any of Embodiments 42-89, wherein at least six of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least six of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 97. The compound of any of Embodiments 42-89, wherein at least seven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least six of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 98. The compound of any of Embodiments 42-89, wherein at least seven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least seven of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 99. The compound of any of Embodiments 42-89, wherein at least eight of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least seven of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 100. The compound of any of Embodiments 42-89, wherein at least eight of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least eight of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 101. The compound of any of Embodiments 42-89, wherein at least nine of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least eight of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 102. The compound of any of Embodiments 42-89, wherein at least nine of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 103. The compound of any of Embodiments 42-89, wherein at least ten of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 104. The compound of any of Embodiments 42-89, wherein at least eleven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 105. The compound of any of Embodiments 42-89, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 106. The compound of any of Embodiments 42-89, wherein at least eleven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 107. The compound of any of Embodiments 42-106, wherein R^q is H, $-NR^{16a}R^{17a}$ or $-OR^{18e}$.

Embodiment 108. The compound of any of Embodiments 42-106, wherein R^q is $-NR^{16a}R^{17a}$ or $-OR^{18e}$.

Embodiment 109. The compound of any of Embodiments 42-108, wherein R^k is H, halogen, –CN, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$.

Embodiment 110. The compound of any of Embodiments 42-108, wherein R^k is H, –CN, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$.

Embodiment 111. The compound of any of Embodiments 42-108, wherein R^k is H, –CN, $–NR^{16}R^{17}$, $–OR^{18c}$, or $–CR^oR^pR^q$.

Embodiment 112. The compound of any of Embodiments 42-108, wherein R^k is H, $–NR^{16}R^{17}$, $–OR^{18c}$, or $–CR^oR^pR^q$.

Embodiment 113. The compound of any of Embodiments 42-108, wherein R^k is $–NR^{16}R^{17}$, $–OR^{18c}$, or $–CR^oR^pR^q$.

Embodiment 114. The compound of any of Embodiments 42-106, wherein R^k is H.

Embodiment 115. The compound of any of Embodiments 42-106, wherein R^k is $–NR^{16}R^{17}$.

Embodiment 116. The compound of any of Embodiments 42-106, wherein R^k is $–OR^{18c}$.

Embodiment 117. The compound of any of Embodiments 42-108, wherein R^k is $–CR^oR^pR^q$.

Embodiment 118. The compound of any of Embodiments 42-117, wherein A is $–NR^1R^2$, $–CR^iR^jR^k$, or $–OR^{18a}$.

Embodiment 119. The compound of any of Embodiments 42-106, wherein A is $–NR^1R^2$ or $–OR^{18a}$.

Embodiment 120. The compound of any of Embodiments 42-117, wherein A is $–CR^iR^jR^k$.

Embodiment 121. The compound of any of Embodiments 42-106, wherein A is $–NR^1R^2$.

Embodiment 122. The compound of any of Embodiments 42-106, wherein A is $–OR^{18a}$.

Embodiment 123. The compound of any of Embodiments 42-122, wherein Q is $–NR^{11}–$, $–CR^mR^n–$, or –O–.

Embodiment 124. The compound of any of Embodiments 42-122, wherein Q is $–NR^{11}–$.

Embodiment 125. The compound of any of Embodiments 42-122, wherein Q is $–CR^mR^n–$.

Embodiment 126. The compound of any of Embodiments 42-122, wherein Q is –O–.

Embodiment 127. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}; Q is –NR^{11}–, –CR^mR^n–, or –O–; and R^k is –$NR^{16}R^{17}$, or –OR^{18c}.

Embodiment 128. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}; Q is –NR^{11}–; and R^k is –$NR^{16}R^{17}$, or –OR^{18c}.

Embodiment 129. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}; Q is –NR^{11}–; and R^k is –OR^{18c}.

Embodiment 130. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2 or –OR^{18a}; and Q is –NR^{11}–.

Embodiment 131. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2; and Q is –NR^{11}–.

Embodiment 132. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 133. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 134. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-9 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 135. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 136. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 137. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –$C(=O)OR^{30}$, –$C(=O)NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, and –OR^{30}.

Embodiment 138. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –$C(=O)OR^{30}$, –$C(=O)NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, and –OR^{30}.

Embodiment 139. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –$C(=O)OR^{30}$, –$C(=O)NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, and –OR^{30}.

Embodiment 140. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, and –OH.

Embodiment 141. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-6 R^{49}), –NH(3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{49}), –NH(4-11 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{49}), and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 142. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-6 R^{49}), –NH(3-10 membered heterocycloalkyl), –NH(4-11 membered

heterocycloalkylalkyl), and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 143. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 144. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-9 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 145. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 146. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 147. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2

members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 148. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 149. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 150. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 151. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, and –OH.

Embodiment 152. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 153. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(benzyl), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 154. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 155. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, and –OH.

Embodiment 156. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}) and –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms).

Embodiment 200. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(=NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 201. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 202. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 203. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-4 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-4 R^{19}, C_{2-6}alkynyl optionally substituted by 1-4 R^{19}, C_{6-10}aryl optionally substituted by 1-4 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-4 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-4 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-4 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-4 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-4 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-4 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-4 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-4 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-4 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-4 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-4 R^{19}.

Embodiment 204. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 205. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 206. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$,$–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 207. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-7}cycloalkyl, C_{4-8}cycloalkylalkyl, 3-7 membered heterocycloalkyl, 4-8 membered heterocycloalkylalkyl, 5-6 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$,$–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can,

together with the atoms linking them, form a C_{6-10}aryl, C_{3-7}cycloalkyl, 3-7 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 208. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 209. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 210. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{3-}

$_{7}$cycloalkyl optionally substituted by 1-3 R^{19}, or a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 211. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{3-7}cycloalkyl, 3-7 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{3-7}cycloalkyl, or a 3-7 membered heterocycloalkyl.

Embodiment 212. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, and $–OR^{20}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 213. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, and $–OR^{20}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl

optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 214. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 215. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 216. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 217. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, and $–S(=O)NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 218. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-10 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, and $–S(=O)NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 219. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–Si(R^{24})_3$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 220. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, –

$C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–Si(R^{24})_3$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 221. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 222. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 222. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 223. The compound of any of Embodiments 1-156 or 200-222, wherein R^8 is not phenyl or morpholinyl.

Embodiment 224. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and –

$S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, halogen, –$NR^{22}R^{23}$, and –OR^{20}; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, –$C(=O)R^{20}$, –$C(=O)OR^{20}$, –$C(=O)NR^{22}R^{23}$, –NC, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)OR^{21}$, –$NR^{24}C(=O)NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$OR^{20}$, –$OC(=O)R^{20}$, –$OC(=O)NR^{22}R^{23}$, –$S(=O)_nR^{20}$, and –$S(=O)_2NR^{22}R^{23}$.

Embodiment 225. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, –$C(=O)R^{20}$, –$C(=O)OR^{20}$, –$C(=O)NR^{22}R^{23}$, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$OR^{20}$, –$OC(=O)R^{20}$, –$S(=O)_nR^{20}$, and –$S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, halogen, –$NR^{22}R^{23}$, and –OR^{20}; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, –$C(=O)R^{20}$, –$C(=O)OR^{20}$, –$C(=O)NR^{22}R^{23}$, –NC, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)OR^{21}$, –$NR^{24}C(=O)NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$OR^{20}$, –$OC(=O)R^{20}$, –$OC(=O)NR^{22}R^{23}$, –$S(=O)_nR^{20}$, and –$S(=O)_2NR^{22}R^{23}$.

Embodiment 226. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, –$C(=O)R^{20}$, –$C(=O)OR^{20}$, –$C(=O)NR^{22}R^{23}$, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$OR^{20}$, –$OC(=O)R^{20}$, –$S(=O)_nR^{20}$, and –$S(=O)_2NR^{22}R^{23}$; R^8 is chosen

from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 227. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 228. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, and $-OC(=O)R^{20}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6

R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 229. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 230. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 231. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 232. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 233. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_nR^{20}$.

Embodiment 234. The compound of any of Embodiments 1-156 or 200-233, wherein R^8 is H.

Embodiment 235. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{1-6}alkyl, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 236. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl, C_{6-10}aryl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 237. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 238. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 239. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and –O(C_{1-6}alkyl); R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –$NR^{22}R^{23}$, –OR^{20}, and –SR^{20}.

Embodiment 240. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and –OR^{20}; R^8 is H; and R^9 is H.

Embodiment 241. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and –O(C_{1-6}alkyl); R^8 is H; and R^9 is H.

Embodiment 242. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and –O(C_{1-6}alkyl); R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –$NR^{22}R^{23}$, –OR^{20}, and –SR^{20}.

Embodiment 243. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and –OR^{20}; R^8 is H; and R^9 is H.

Embodiment 244. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and –O(C_{1-6}alkyl); R^8 is H; and R^9 is H.

Embodiment 245. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and –O(CH_3); R^8 is H; and R^9 is H.

Embodiment 246. The compound of any of Embodiments 1-156, wherein R^7 is H; R^8 is H; and R^9 is H.

Embodiment 247. The compound of any of Embodiments 1-156, wherein R^7 is cyclopropyl; R^8 is H; and R^9 is H.

Embodiment 248. The compound of any of Embodiments 1-156, wherein R^7 is –O(CH_3); R^8 is H; and R^9 is H.

Embodiment 249. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and –O(C_{1-6}alkyl); R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9

membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 250. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-O(CH_3)$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 300. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them,

form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 301. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $–P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 302. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, –

$NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 303. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 304. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-11}aryl optionally substituted by 1-3 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, –

$NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 305. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 306. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them,

form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 307. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 308. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 309. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, –

$NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, and $-S(=O)NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 310. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, and $-S(=O)NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 311. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, –SCN, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 312. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 313. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl

optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 314. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, –SCN, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 315. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 316. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, –

$C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 317. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 318. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 319. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-$

$OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 320. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 321. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 322. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 323. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 324. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen

from H, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 325. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 326. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 327. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 328. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 329. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 330. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 331. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 332. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 333. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 334. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 335. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 336. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 337. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 338. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 339. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 340. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 341. The compound of any of Embodiments 300-340, wherein R^{14} is H.

Embodiment 342. The compound of any of Embodiments 300-341, wherein R^{15} is H.

Embodiment 343. The compound of any of Embodiments 300-342, wherein R^{12} is H.

Embodiment 344. The compound of any of Embodiments 300-343, wherein R^{13} is H.

Embodiment 345. The compound of any of Embodiments 300-340, wherein R^{14} and R^{15} are H.

Embodiment 346. The compound of any of Embodiments 300-340, wherein R^{12} are R^{15} are H.

Embodiment 347. The compound of any of Embodiments 300-340, wherein R^{12}, R^{14}, and R^{15} are H.

Embodiment 348. The compound of any of Embodiments 300-340, wherein R^{12} are R^{14} are H.

Embodiment 349. The compound of any of Embodiments 1, 2, 4-156, 200-250, or 300-340, wherein R^{12}, R^{13}, R^{14}, and R^{15} are H.

Embodiment 350. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 351. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 352. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 353. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a pyrrolyl ring.

Embodiment 354. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 355. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 356. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 357. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 358. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by

1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 359. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 360. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 361. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 362. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 363. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted

by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 364. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 365. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 366. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 367. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 368. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 369. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can,

together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 370. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 371. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 400. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-$

SO_3R^{27}, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 401. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-

6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 402. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, and $–S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 403. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –

SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 404. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 405. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d

and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 406. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 407. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 408. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–NR^{24}S(=O)_2R^{21}$.

Embodiment 409. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–NR^{24}S(=O)_2R^{21}$.

Embodiment 410. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $–NR^{22}R^{23}$,and $–NR^{24}C(=O)R^{20}$.

Embodiment 411. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}.

Embodiment 412. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and benzyl optionally substituted by 1-3 R^{19}.

Embodiment 413. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 414. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 415. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 416. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 417. The compound of any of Embodiments 400-416, wherein at least three of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 418. The compound of any of Embodiments 400-416, wherein at least four of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 419. The compound of any of Embodiments 400-416, wherein at least five of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 420. The compound of any of Embodiments 400-416, wherein at least six of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 421. The compound of any of Embodiments 400-416, wherein at least seven of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 422. The compound of any of Embodiments 400-416, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H.

Embodiment 423. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-}

$_{17}$cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(=NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 424. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21

membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)OR^{20}, –C(=O)$NR^{22}R^{23}$, –C(=O)C(=O)R^{20}, –NC, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}NR^{22}R^{23}$, –N=NR^{24}, –$NR^{24}OR^{26}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)C(=O)R^{20}, –NR^{24}C(=O)OR^{21}, –NR^{24}C(=O)C(=O)OR^{21}, –NR^{24}C(=O)$NR^{22}R^{23}$, –NR^{24}C(=O)NR^{24}C(=O)R^{20}, –NR^{24}C(=O)NR^{24}C(=O)OR^{20}, –NR^{24}C(=O)C(=O)$NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$NR^{24}$P(=O)$R^{78}R^{78}$, –$NR^{24}$P(=O)($NR^{22}R^{23}$)($NR^{22}R^{23}$), –$NR^{24}$P(=O)($OR^{20}$)($OR^{20}$), –$NR^{24}$P(=O)($SR^{20}$)($SR^{20}$), –$OR^{20}$, –OCN, –OC(=O)$R^{20}$, –OC(=O)$NR^{22}R^{23}$, –OC(=O)$OR^{20}$, –OC(=$NR^{25}$)$NR^{22}R^{23}$, –OS(=O)$R^{20}$, –$OS(=O)_2R^{20}$, –$OS(=O)_2OR^{20}$, –$OS(=O)_2NR^{22}R^{23}$, –OP(=O)$R^{78}R^{78}$, –OP(=O)($NR^{22}R^{23}$)($NR^{22}R^{23}$), –OP(=O)($OR^{20}$)($OR^{20}$), –OP(=O)($SR^{20}$)($SR^{20}$), –$Si(R^{24})_3$, –SCN, –$S(=O)_nR^{20}$, –$S(=O)_2OR^{20}$, –SO_3R^{27}, –$S(=O)_2NR^{22}R^{23}$, –S(=O)$NR^{22}R^{23}$, –SP(=O)$R^{78}R^{78}$, –SP(=O)($NR^{22}R^{23}$)($NR^{22}R^{23}$), –SP(=O)(OR^{20})(OR^{20}), –SP(=O)(SR^{20})(SR^{20}), –P(=O)$R^{78}R^{78}$, –P(=O)($NR^{22}R^{23}$)($NR^{22}R^{23}$), –P(=O)(OR^{20})(OR^{20}), and –P(=O)(SR^{20})(SR^{20}); or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 425. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)OR^{20}, –C(=O)$NR^{22}R^{23}$, –NC, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}NR^{22}R^{23}$, –$NR^{24}OR^{26}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)C(=O)R^{20}, –NR^{24}C(=O)OR^{21}, –NR^{24}C(=O)C(=O)OR^{21}, –NR^{24}C(=O)$NR^{22}R^{23}$, –NR^{24}C(=O)NR^{24}C(=O)R^{20}, –NR^{24}C(=O)NR^{24}C(=O)OR^{20}, –NR^{24}C(=O)C(=O)$NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$OR^{20}$, –OCN, –OC(=O)$R^{20}$, –OC(=O)$NR^{22}R^{23}$, –OC(=O)$OR^{20}$, –OS(=O)$R^{20}$, –$OS(=O)_2R^{20}$, –$OS(=O)_2OR^{20}$, –$OS(=O)_2NR^{22}R^{23}$, –$Si(R^{24})_3$, –SCN, –$S(=O)_nR^{20}$, –$S(=O)_2OR^{20}$, –SO_3R^{27}, and –$S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g,

R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 426. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, and $–S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 427. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and

R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 428. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 429. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 430. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 431. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-NR^{24}S(=O)_2R^{21}$.

Embodiment 432. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-NR^{24}S(=O)_2R^{21}$.

Embodiment 433. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$,and $-NR^{24}C(=O)R^{20}$.

Embodiment 434. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}.

Embodiment 435. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and benzyl optionally substituted by 1-3 R^{19}.

Embodiment 436. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 437. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 438. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 439. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 440. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 500. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–C(=O)C(=O)R^{30}$, $–C(=NR^{35})R^{30}$, $–C(=NR^{35})NR^{32}R^{33}$, $–C(=NOH)NR^{32}R^{33}$, $–C(=NOR^{36})R^{30}$, $–C(=NNR^{32}R^{33})R^{30}$, $–C(=NNR^{34}C(=O)R^{31})R^{30}$, $–C(=NNR^{34}C(=O)OR^{31})R^{30}$, $–C(=S)NR^{32}R^{33}$, –NC, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $–NR^{34}C(=NR^{35})NR^{32}R^{33}$, $–NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $–NR^{34}C(=S)R^{30}$, $–NR^{34}C(=S)OR^{30}$, $–NR^{34}C(=S)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–NR^{34}P(=O)R^{78}R^{78}$, $–NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–NR^{34}P(=O)(OR^{30})(OR^{30})$, $–NR^{34}P(=O)(SR^{30})(SR^{30})$, $–OR^{30}$, =O, –OCN, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–OC(=O)OR^{30}$, $–OC(=NR^{35})NR^{32}R^{33}$, $–OS(=O)R^{30}$, $–OS(=O)_2R^{30}$, $–OS(=O)_2OR^{30}$, $–OS(=O)_2NR^{32}R^{33}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–OP(=O)(OR^{30})(OR^{30})$, $–OP(=O)(SR^{30})(SR^{30})$, $–Si(R^{34})_3$, –SCN, =S, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–SP(=O)(OR^{30})(OR^{30})$, $–SP(=O)(SR^{30})(SR^{30})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 501. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{39}, C_{2-6}alkenyl optionally substituted by 1-6 R^{39}, C_{2-6}alkynyl optionally substituted by 1-6 R^{39}, C_{6-11}aryl optionally substituted by 1-6 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{39}, 6-21

membered heteroarylalkyl optionally substituted by 1-6 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–C(=O)C(=O)R^{30}$, $–C(=NR^{35})R^{30}$, $–C(=NR^{35})NR^{32}R^{33}$, $–C(=NOH)NR^{32}R^{33}$, $–C(=NOR^{36})R^{30}$, $–C(=NNR^{32}R^{33})R^{30}$, $–C(=NNR^{34}C(=O)R^{31})R^{30}$, $–C(=NNR^{34}C(=O)OR^{31})R^{30}$, $–C(=S)NR^{32}R^{33}$, –NC, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $–NR^{34}C(=NR^{35})NR^{32}R^{33}$, $–NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $–NR^{34}C(=S)R^{30}$, $–NR^{34}C(=S)OR^{30}$, $–NR^{34}C(=S)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–NR^{34}P(=O)R^{78}R^{78}$, $–NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–NR^{34}P(=O)(OR^{30})(OR^{30})$, $–NR^{34}P(=O)(SR^{30})(SR^{30})$, $–OR^{30}$, =O, –OCN, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–OC(=O)OR^{30}$, $–OC(=NR^{35})NR^{32}R^{33}$, $–OS(=O)R^{30}$, $–OS(=O)_2R^{30}$, $–OS(=O)_2OR^{30}$, $–OS(=O)_2NR^{32}R^{33}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–OP(=O)(OR^{30})(OR^{30})$, $–OP(=O)(SR^{30})(SR^{30})$, $–Si(R^{34})_3$, –SCN, =S, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–SP(=O)(OR^{30})(OR^{30})$, $–SP(=O)(SR^{30})(SR^{30})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 502. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{39}, C_{2-6}alkenyl optionally substituted by 1-6 R^{39}, C_{2-6}alkynyl optionally substituted by 1-6 R^{39}, C_{6-11}aryl optionally substituted by 1-6 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–C(=O)C(=O)R^{30}$, –NC, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $–NR^{34}C(=NR^{35})NR^{32}R^{33}$, $–NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–OR^{30}$, =O, –OCN, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–OC(=O)OR^{30}$, $–OC(=NR^{35})NR^{32}R^{33}$, $–Si(R^{34})_3$, –SCN, =S, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, –

SO_3R^{37}, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 503. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OCN$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-Si(R^{34})_3$, $-SCN$, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 504. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OCN$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-Si(R^{34})_3$, $-SCN$, =S,

$-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 505. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, $=O$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, $=S$, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 506. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, $=O$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, $=S$, $-S(=O)_nR^{30}$, $-S(=O)_2NR^{32}R^{33}$, and $-S(=O)NR^{32}R^{33}$.

Embodiment 507. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-$

$NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, =S, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 508. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, =S, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 509. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}S(=O)_2R^{31}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 510. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}S(=O)_2R^{31}$, $-OR^{30}$, =O, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 511. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl

optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)R^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, –OR^{30}, and =O.

Embodiment 512. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, –C(=O)R^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, –OR^{30}, and =O.

Embodiment 513. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –C(=O)R^{30}, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, and –OR^{30}.

Embodiment 514. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, –CN, –C(=O)$NR^{32}R^{33}$, –NO_2, –$NR^{32}R^{33}$, and –OR^{30}.

Embodiment 515. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}.

Embodiment 516. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –C(=O)OR^{30}, –$NR^{32}R^{33}$, and –OR^{30}.

Embodiment 517. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl

optionally substituted by 1-3 R^{39}, phenyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 518. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 519. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl optionally substituted by 1 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl optionally substituted by 1 R^{39}, 5-6 membered heteroaryl, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 520. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 521. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, $=O$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, $=S$, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 522. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl

optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, –$NR^{34}S(=O)_2R^{31}$, –OR^{30}, =O, –OC(=O)R^{30}, –$S(=O)_nR^{30}$, and –$S(=O)_2NR^{32}R^{33}$.

Embodiment 523. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –OR^{30}, and =O.

Embodiment 524. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, and –OR^{30}.

Embodiment 525. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, 6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –OR^{30}, and =O.

Embodiment 526. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, 6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, and –OR^{30}.

Embodiment 527. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, morpholinyl optionally substituted by 1-3 R^{39}, pyrazolyl optionally substituted by 1-3 R^{39}, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 528. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, morpholinyl optionally substituted by 1-3 R^{39}, pyrazolyl optionally substituted by 1-3 R^{39}, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, and $–OR^{30}$.

Embodiment 529. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 530. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, and $–OR^{30}$.

Embodiment 531. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, benzyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 532. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, benzyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, and $–OR^{30}$.

Embodiment 533. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl, morpholinyl, pyrazolyl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 600. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-6 R^{49}, C_{2-6}alkynyl optionally substituted by 1-6 R^{49}, C_{6-11}aryl optionally substituted by 1-6 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{49}.

Embodiment 601. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-6 R^{49}, C_{2-6}alkynyl optionally substituted by 1-6 R^{49}, C_{6-10}aryl optionally substituted by 1-6 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{49}.

Embodiment 602. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{2-6}alkenyl optionally substituted by 1-3 R^{49}, C_{2-6}alkynyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 603. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 604. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 605. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 606. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}.

Embodiment 607. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 608. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 609. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 610. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{49}.

Embodiment 611. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 612. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 613. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 614. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37}

at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 615. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and cyclopropyl optionally substituted by 1-3 R^{49}.

Embodiment 616. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl.

Embodiment 617. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl.

Embodiment 618. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 619. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 620. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 621. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37}

at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 622. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 623. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 624. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 625. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 626. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 627. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 628. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 629. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 630. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 631. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 632. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 633. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and cyclopropyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 634. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 635. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 636. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 637. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 638. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 639. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 640. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 641. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 642. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 643. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 644. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H,

C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 645. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 646. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 647. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 648. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 649. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 650. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered

heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 651. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 652. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 653. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 654. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 655. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 656. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-}

$_6$cycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 657. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 658. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 659. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 660. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and cyclopropyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 661. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 662. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 663. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H,

phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 664. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 665. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 666. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 667. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 668. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 700. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-6}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49}.

Embodiment 701. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-3 R^{49}, C_{2-6}alkynyl optionally substituted by 1-3 R^{49}, C_{6-11}aryl optionally substituted by 1-3 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{49}.

Embodiment 702. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-3 R^{49}, C_{2-6}alkynyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 703. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 704. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 705. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 706. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}.

Embodiment 707. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}.

Embodiment 708. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5-6 membered heterocycloalkyl.

Embodiment 709. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5 membered heterocycloalkyl optionally substituted by 1-6 R^{49}.

Embodiment 710. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5 membered heterocycloalkyl.

Embodiment 711. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and pyrrolidinyl.

Embodiment 712. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{49} and 5 membered heterocycloalkyl.

Embodiment 713. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is C_{1-6}alkyl optionally substituted by 1-6 R^{49}.

Embodiment 714. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 750. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each

occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 751. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-11}aryl optionally substituted by 1-3 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 752. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 753. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 754. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 755. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 756. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 757. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 4-5 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 758. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 759. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 760. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 761. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, and 6 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 762. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1 R^{59}, and 6 membered heteroaryl optionally substituted by 1 R^{59}.

Embodiment 763. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21

membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 764. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-11}aryl optionally substituted by 1-3 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 765. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, bezyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 766. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally

substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence are independently chosen from H and C_{1-6}alkyl.

Embodiment 767. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, benzyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence are independently chosen from H and C_{1-6}alkyl.

Embodiment 768. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 4-5 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 769. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{23} and R^{33} at each occurrence are independently chosen from H and C_{1-6}alkyl.

Embodiment 770. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{59}.

Embodiment 771. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, benzyl, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-9

membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{59}.

Embodiment 772. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 773. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 774. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, benzyl, and 6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 775. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{59}, and 6 membered heteroaryl optionally substituted by 1 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 776. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or

R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 777. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-11}aryl optionally substituted by 1-3 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 778. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 779. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered

heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 780. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 781. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 782. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 783. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 784. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 785. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 786. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 787. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, and 6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 788. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{59}, and 6 membered heteroaryl optionally substituted by 1 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 789. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 790. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 791. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 792. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they

are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{69}.

Embodiment 793. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{69}.

Embodiment 794. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-6 membered heterocycloalkyl optionally substituted by 1-6 R^{69} or a 5-6 membered heteroaryl optionally substituted by 1-6 R^{69}.

Embodiment 795. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 800. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkenyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–C(=O)C(=O)R^{70}$, $–C(=NR^{75})R^{70}$, $–C(=NR^{75})NR^{72}R^{73}$, $–C(=NOH)NR^{72}R^{73}$, $–C(=NOR^{76})R^{70}$, $–C(=NNR^{72}R^{73})R^{70}$, $–C(=NNR^{74}C(=O)R^{71})R^{70}$, $–C(=NNR^{74}C(=O)OR^{71})R^{70}$, $–C(=S)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}NR^{72}R^{73}$, $–N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, –

$NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, =O, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, –SCN, =S, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$.

Embodiment 801. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-Si(R^{74})_3$, –SCN, =S, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 802. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{6-10}aryl optionally substituted by 1-6 R^{79}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-Si(R^{74})_3$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 803. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, C_{6-10}aryl optionally substituted by 1-3 R^{79}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, =O, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OC(=O)OR^{70}$, $–Si(R^{74})_3$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

Embodiment 804. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, =O, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OC(=O)OR^{70}$, $–Si(R^{74})_3$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

Embodiment 805. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}S(=O)_2R^{71}$, $–OR^{70}$, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

Embodiment 806. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl

optionally substituted by 1-3 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –OR^{70}, and –$S(=O)_nR^{70}$.

Embodiment 807. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –OR^{70}, and –$S(=O)_nR^{70}$.

Embodiment 808. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, cyclopropyl, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –OR^{70}, and –$S(=O)_nR^{70}$.

Embodiment 809. The compound of any of Embodiments 800-808, wherein R^{39} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, and 5-6 membered heteroaryl.

Embodiment 810. The compound of any of Embodiments 800-808, wherein R^{39} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, and 6 membered heteroaryl.

Embodiment 811. The compound of any of Embodiments 800-810, wherein R^{49} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –$C(=O)NR^{72}R^{73}$, and –$NR^{72}R^{73}$.

Embodiment 812. The compound of any of Embodiments 800-810, wherein R^{49} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, 5-6 membered heterocycloalkyl, 6 membered heteroaryl, halogen, –$C(=O)NR^{72}R^{73}$, and –$NR^{72}R^{73}$.

Embodiment 813. The compound of any of Embodiments 800-812, wherein R^{59} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79},

phenyl optionally substituted by 1-3 R^{79}, cyclopropyl, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–NR^{72}R^{73}$, $–OR^{70}$, and $–S(=O)_nR^{70}$.

Embodiment 814. The compound of any of Embodiments 800-812, wherein R^{59} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, cyclopropyl, 6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–NR^{72}R^{73}$, $–OR^{70}$, and $–S(=O)_nR^{70}$.

Embodiment 815. The compound of any of Embodiments 800-814, wherein R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}.

Embodiment 816. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}.

Embodiment 817. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently C_{1-6}alkyl.

Embodiment 850. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}.

Embodiment 851. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{89}, C_{2-6}alkenyl optionally substituted by 1-6 R^{89}, C_{2-6}alkynyl optionally substituted by 1-6 R^{89}, C_{6-10}aryl optionally substituted by 1-6 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{89}.

Embodiment 852. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{2-6}alkenyl optionally substituted by 1-3 R^{89}, C_{2-6}alkynyl optionally substituted by 1-3 R^{89}, C_{6-10}aryl optionally substituted by 1-3 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}.

Embodiment 853. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, benzyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}.

Embodiment 854. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 855. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, benzyl optionally substituted by 1-3 R^{89}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{89}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{89}.

Embodiment 856. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 857. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75},

R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 858. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{89}, and 5-6 membered heteroaryl.

Embodiment 859. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{89}.

Embodiment 860. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 861. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is H.

Embodiment 862. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkynyl optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109}.

Embodiment 863. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-

6 R^{99}, C_{2-6}alkenyl optionally substituted by 1-6 R^{99}, C_{2-6}alkynyl optionally substituted by 1-6 R^{99}, C_{6-11}aryl optionally substituted by 1-6 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{109}.

Embodiment 864. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{99}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{109}.

Embodiment 865. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{99}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{99}.

Embodiment 866. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{99}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-10

membered heterocycloalkyl optionally substituted by 1-3 R^{109} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{109}.

Embodiment 867. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{99}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{99}.

Embodiment 868. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{99}.

Embodiment 869. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 870. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 871. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, and benzyl optionally substituted by 1-3 R^{99}.

Embodiment 872. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{99}.

Embodiment 873. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 874. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 875. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is H.

Embodiment 876. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89}.

Embodiment 877. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{2-6}alkenyl optionally substituted by 1-3 R^{89}, C_{2-6}alkynyl optionally substituted by 1-3 R^{89}, C_{6-11}aryl optionally substituted by 1-3 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89}.

Embodiment 878. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{2-6}alkenyl optionally substituted by 1-3 R^{89}, C_{2-6}alkynyl optionally substituted by 1-3 R^{89}, C_{6-10}aryl optionally substituted by 1-3 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 879. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{6-10}aryl optionally substituted by 1-3 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 880. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, benzyl optionally substituted by 1-3 R^{89}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{89}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 881. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 882. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl, and benzyl.

Embodiment 883. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, and benzyl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 884. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form an azaphosphinane ring optionally substituted by 1-3 C_{1-6}alkyl.

Embodiment 885. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form an azaphosphinane ring optionally substituted by 1-3 R^{89}.

Embodiment 886. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is C_{1-6}alkyl.

Embodiment 900. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{119}, C_{2-6}alkenyl optionally substituted by 1-6 R^{119}, C_{2-6}alkynyl optionally substituted by 1-6 R^{119}, C_{6-11}aryl optionally substituted by 1-6 R^{119}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{119}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{119}, 6-21 membered heteroarylalkyl optionally

substituted by 1-6 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{115})R^{110}$, $–C(=NR^{115})NR^{112}R^{113}$, $–C(=NOH)NR^{112}R^{113}$, $–C(=NOR^{116})R^{110}$, $–C(=NNR^{112}R^{113})R^{110}$, $–C(=NNR^{114}C(=O)R^{111})R^{110}$, $–C(=NNR^{114}C(=O)OR^{111})R^{110}$, $–C(=S)NR^{112}R^{113}$, –NC, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}NR^{112}R^{113}$, $–N=NR^{114}$, $=NR^{110}$, $=NOR^{110}$, $–NR^{114}OR^{116}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $–NR^{114}C(=NR^{115})NR^{112}R^{113}$, $–NR^{114}C(=O)C(=O)NR^{112}R^{113}$, $–NR^{114}C(=S)R^{110}$, $–NR^{114}C(=S)OR^{110}$, $–NR^{114}C(=S)NR^{112}R^{113}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–NR^{114}P(=O)R^{118}R^{118}$, $–NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–NR^{114}P(=O)(OR^{110})(OR^{110})$, $–NR^{114}P(=O)(SR^{110})(SR^{110})$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–OC(=NR^{115})NR^{112}R^{113}$, $–OS(=O)R^{110}$, $–OS(=O)_2R^{110}$, $–OS(=O)_2OR^{110}$, $–OS(=O)_2NR^{112}R^{113}$, $–OP(=O)R^{118}R^{118}$, $–OP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–OP(=O)(OR^{110})(OR^{110})$, $–OP(=O)(SR^{110})(SR^{110})$, $–Si(R^{114})_3$, –SCN, =S, $–S(=O)_nR^{110}$, $–S(=O)_2OR^{110}$, $–SO_3R^{1111}$, $–S(=O)_2NR^{112}R^{113}$, $–S(=O)NR^{112}R^{113}$, $–SP(=O)R^{118}R^{118}$, $–SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–SP(=O)(OR^{110})(OR^{110})$, $–SP(=O)(SR^{110})(SR^{110})$, $–P(=O)R^{118}R^{118}$, $–P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–P(=O)(OR^{110})(OR^{110})$, and $–P(=O)(SR^{110})(SR^{110})$.

Embodiment 901. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{119}, C_{6-11}aryl optionally substituted by 1-6 R^{119}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, –NC, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}NR^{112}R^{113}$, $–NR^{114}OR^{116}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–Si(R^{114})_3$, –SCN, =S, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 902. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted

by 1-6 R^{119}, C_{6-10}aryl optionally substituted by 1-6 R^{119}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{119}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{119}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{119}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–OR^{110}$, =O, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–Si(R^{114})_3$, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 903. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, C_{6-10}aryl optionally substituted by 1-3 R^{119}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{119}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{119}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{119}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–OR^{110}$, =O, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–Si(R^{114})_3$, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 904. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, phenyl optionally substituted by 1-3 R^{119}, benzyl optionally substituted by 1-3 R^{119}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{119}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{119}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–OR^{110}$, =O, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–Si(R^{114})_3$, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 905. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89},

R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, phenyl optionally substituted by 1-3 R^{119}, benzyl optionally substituted by 1-3 R^{119}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{119}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{119}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–OR^{110}$, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 906. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–OR^{110}$, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 907. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, –CN, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–OR^{110}$, and $–S(=O)_nR^{110}$.

Embodiment 908. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, phenyl optionally substituted by 1-3 R^{119}, benzyl optionally substituted by 1-3 R^{119}, halogen, –CN, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–NO_2$, $–NR^{112}R^{113}$, $–OR^{110}$, and $–S(=O)_nR^{110}$.

Embodiment 909. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $–NR^{112}R^{113}$, and $–OR^{110}$.

Embodiment 910. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89},

R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, $-NR^{112}R^{113}$, and $-OR^{110}$.

Embodiment 911. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119} and halogen.

Embodiment 912. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}.

Embodiment 913. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently C_{1-6}alkyl.

Embodiment 914. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129}.

Embodiment 915. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{129}, C_{2-6}alkenyl optionally substituted by 1-6 R^{129}, C_{2-6}alkynyl optionally substituted by 1-6 R^{129}, C_{6-10}aryl optionally substituted by 1-6 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{129}.

Embodiment 916. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{129}, C_{2-6}alkenyl optionally substituted by 1-3 R^{129}, C_{2-6}alkynyl optionally substituted by 1-3 R^{129}, C_{6-10}aryl optionally substituted by 1-3 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 917. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, benzyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 918. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 919. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, benzyl optionally substituted by 1-3 R^{129}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{129}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 920. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 921. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 922. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{129}, and 5-6 membered heteroaryl.

Embodiment 923. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{129}.

Embodiment 924. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 925. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is H.

Embodiment 926. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered

heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149}.

Embodiment 927. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{139}, C_{2-6}alkenyl optionally substituted by 1-6 R^{139}, C_{2-6}alkynyl optionally substituted by 1-6 R^{139}, C_{6-11}aryl optionally substituted by 1-6 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{149}.

Embodiment 928. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{139}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{149}.

Embodiment 929. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{139}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{139}.

Embodiment 930. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{139}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{149} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{149}.

Embodiment 931. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{139}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{139}.

Embodiment 932. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{139}.

Embodiment 933. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 934. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 935. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, and benzyl optionally substituted by 1-3 R^{139}.

Embodiment 936. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{139}.

Embodiment 937. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 938. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 939. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is H.

Embodiment 940. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129}.

Embodiment 941. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3

R^{129}, C_{2-6}alkenyl optionally substituted by 1-3 R^{129}, C_{2-6}alkynyl optionally substituted by 1-3 R^{129}, C_{6-11}aryl optionally substituted by 1-3 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{129}.

Embodiment 942. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, C_{2-6}alkenyl optionally substituted by 1-3 R^{129}, C_{2-6}alkynyl optionally substituted by 1-3 R^{129}, C_{6-10}aryl optionally substituted by 1-3 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 943. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, C_{6-10}aryl optionally substituted by 1-3 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 944. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, benzyl optionally substituted by 1-3 R^{129}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{129}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 945. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 946. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl, and benzyl.

Embodiment 947. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, and benzyl optionally substituted by 1-3 R^{129}.

Embodiment 948. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 949. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{129}.

Embodiment 950. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is C_{1-6}alkyl.

Embodiment 951. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{159}, C_{2-6}alkenyl optionally substituted by 1-6 R^{159}, C_{2-6}alkynyl optionally substituted by 1-6 R^{159}, C_{6-11}aryl optionally substituted by 1-6 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{159}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{159}, halogen, –CN, $–C(=O)R^{150}$, $–C(=O)OR^{150}$, $–C(=O)NR^{152}R^{153}$, $–C(=O)C(=O)R^{150}$, $–C(=NR^{155})R^{150}$, $–C(=NR^{155})NR^{152}R^{153}$, $–C(=NOH)NR^{152}R^{153}$, $–C(=NOR^{156})R^{150}$, $–C(=NNR^{152}R^{153})R^{150}$, $–C(=NNR^{154}C(=O)R^{151})R^{150}$, $–C(=NNR^{154}C(=O)OR^{151})R^{150}$, $–C(=S)NR^{152}R^{153}$, –NC, $–NO_2$, $–NR^{152}R^{153}$, $–NR^{154}NR^{152}R^{153}$, $–N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, $–NR^{154}OR^{156}$, $–NR^{154}C(=O)R^{150}$, $–NR^{154}C(=O)C(=O)R^{150}$, $–NR^{154}C(=O)OR^{151}$, $–NR^{154}C(=O)C(=O)OR^{151}$, –

$NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, $-NR^{154}C(=NR^{155})NR^{152}R^{153}$, $-NR^{154}C(=O)C(=O)NR^{152}R^{153}$, $-NR^{154}C(=S)R^{150}$, $-NR^{154}C(=S)OR^{150}$, $-NR^{154}C(=S)NR^{152}R^{153}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-NR^{154}P(=O)R^{158}R^{158}$, $-NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-NR^{154}P(=O)(OR^{150})(OR^{150})$, $-NR^{154}P(=O)(SR^{150})(SR^{150})$, $-OR^{150}$, =O, –OCN, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-OC(=NR^{155})NR^{152}R^{153}$, $-OS(=O)R^{150}$, $-OS(=O)_2R^{150}$, $-OS(=O)_2OR^{150}$, $-OS(=O)_2NR^{152}R^{153}$, $-OP(=O)R^{158}R^{158}$, $-OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-OP(=O)(OR^{150})(OR^{150})$, $-OP(=O)(SR^{150})(SR^{150})$, $-Si(R^{154})_3$, –SCN, =S, $-S(=O)_nR^{150}$, $-S(=O)_2OR^{150}$, $-SO_3R^{1515}$, $-S(=O)_2NR^{152}R^{153}$, $-S(=O)NR^{152}R^{153}$, $-SP(=O)R^{158}R^{158}$, $-SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-SP(=O)(OR^{150})(OR^{150})$, $-SP(=O)(SR^{150})(SR^{150})$, $-P(=O)R^{158}R^{158}$, $-P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-P(=O)(OR^{150})(OR^{150})$, and $-P(=O)(SR^{150})(SR^{150})$.

Embodiment 952. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{159}, C_{6-11}aryl optionally substituted by 1-6 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{159}, halogen, –CN, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, –NC, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}NR^{152}R^{153}$, $-NR^{154}OR^{156}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, =O, –OCN, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, –SCN, =S, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 953. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{159}, C_{6-10}aryl optionally substituted by 1-6 R^{159}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{159}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{159}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{159}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{159}, halogen, –CN, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, =O, –

$OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 954. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, C_{6-10}aryl optionally substituted by 1-3 R^{159}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{159}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{159}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{159}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, =O, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 955. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, phenyl optionally substituted by 1-3 R^{159}, benzyl optionally substituted by 1-3 R^{159}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{159}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{159}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, =O, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 956. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, phenyl optionally substituted by 1-3 R^{159}, benzyl optionally substituted by 1-3 R^{159}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{159}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{159}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$,

$-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-OR^{150}$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 957. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-OR^{150}$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 958. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-CN$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-OR^{150}$, and $-S(=O)_nR^{150}$.

Embodiment 959. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, phenyl optionally substituted by 1-3 R^{159}, benzyl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-OR^{150}$, and $-S(=O)_nR^{150}$.

Embodiment 960. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-NR^{152}R^{153}$, and $-OR^{150}$.

Embodiment 961. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, $-NR^{152}R^{153}$, and $-OR^{150}$.

Embodiment 962. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159} and halogen.

Embodiment 963. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}.

Embodiment 964. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently C_{1-6}alkyl.

Embodiment 965. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169}.

Embodiment 966. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{169}, C_{2-6}alkenyl optionally substituted by 1-6 R^{169}, C_{2-6}alkynyl optionally substituted by 1-6 R^{169}, C_{6-10}aryl optionally substituted by 1-6 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{169}.

Embodiment 967. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{2-6}alkenyl optionally substituted by 1-3 R^{169}, C_{2-6}alkynyl optionally substituted by 1-3 R^{169}, C_{6-10}aryl optionally substituted by 1-3 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3

R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 968. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, benzyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 969. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 970. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, benzyl optionally substituted by 1-3 R^{169}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{169}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 971. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 972. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 973. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein

R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{169}, and 5-6 membered heteroaryl.

Embodiment 974. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{169}.

Embodiment 975. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 976. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is H.

Embodiment 977. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{179}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{189}.

Embodiment 978. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{179}, C_{2-6}alkenyl optionally substituted by 1-6 R^{179}, C_{2-6}alkynyl optionally substituted by 1-6 R^{179}, C_{6-11}aryl optionally substituted by 1-6 R^{179}, C_{7-16}arylalkyl optionally

substituted by 1-6 R^{179}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{189}.

Embodiment 979. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{179}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{189}.

Embodiment 980. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{179}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{179}.

Embodiment 981. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{179}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to

which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{189} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{189}.

Embodiment 982. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{179}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{179}.

Embodiment 983. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{179}.

Embodiment 984. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 985. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 986. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, and benzyl optionally substituted by 1-3 R^{179}.

Embodiment 987. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein

R^{152} and R^{153} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{179}.

Embodiment 988. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 989. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 990. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is H.

Embodiment 991. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169}.

Embodiment 992. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{2-6}alkenyl optionally substituted by 1-3 R^{169}, C_{2-6}alkynyl optionally substituted by 1-3 R^{169}, C_{6-11}aryl optionally substituted by 1-3 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{169}.

Embodiment 993. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{2-6}alkenyl optionally substituted by 1-3 R^{169}, C_{2-6}alkynyl optionally substituted by 1-3 R^{169}, C_{6-10}aryl optionally substituted by 1-3 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 994. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{6-10}aryl optionally substituted by 1-3 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 995. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, benzyl optionally substituted by 1-3 R^{169}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{169}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 996. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 997. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl, and benzyl.

Embodiment 998. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, and benzyl optionally substituted by 1-3 R^{169}.

Embodiment 999. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 1000. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{169}.

Embodiment 1001. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is C_{1-6}alkyl.

Embodiment 1002. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{199}, C_{2-6}alkenyl optionally substituted by 1-6 R^{199}, C_{2-6}alkynyl optionally substituted by 1-6 R^{199}, C_{6-11}aryl optionally substituted by 1-6 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{199}, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–C(=O)C(=O)R^{190}$, $–C(=NR^{195})R^{190}$, $–C(=NR^{195})NR^{192}R^{193}$, $–C(=NOH)NR^{192}R^{193}$, $–C(=NOR^{196})R^{190}$, $–C(=NNR^{192}R^{193})R^{190}$, $–C(=NNR^{194}C(=O)R^{191})R^{190}$, $–C(=NNR^{194}C(=O)OR^{191})R^{190}$, $–C(=S)NR^{192}R^{193}$, –NC, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}NR^{192}R^{193}$, $–N=NR^{194}$, $=NR^{190}$, $=NOR^{190}$, $–NR^{194}OR^{196}$, $–NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)C(=O)R^{190}$, $–NR^{194}C(=O)OR^{191}$, $–NR^{194}C(=O)C(=O)OR^{191}$, $–NR^{194}C(=O)NR^{192}R^{193}$, $–NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)NR^{194}C(=O)OR^{190}$, $–NR^{194}C(=NR^{195})NR^{192}R^{193}$, $–NR^{194}C(=O)C(=O)NR^{192}R^{193}$, $–NR^{194}C(=S)R^{190}$, $–NR^{194}C(=S)OR^{190}$, $–NR^{194}C(=S)NR^{192}R^{193}$, $–NR^{194}S(=O)_2R^{191}$, $–NR^{194}S(=O)_2NR^{192}R^{193}$, $–NR^{194}P(=O)R^{198}R^{198}$, $–NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $–NR^{194}P(=O)(OR^{190})(OR^{190})$, $–NR^{194}P(=O)(SR^{190})(SR^{190})$, $–OR^{190}$, =O, –OCN, $–OC(=O)R^{190}$, $–OC(=O)NR^{192}R^{193}$, $–OC(=O)OR^{190}$, $–OC(=NR^{195})NR^{192}R^{193}$, $–OS(=O)R^{190}$, $–OS(=O)_2R^{190}$, $–OS(=O)_2OR^{190}$, –

$OS(=O)_2NR^{192}R^{193}$, $-OP(=O)R^{198}R^{198}$, $-OP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-OP(=O)(OR^{190})(OR^{190})$, $-OP(=O)(SR^{190})(SR^{190})$, $-Si(R^{194})_3$, $-SCN$, $=S$, $-S(=O)_nR^{190}$, $-S(=O)_2OR^{190}$, $-SO_3R^{1919}$, $-S(=O)_2NR^{192}R^{193}$, $-S(=O)NR^{192}R^{193}$, $-SP(=O)R^{198}R^{198}$, $-SP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-SP(=O)(OR^{190})(OR^{190})$, $-SP(=O)(SR^{190})(SR^{190})$, $-P(=O)R^{198}R^{198}$, $-P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-P(=O)(OR^{190})(OR^{190})$, and $-P(=O)(SR^{190})(SR^{190})$.

Embodiment 1003. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{199}, C_{6-11}aryl optionally substituted by 1-6 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{199}, halogen, $-CN$, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NC$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}NR^{192}R^{193}$, $-NR^{194}OR^{196}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}C(=O)OR^{191}$, $-NR^{194}C(=O)NR^{192}R^{193}$, $-NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-NR^{194}S(=O)_2NR^{192}R^{193}$, $-OR^{190}$, $=O$, $-OCN$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-Si(R^{194})_3$, $-SCN$, $=S$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1004. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{199}, C_{6-10}aryl optionally substituted by 1-6 R^{199}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{199}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{199}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{199}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{199}, halogen, $-CN$, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}C(=O)OR^{191}$, $-NR^{194}C(=O)NR^{192}R^{193}$, $-NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-NR^{194}S(=O)_2NR^{192}R^{193}$, $-OR^{190}$, $=O$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-Si(R^{194})_3$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1005. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, C_{6-10}aryl optionally substituted by 1-3 R^{199}, C_{7-11}arylalkyl optionally

substituted by 1-3 R^{199}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{199}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{199}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{199}, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)OR^{191}$, $–NR^{194}C(=O)NR^{192}R^{193}$, $–NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $–NR^{194}S(=O)_2R^{191}$, $–NR^{194}S(=O)_2NR^{192}R^{193}$, $–OR^{190}$, =O, $–OC(=O)R^{190}$, $–OC(=O)NR^{192}R^{193}$, $–OC(=O)OR^{190}$, $–Si(R^{194})_3$, $–S(=O)_nR^{190}$, and $–S(=O)_2NR^{192}R^{193}$.

Embodiment 1006. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, phenyl optionally substituted by 1-3 R^{199}, benzyl optionally substituted by 1-3 R^{199}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{199}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{199}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{199}, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)OR^{191}$, $–NR^{194}C(=O)NR^{192}R^{193}$, $–NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $–NR^{194}S(=O)_2R^{191}$, $–NR^{194}S(=O)_2NR^{192}R^{193}$, $–OR^{190}$, =O, $–OC(=O)R^{190}$, $–OC(=O)NR^{192}R^{193}$, $–OC(=O)OR^{190}$, $–Si(R^{194})_3$, $–S(=O)_nR^{190}$, and $–S(=O)_2NR^{192}R^{193}$.

Embodiment 1007. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, phenyl optionally substituted by 1-3 R^{199}, benzyl optionally substituted by 1-3 R^{199}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{199}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{199}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{199}, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}C(=O)R^{190}$, $–NR^{194}S(=O)_2R^{191}$, $–OR^{190}$, $–OC(=O)R^{190}$, $–OC(=O)NR^{192}R^{193}$, $–S(=O)_nR^{190}$, and $–S(=O)_2NR^{192}R^{193}$.

Embodiment 1008. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}C(=O)R^{190}$, –

$NR^{194}S(=O)_2R^{191}$, $-OR^{190}$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1009. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-CN$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-OR^{190}$, and $-S(=O)_nR^{190}$.

Embodiment 1010. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, phenyl optionally substituted by 1-3 R^{199}, benzyl optionally substituted by 1-3 R^{199}, halogen, $-CN$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-OR^{190}$, and $-S(=O)_nR^{190}$.

Embodiment 1011. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-NR^{192}R^{193}$, and $-OR^{190}$.

Embodiment 1012. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, $-NR^{192}R^{193}$, and $-OR^{190}$.

Embodiment 1013. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199} and halogen.

Embodiment 1014. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}.

Embodiment 1015. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently C_{1-6}alkyl.

Embodiment 1016. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209}.

Embodiment 1017. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{209}, C_{2-6}alkenyl optionally substituted by 1-6 R^{209}, C_{2-6}alkynyl optionally substituted by 1-6 R^{209}, C_{6-10}aryl optionally substituted by 1-6 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{209}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{209}.

Embodiment 1018. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{2-6}alkenyl optionally substituted by 1-3 R^{209}, C_{2-6}alkynyl optionally substituted by 1-3 R^{209}, C_{6-10}aryl optionally substituted by 1-3 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1019. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, benzyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10

membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1020. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 1021. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, benzyl optionally substituted by 1-3 R^{209}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{209}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1022. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1023. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1024. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{209}, and 5-6 membered heteroaryl.

Embodiment 1025. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{209}.

Embodiment 1026. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 1027. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is H.

Embodiment 1028. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{219}, C_{2-6}alkenyl optionally substituted by 1-11 R^{219}, C_{2-6}alkynyl optionally substituted by 1-9 R^{219}, C_{6-11}aryl optionally substituted by 1-11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229}.

Embodiment 1029. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{219}, C_{2-6}alkenyl optionally substituted by 1-6 R^{219}, C_{2-6}alkynyl optionally substituted by 1-6 R^{219}, C_{6-11}aryl optionally substituted by 1-6 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered

heterocycloalkyl optionally substituted by 1-6 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{229}.

Embodiment 1030. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{219}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{229}.

Embodiment 1031. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{219}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{219}.

Embodiment 1032. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{219}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{229} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{229}.

Embodiment 1033. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{219}, 5-6 membered

heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{219}.

Embodiment 1034. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{219}.

Embodiment 1035. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 1036. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1037. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, and benzyl optionally substituted by 1-3 R^{219}.

Embodiment 1038. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{219}.

Embodiment 1039. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 1040. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 1041. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is H.

Embodiment 1042. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209}.

Embodiment 1043. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{2-6}alkenyl optionally substituted by 1-3 R^{209}, C_{2-6}alkynyl optionally substituted by 1-3 R^{209}, C_{6-11}aryl optionally substituted by 1-3 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{209}.

Embodiment 1044. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{2-6}alkenyl optionally substituted by 1-3 R^{209}, C_{2-6}alkynyl optionally substituted by 1-3 R^{209}, C_{6-10}aryl optionally substituted by 1-3 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10 membered heterocycloalkyl

optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1045. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{6-10}aryl optionally substituted by 1-3 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1046. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, benzyl optionally substituted by 1-3 R^{209}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{209}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1047. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1048. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl, and benzyl.

Embodiment 1049. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, and benzyl optionally substituted by 1-3 R^{209}.

Embodiment 1050. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 1051. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{209}.

Embodiment 1052. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is C_{1-6}alkyl.

Embodiment 1053. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(=O)C(=O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}R^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=NR^{230})NR^{230}R^{230}$, $–NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $–NR^{230}C(=S)R^{230}$, $–NR^{230}C(=S)OR^{230}$, $–NR^{230}C(=S)NR^{230}R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–NR^{230}P(=O)(SR^{230})(SR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OC(=O)OR^{230}$, $–OC(=NR^{230})NR^{230}R^{230}$, $–OS(=O)R^{230}$, $–OS(=O)_2R^{230}$, $–OS(=O)_2OR^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–OP(=O)(OR^{230})(OR^{230})$, $–OP(=O)(SR^{230})(SR^{230})$, $–Si(R^{230})_3$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2OR^{230}$, $–SO_3R^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–SP(=O)R^{231}R^{231}$, $–SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–SP(=O)(OR^{230})(OR^{230})$, $–SP(=O)(SR^{230})(SR^{230})$, $–P(=O)R^{231}R^{231}$, $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–P(=O)(OR^{230})(OR^{230})$, and $–P(=O)(SR^{230})(SR^{230})$.

Embodiment 1054. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally

substituted by 1-6 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-15 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-15 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(=O)C(=O)R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OC(=O)OR^{230}$, $–OS(=O)R^{230}$, $–OS(=O)_2R^{230}$, $–OS(=O)_2OR^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–OP(=O)(OR^{230})(OR^{230})$, $–Si(R^{230})_3$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2OR^{230}$, $–SO_3R^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–P(=O)R^{231}R^{231}$, $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, and $–P(=O)(OR^{230})(OR^{230})$.

Embodiment 1055. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-10 membered heterocycloalkyl, 4-10 membered heterocycloalkylalkyl, 5-10 membered heteroaryl, 6-10 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–P(=O)R^{231}R^{231}$, and $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$.

Embodiment 1056. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, halogen, –CN, $–C(=O)R^{230}$, –

$C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NO_2$, $-NR^{230}R^{230}$, $-NR^{230}OR^{230}$, $-NR^{230}C(=O)R^{230}$, $-NR^{230}C(=O)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-OR^{230}$, =O, –OCN, $-OC(=O)R^{230}$, $-S(=O)_nR^{230}$, $-S(=O)_2NR^{230}R^{230}$, and $-S(=O)NR^{230}R^{230}$.

Embodiment 1057. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from $C_{1\text{-}6}$alkyl optionally substituted by 1-3 halogen, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, phenyl, benzyl, $C_{3\text{-}6}$cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{230}$, $-C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NO_2$, $-NR^{230}R^{230}$, $-NR^{230}C(=O)R^{230}$, $-NR^{230}C(=O)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-OR^{230}$, =O, $-S(=O)_nR^{230}$, and $-S(=O)_2NR^{230}R^{230}$.

Embodiment 1058. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from $C_{1\text{-}6}$alkyl optionally substituted by 1-3 halogen, $C_{2\text{-}6}$alkenyl, $C_{2\text{-}6}$alkynyl, phenyl, benzyl, $C_{3\text{-}6}$cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{230}$, $-C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NR^{230}R^{230}$, $-NR^{230}C(=O)R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-OR^{230}$, =O, $-S(=O)_nR^{230}$, and $-S(=O)_2NR^{230}R^{230}$.

Embodiment 1059. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from $C_{1\text{-}6}$alkyl optionally substituted by 1-3 halogen, phenyl, benzyl, $C_{3\text{-}6}$cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{230}$, $-C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NR^{230}R^{230}$, $-OR^{230}$, =O, $-S(=O)_nR^{230}$, and $-S(=O)_2NR^{230}R^{230}$.

Embodiment 1060. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from $C_{1\text{-}6}$alkyl optionally substituted by 1-3 halogen, halogen, and $-NR^{230}R^{230}$.

Embodiment 1061. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from $C_{1\text{-}6}$alkyl, halogen, and $-NR^{230}R^{230}$.

Embodiment 1062. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{230}R^{230}$.

Embodiment 1063. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is $-NR^{230}R^{230}$.

Embodiment 1064. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is C_{1-6}alkyl.

Embodiment 1065. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{230}R^{230}$; R^{209}, R^{219} and R^{229} at each occurrence is C_{1-6}alkyl.

Embodiment 1066. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{230}R^{230}$; R^{209}, R^{219} and R^{229} at each occurrence is $-NR^{230}R^{230}$.

Embodiment 1067. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199} at each occurrence is $-NR^{230}R^{230}$; R^{209}, R^{219} and R^{229} at each occurrence is C_{1-6}alkyl.

Embodiment 1068. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl.

Embodiment 1069. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 1070. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is C_{1-6}alkyl.

Embodiment 1071. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is H.

Embodiment 1072. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1071, wherein R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl.

Embodiment 1073. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1071, wherein R^{231} at each occurrence is C_{1-6}alkyl.

Embodiment 1074. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1071, wherein R^{231} at each occurrence is C_{1-6}-haloalkyl.

Embodiment 1075. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 0, 1, and 2.

Embodiment 1076. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 0 and 2.

Embodiment 1077. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 1 and 2.

Embodiment 1078. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 0 and 1.

Embodiment 1079. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is 0.

Embodiment 1080. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is 1.

Embodiment 1081. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is 2.

The above Embodiments include salts of acidic and basic compounds of formula (I). Preferably, the salts are pharmaceutically acceptable. Pharmaceutically acceptable acid addition salts of basic compounds of formula (I) include, but are not limited to, salts derived from inorganic acids such as hydrochloric, nitric, phosphoric, sulfuric, hydrobromic, hydriodic, and phosphorus, as well as the salts derived from organic acids, such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, alkanedioic acids, aromatic acids, and aliphatic and aromatic sulfonic acids. Such salts thus include, but are not limited to, sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, nitrate, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, propionate, caprylate, isobutyrate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, mandelate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, phthalate, benzenesulfonate, toluenesulfonate, phenylacetate, citrate, lactate, maleate, tartrate, and methanesulfonate. See, for example, Berge et al., "Pharmaceutical Salts," J. of Pharmaceutical Science, 1977; 66:1-19.

Acid addition salts may be prepared by contacting a compound of formula (I) with a sufficient amount of the desired acid to produce the salt in the conventional manner. The free base form of the compound of formula (I) may be regenerated by contacting the salt form with a base and isolating the free base in the conventional manner.

Pharmaceutically acceptable base salts of acidic compounds of formula (I) are formed with metals or amines, such as alkali and alkaline earth metal hydroxides, or of organic amines. Examples of metals used as cations include, but are not limited to, sodium, potassium, magnesium, and calcium. Examples of suitable amines include, but are not limited to, N,N'- dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine (ethane-1,2-diamine), N-methylglucamine, and procaine. See, for example, Berge et al., "Pharmaceutical Salts," J. of Pharmaceutical Science, 1977; 66:1-19.

Base salts may be prepared by contacting a compound of formula (I) with a sufficient amount of the desired base to produce the salt in the conventional manner. The acid form of the compound of formula (I) may be regenerated by contacting the salt form with an acid and isolating the acid in a conventional manner.

Some compounds of the present invention may exist as stereoisomers, including enantiomers, diastereomers, and geometric isomers. Geometric isomers include compounds of the present invention that have alkenyl groups, which may exist as entgegen or zusammen conformations, in which case all geometric forms thereof, both entgegen and zusammen, cis and trans, and mixtures thereof, are within the scope of the present invention. Some compounds of the present invention have cycloalkyl groups, which may be substituted at more than one carbon atom, in which case all geometric forms thereof, both cis and trans, and mixtures thereof, are within the scope of the present invention. All of these forms, including (R), (S), epimers, diastereomers, cis, trans, syn, anti, (E), (Z), tautomers, and mixtures thereof, are included in the compounds of the present invention.

The compounds of the present invention may be in any physical form, including amorphous or crystalline solids in any polymorphic form, in any state of purity. Crystalline polymorphic forms include unsolvated forms as well as solvated forms, such as hydrated forms.

III. Pharmaceutical Compositions

The present invention further provides pharmaceutical compositions comprising a compound of any of the above Embodiments (e.g., a compound of formula (I) or a pharmaceutically acceptable salt thereof), together with a pharmaceutically acceptable excipient. For preparing a pharmaceutical composition from a compound of the present invention, pharmaceutically acceptable excipients can be either solid or liquid. An excipient can be one or more substances which may act as, e.g., a carrier, diluent, flavoring agent, binder, preservative, tablet disintegrating agent, or an encapsulating material. The pharmaceutical composition may contain two or more compounds of the present invention (e.g., two different salt forms of a compound of formula (I), may be used together in the same pharmaceutical composition). Preferably, the pharmaceutical composition contains a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt form thereof. In one embodiment, the composition contains an amount of a compound of formula (I) or a pharmaceutically acceptable salt form thereof effective to treat an atypical protein kinase C (aPKC)-dependent disorder or condition. Preferably, a compound of the present invention will cause a decrease in symptoms or disease indicia associated with an aPKC-dependent disorder as measured quantitatively or qualitatively. The

composition may also contain, in addition to a compound of formula (I) or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable excipient, another therapeutic compound, such as a compound useful in the treatment of cancer.

A compound of the present invention can be formulated as a pharmaceutical composition in any delivery form, such as a syrup, an elixir, a suspension, a powder, a granule, a tablet, a capsule, a lozenge, a troche, an aqueous solution, a cream, an ointment, a lotion, a gel, an emulsion, etc. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. Preferably, the pharmaceutical composition is a tablet or capsule. In one embodiment, the pharmaceutical composition is a tablet. In another embodiment, the pharmaceutical composition is a capsule.

In powders, the excipient may be a finely divided solid in a mixture with a finely divided active component (i.e., compound of the present invention). In tablets, the active component may be mixed with an excipient having the necessary binding properties in suitable proportions and compacted in the shape and size desired. Suitable excipients include magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, low melting wax, cocoa butter, and the like.

The pharmaceutical composition preferably contains from 1% to 95% (w/w) of the active compound (i.e., compound of the present invention). More preferably, the pharmaceutical composition contains from 5% to 70% (w/w) of the active compound.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides or cocoa butter, may be melted and the active component dispersed homogeneously therein, as by stirring. The molten homogeneous mixture may then be poured into convenient sized molds, allowed to cool, and thereby to solidify.

Liquid form preparations include solutions, suspensions, and emulsions. Formulations suitable for parenteral administration, such as, for example, by intravenous, intramuscular, intradermal, and subcutaneous routes, include aqueous and non-aqueous, isotonic sterile injection solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and nonaqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. In the practice of this invention, compositions can be administered, for example, by intravenous infusion, orally, topically,

intraperitoneally, intravesically or intrathecally. The formulations of compounds can be presented in unit-dose or multi-dose sealed containers, such as ampoules and vials. Injection solutions and suspensions can be prepared from sterile powders, granules, and tablets of the kind previously described.

A compound of the present invention, alone or in combination with other suitable components, can be made into aerosol formulations (e.g., they can be "nebulized") to be administered via inhalation. Aerosol formulations can be placed into pressurized acceptable propellants, such as dichlorodifluoromethane, propane, nitrogen, and the like.

Pharmaceutically acceptable excipients are determined in part by the particular composition being administered, as well as by the particular method used to administer the composition. Accordingly, there is a wide variety of suitable formulations of pharmaceutical compositions of the present invention (see, e.g., *Remington: The Science and Practice of Pharmacy*, 20th ed., Gennaro et al. Eds., Lippincott Williams and Wilkins, **2000**).

The quantity of active component in a pharmaceutical composition may be varied or adjusted from, e.g., 1 mg to 1,000 mg, 5 mg to 500 mg, 10 mg to 300 mg, or 25 mg to 250 mg, according to the particular application and the desired size of the dosage form.

The dose administered to a subject is preferably sufficient to induce a beneficial therapeutic response in the subject over time. The beneficial dose can vary from subject to subject depending upon, e.g., the subject's condition, body weight, surface area, and side effect susceptibility. Administration can be accomplished via single or divided doses.

IV. Method of Treatment

In another aspect, the present invention provides a method of treating an aPKC-dependent disorder or condition in a subject comprising: administering to the subject a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in treating an aPKC-dependent disorder or condition in a subject. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in the preparation of a medicament for treating an aPKC-dependent disorder or condition in a subject. Preferably, the compound is administered to the subject as a pharmaceutical

composition comprising a pharmaceutically acceptable excipient. Preferably, the compound is administered to the subject in a pharmaceutically acceptable amount. In one embodiment, the aPKC-dependent condition or disorder is cancer. In another embodiment, the aPKC-dependent condition is selected from non-small cell lung cancer (NSCLC), squamous cell carcinoma (e.g., oesophageal squamous cell carcinoma), leukaemia, prostate cancer, non-Hodgkin's lymphoma (e.g., follicular lymphoma), endometrial cancer, lung cancer and breast cancer.

The aPKC-dependent disorder or condition can be treated prophylactically, acutely, or chronically using compounds of the present invention, depending on the nature of the disorder or condition. Typically, the subject in each of these methods is human, although other mammals can also benefit from the administration of a compound of the present invention.

In another embodiment, the present invention provides a method of treating a proliferative disorder in a subject, comprising administering to the subject a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in treating a proliferative disorder in a subject. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in the preparation of a medicament for treating a proliferative disorder in a subject. Preferably, the compound is administered to the subject in a pharmaceutical composition comprising a pharmaceutically acceptable excipient. Preferably, the compound is administered to the subject in a pharmaceutically acceptable amount. In certain embodiments, the proliferative disorder is aPKC-dependent. In certain embodiments, the proliferative disorder is cancer. In certain embodiments, the proliferative disorder is selected from non-small cell lung cancer (NSCLC), squamous cell carcinoma (e.g., oesophageal squamous cell carcinoma), leukaemia, prostate cancer, non-Hodgkin's lymphoma (e.g., follicular lymphoma), endometrial cancer, lung cancer and breast cancer.

The proliferative disorder can be treated prophylactically, acutely, or chronically using a compound of the present invention, depending on the nature of the disorder or condition. Typically, the subject in each of these methods is human, although other mammals can also benefit from the administration of a compound of the present invention.

In therapeutic applications, the compounds of the present invention can be prepared and administered in a wide variety of oral and parenteral dosage forms. Thus, the compounds of the present invention can be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, or intraperitoneally. Also, the compounds described herein can be administered by inhalation, for example, intranasally. Additionally, the compounds of the present invention can be administered transdermally. In another embodiment, the compounds of the present invention are delivered orally. The compounds can also be delivered rectally, bucally or by insufflation.

Determination of the proper dosage for a particular situation is within the skill of the practitioner. Generally, treatment is initiated with smaller dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day, if desired. A typical dose is about 1 mg to about 1,000 mg per day, such as about 5 mg to about 500 mg per day. In certain embodiments, the dose is about 10 mg to about 300 mg per day, such as about 25 mg to about 250 mg per day.

V. Chemistry

Abbreviations

For convenience, the following common abbreviations are used herein:

LCMS for Liquid Chromatography-Mass Spectrometry.

HPLC for High Pressure Liquid Chromatography.

NMR for Nuclear Magnetic Resonance.

RT for Retention Time.

MI for Molecular Ion

h for hours

min for minutes

$AlCl_3$ for aluminium chloride

BBr_3 for boron tribromide

Boc for *tert*-butoxycarbonyl

cataCXium C for trans-Bis(acetato)bis[o-(di-o-tolylphosphino)benzyl] dipalladium(II).

Cs_2CO_3 for cesium carbonate

CuI for copper(I)iodide

DAST for diethylaminosulfur trifluoride

DBU for 1,8-diazabicyclo(5.4.0)undec-7-ene

DMAP for 4-(dimethylamino) pyridine

DCE for 1,1-dichloroethane or ethylidene chloride

DCM for dichloromethane or methylene chloride

DEA for diethanolamine

DIPEA for *N*,*N*,-di-isopropyethylamine, Hunig's base

DMA for *N*,*N*-dimethylacetamide

DMF for *N*,*N*-dimethylformamide

DMSO for dimethylsulfoxide.

Et_3N for triethylamine

EtOH for ethyl alcohol, ethanol

Ex for example

HCl for hydrochloric acid

H_2SO_4 for sulfuric acid

Int for intermediate

KOH for potassium hydroxide

MW for microwave

mCPBA for meta-Chloroperoxybenzoic acid

MeOH for methyl alcohol, methanol

$Mo(CO)_6$ for Molybdenum hexacarbonyl

MP-BH_4 for macroporous triethylammonium methyl polystyrene borohydride

NaOH for sodium hydroxide

Na_2CO_3 for sodium carbonate

Na_2SO_4 for sodium sulphate

NaOAc for sodium acetate

NaOtBu for sodium t-butoxide

NMP for 1-methyl-2-pyrrolidinone

NMM for N-methylmorpholine

$Pd(dba)_2$ for Bis(dibenzylideneacetone)palladium

$Pd(OAc)_2$ for Palladium diacetate

$Pd(Ph_3)_4$ for tetrakis(triphenylphosphine)palladium

$Pd(PPh_3)_2Cl_2$ for Bis(triphenylphosphine)palladium(II) dichloride

$POCl_3$ for phosphorus oxychloride

PPh_3 for triphenylphosphine

PS-TsCl for polystyrene sulfonyl chloride

PS-PPh_3-Pd for polystyrene triphenylphosphine-Pd(0)

SCX-2 for a silica-based sorbent with a chemically bonded propylsulfonic acid functional group

TBAF for Tetra-n-butylammonium fluoride

TBDMS for tert-butyldimethylsilyl

TCA for trichloroacetic acid

TFA for trifluoroacetic acid

THF for tetrahydrofuran

TMS azide for trimethylsilyl azide

Xantphos for 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene

XPhos for 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl

LCMS Methods

Samples analysed by High Performance Liquid Chromatography-Mass Spectrometry employed the following conditions. Unless otherwise noted, Method X was utilized.

Method 1

Method 1 employed Gilson 306 pumps, Gilson 811C mixer, Gilson 806 manometric module, and Gilson UV/VIS 152 detector at 254 nm wavelength. The mass spectrometer was a Finnigan AQA and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 4.60 mm. The injection volume was 10 μl. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 1.5 mL/min, using 95% water: 5% acetonitrile, changed linearly to 5% water: 95% acetonitrile over 5.5 minutes and then maintained at this mixture for 2 minutes.

Method 2

Method 2 employed Waters 515 pumps, a Waters 2525 mixer and a Waters 2996 diode array detector. The detection was performed between 210 nm and 650 nm. The mass

spectrometer was a Waters micromass ZQ and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 4.60 mm. The injection volume was 10 μl. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 1.5 mL/min, using 95% water: 5% acetonitrile, changed linearly to 5% water: 95% acetonitrile over 5.5 minutes and then maintained at this mixture for 2 minutes.

Method 3

Method 3 employed Waters 515 pumps, a Waters 2525 mixer and a Waters 2487 UV detector (single wavelength 254 nm). The mass spectrometer was a Waters micromass ZQ and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 4.60 mm. The injection volume was 10 μl. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 1.5 mL/min, using 95% water: 5% acetonitrile, changed linearly to 5% water: 95% acetonitrile over 5.5 minutes and then maintained at this mixture for 2 minutes.

Method 4

Method 4 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2996 diode array detector. The detection was performed between 210 nm and 650 nm. The mass spectrometer used was a Waters 3100 which detected masses between 100 and 700 g/mol. The column used was a XBridge, 5 micron pore size, C18, 50x4.60 mm.The injection volume was 10 μl of a solution (around 1mg/ml). The flow rate was 1.5 mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide) (3 ml/10l) and acetonitrile 0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 95% water: 5% acetonitrile ramping up to 5% water:95% acetonitrile over 5.50 minutes. The eluent level was returned to the starting conditions of 95% water: 5% acetonitrile over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 5

Method 5 employed Waters 515 pumps, a Waters 2525 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254 nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a SunFire, 5 micron pore size, C18 column of dimensions 50x4.60 mm was used. The injection volume was 10μL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water and methanol

contained 0.1% formic acid. The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5 minutes, these conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 6

Method 6 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2996 diode array detector. The detection was done between 210 nm and 650 nm. The mass spectrometer used was a Waters 3100 which detected masses between 100 and 700g/mol. The column used was a XBridge, 5 micron pore size, C18 ,50x4.60 mm. The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide) (3 ml/10l) and methanol0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5 minutes. These conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 7

Method 7 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a SunFire, 5 micron pore size, C18 column of dimensions 50x4.60 mm was used. The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water and methanol contained 0.1% formic acid. The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5minutes., these conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 8

Method 8 employed Waters 515 pumps, a Waters 2525 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a SunFire, 5 micron pore size, C18 column of dimensions 50x4.60 mm was used. The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water and methanol contained 0.1% formic acid. The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 3 minutes., these conditions were held for 2.5 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected.The run lasted 7 minutes in total.

Method 9

Method 9 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a XBridge, 5 micron pore size, C18 ,50x4.60 mm.The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide) (3 ml/10l)and methanol0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5 minutes. These conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected.The run lasted 7 minutes in total.

Method 10

LCMS results were obtained on either of two instruments. LCMS analysis was performed on a Waters Aquity Ultra Performance LC with a 2.1 mm x 50 mm Waters Aquity UPLC BEH C18 1.7 µm column. The target column temperature was 45°C, with a run time of two (2) minutes, a flow rate of 0.600 mL/min, and a solvent mixture of 5% (0.1% formic acid/water):95% (acetonitrile/0.1% formic acid). The mass spectrometry data was acquired on a Micromass LC-ZQ 2000 quadrupole mass spectrometer. Alternatively, LCMS analysis was performed on a Bruker Esquire 200 ion trap.

Preparative HPLC Methods

Samples purified by Mass Spectrometry directed High Performance Liquid Chromatography employed the following conditions.

Method A

Method A employed Waters 515 pumps, a Waters 2525 mixer and a Waters 2487 UV detector (single wavelength 254 nm). The mass spectrometer was a Waters micromass ZQ and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 19mm. The injection volume was up to 500 μL of solution at a maximum concentration of 50 mg/mL. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 25 mL/min using 95% water, 5% acetonitrile, changing linearly over 5.3 minutes to 95% acetonitrile, 5% water, and maintaining for 0.5 minutes.

Method B

Method B employed Waters 515 pumps a Waters 2545 mixer with valves directing to the different columns and a Waters 2996 diode array detector. The detection was performed between 210 nm and 650 nm. The mass spectrometer used was a Waters 3100 which detected masses between 100 and 700 g/mol. The column used was a XBridge, 5 micron pore size, C18, 50x19 mm. The injection volume was chosen by the user and can be up to 500μL of the solution (max 50mg/mL). The flow rate was 25mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide (3 ml/10l)and acetonitrile 0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 95% water:5% acetonitrile ramping up to 5% water:95% acetonitrile over 5.30 minutes. The eluent level was returned to the starting conditions of 95% water: 5% acetonitrile over 0.6 minutes. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

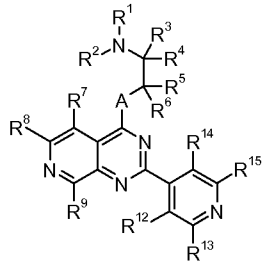
Analytical HPLC Methods

Method X

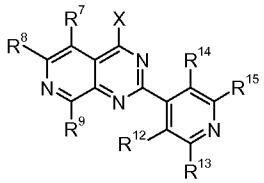
Method X employs gradient elution (0 to 100%) acetonitrile (containing 0.1% trifluoroacetic acid):water (containing 0.1% trifluoroacetic acid) over five minutes on a 4.6 X 75 mm (2.5 micron) Zorbax XDB-C8 column at 2.5 ml/min on an Agilent 1100 series HPLC.

Synthesis

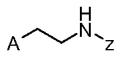
Several methods for the chemical synthesis of 4-substituted-2-(pyridin-4-yl)-azaquinazoline compounds (for convenience, collectively referred to herein as "4PAZ compounds") of the present invention are described herein. These and/or other well known methods may be modified and/or adapted in known ways in order to facilitate the synthesis of additional compounds within the scope of the present invention.



[F-001]



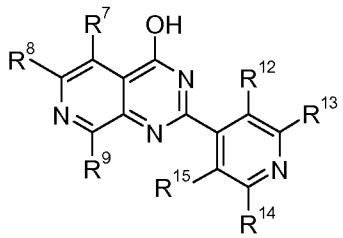
[F-002]



[F-003]

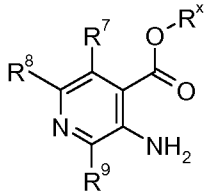
In one approach, 4PAZ compounds of general formula [F-001] (where A = NH or N alkyl) are prepared by reacting a compound of formula [F-002] (where X is a halogen such as chlorine or a sulfonate) with a compound of formula [F-003] (where A is NH or NH2 and Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) in a suitable solvent such as DMF in the presence of a suitable base such as triethylamine. The reaction is suitably conducted at an elevated temperature for example 40 °C. Where Z is a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc, compounds of formula [F-001] are prepared by a suitable deprotection reaction. For example: where Z is a Boc protecting group reaction with an acid such as TFA in a suitable solvent such as DCM. The reaction is suitably conducted at ambient temperature. In one approach, compounds of formula [F-001] (where A = O) are prepared by reacting a compound of formula [F-002] (where X is a halogen such as chlorine or sulfonate) with a

compound of formula [F-003] (where A is OH and Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) in a suitable solvent such as DMA in the presence of a suitable base such as sodium hydride. The reaction is suitably conducted at ambient temperature. Where Z is a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc, compounds of formula [F-001] are prepared by a suitable deprotection reaction. For example: where Z is a Boc protecting group reaction with an acid such as TFA in a suitable solvent such as DCM. The reaction is suitably conducted at ambient temperature.

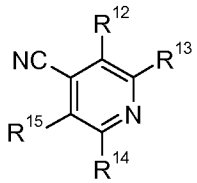


[F-004]

In one approach, compounds of formula [F-002] (where X is a halogen such as chlorine) are prepared by reacting a compound of formula [F-004] with a suitable halogenating agent such as phosphorous oxychloride. The reaction is suitably conducted at elevated temperature such as 125 °C. Compounds of formula [F-002] (where X is a sulfonate) are prepared by reacting a compound of formula [F-004] with a suitably substituted sulfonyl chloride in a suitable solvent such as DMA in the presence of a suitable base such as triethylamine and a catalytic amount of DMAP. The reaction is suitably conducted at ambient temperature.



[F-005]

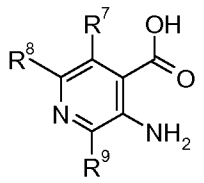


[F-006]

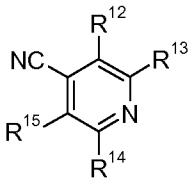
In one approach, compounds of formula [F-004] are prepared by reacting a compound of formula [F-005] (where Rx is an alkyl group such as methyl or ethyl) with a compound of formula [F-006] in a suitable solvent in a dry non-aprotic solvent such as dioxane or THF in

the presence of a hindered alkoxide base such as potassium-tert-pentylate 1.7M in toluene or potassium-tert-butoxide. The reaction is suitably conducted at ambient temperature.

In one approach, compounds of formula [F-004] are prepared by reacting a compound of formula [F-007] with a compound of formula [F-006] in a suitable solvent in a protic solvent such as methanol in the presence of a base such as sodium methoxide. The reaction is suitably conducted first at ambient temperature then at reflux overnight.



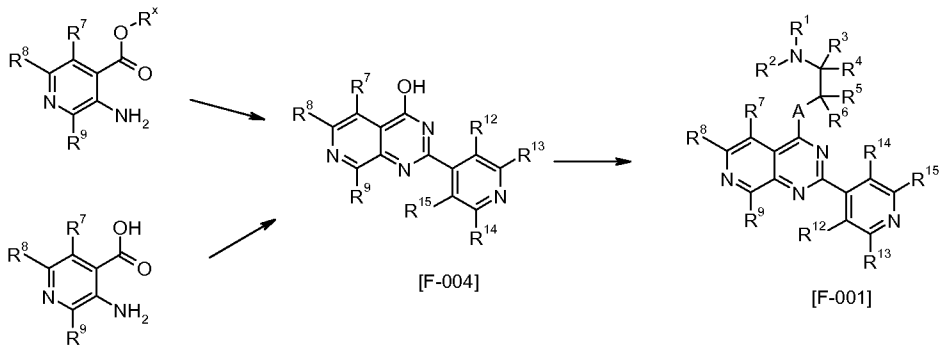
[F-007]



[F-006]

An example of a method as described above is illustrated in the following scheme.

[F-005]



[F-007]

[F-004]

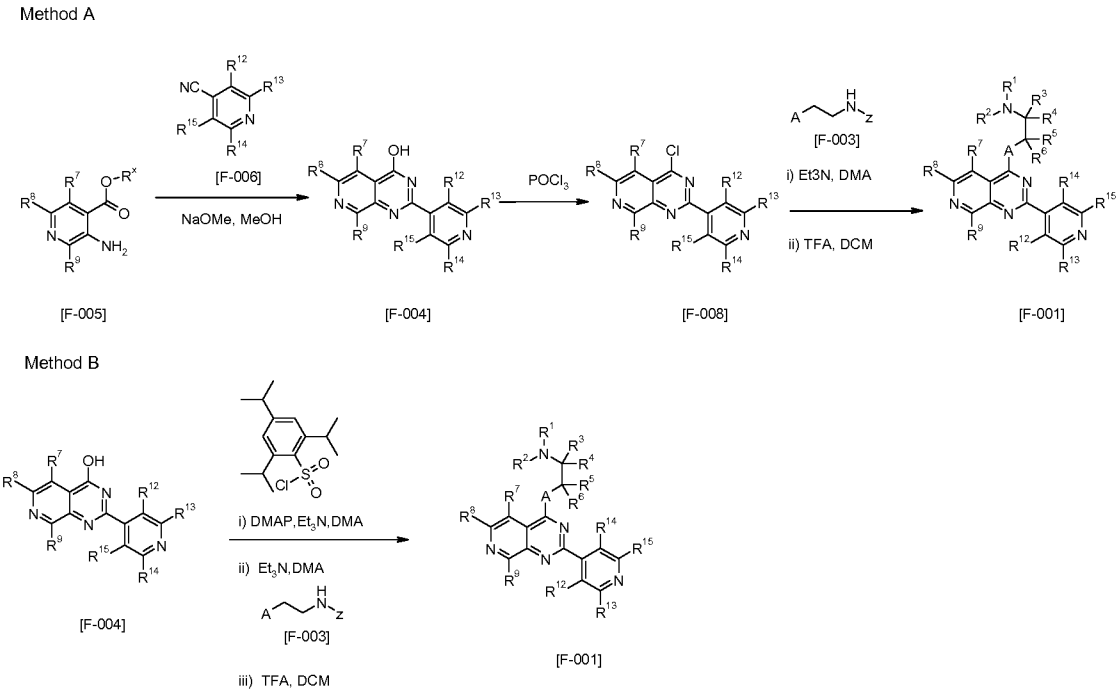
[F-001]

General synthesis of 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A1

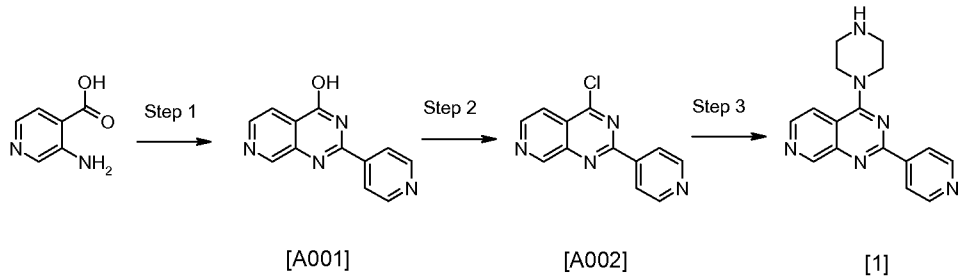
Substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-001] were prepared by the reaction of a 2-amino-pyridyl derivative of general formula [F-005] with a 4-cyanopyridyl derivative of general formula [F-006] in the presence of a base such as sodium methoxide in a polar aprotic solvent such as methanol. The reaction is suitably conducted at elevated temperature to yield the cyclised 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol product of general formula [F-004]. 4-substituted-1-yl-2-pyridin-4-yl-

pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride to yield 4-chloro-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-008] which were reacted with primary or secondary amino derivative of general formula [F-003], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-003], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC

Scheme A1



Synthesis of 4-Piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [1] Method A



Synthesis of 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [A001]

A mixture of 4-Cyanopyridine (8.25 g, 79.2 mmol), sodium methoxide (891 mg, 16.5 mmol) and methanol (400 mL) was stirred at room temperature for 60 minutes. 3-Amino-isonicotinic acid (9.12g, 66.0 mmol) was added and the mixture heated to reflux for 3 days. After cooling to room temperature the solid precipitate was collected by filtration then dried in the vacuum oven to yield the title compound as an off-white solid (6.02 g): (1H, 300MHz, d6-dmso) 13.10 (1H, br s), 9.16 (1H, s), 8.80 (2H, dd), 8.70 (1H, d), 8.10 (2H, dd), 8.00 (1H, dd)

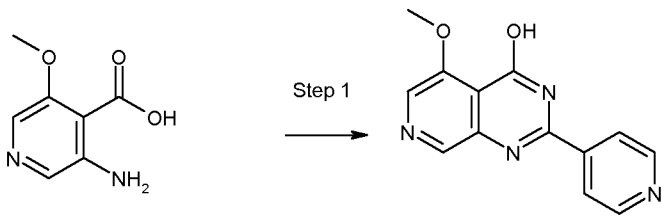
Synthesis of 4-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [A002]

2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [A001] (4 g, 17.8 mmol) in $POCl_3$ (50 mL, 538 mmol) was heated to 110°C for 3 hours. The reaction mixture was concentrated under vacuum, quenched with saturated $NaHCO_3$ solution, extracted into DCM, washed with water then brine, passed through a phase separator cartridge and evaporated to yield the title compound [A002] (2.6 g) as a yellow / brown solid which was used without further purification: LCMS method: 1, RT:4.09 min, MI 243 [M+H].

Synthesis of 1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [1]

A solution of 4-Chloro-2-pyridin-4-yl-pyrido[3,4- d]pyrimidine [A002] (100 mg, 0.43 mmol), piperazine (172mg, 2 mmol) in anhydrous DMA (5 mL) was stirred at room temperature for 3 days. The reaction mixture was partitioned between NaOH (2M aqueous solution) and ethyl acetate. The organic layer was further washed with water then brine, dried ($MgSO_4$), passed through a phase separator cartridge and evaporated to yield the crude material, which was purified by preparative HPLC (method A) to yield the title compound (1.87mg). LCMS method: 1, RT:3.49 min, MI 293 [M+H]; 1H-NMR (300MHz; DMSO-d6): 9.26 (1H, s), 8.76 (2H, d), 8.58 (1H, d),8.32 (2H, d), 8.24 (1H, s), 7.92 (1H, d), 3.96 (4H, br tr), 2.99 (4H, br tr)

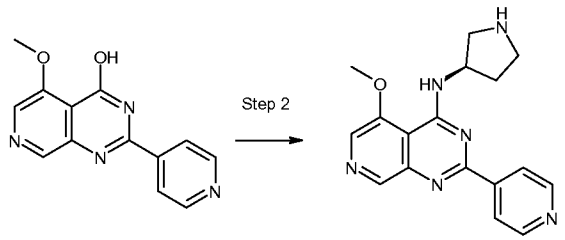
Synthesis of (5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine [2] method B



[A003]

Synthesis of 5-Methoxy-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A003]

To a stirred solution of 2-chloro-4-pyridinecarbonitrile (1g, 9.6 mmol) in MeOH (20 mL) was added 0.5 M NaOMe (2 mmol, 4 mL) followed by 3-Amino-5-methoxy-isonicotinic acid (1.35g, 8 mmol). The RM was heated at 75° C over night. The RM was left to cool and a solid ppt formed which was collected by filtration, washed with cold MeOH and dried in a vac oven to give the title compound as a pale brown solid (610 mg, 30% yield). LCMS method: 1, RT:3.82 min, MI 255.09 [M+H].



[A003] [2]

Synthesis of (5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine [2]

5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4- [A003] (0.157 mmol, 0.04 g), 2,4,6-triisopropylbenzenesulfonyl chloride (0.173 mmol, 0.052 g), were dissolved in anhydrous DMA (2mL), and Et_3N (0.314mmol, 0.045 mL), and DMAP (5mg) were added sequentially. The mixture was stirred at room temperature for 1 hour and (R)-3-amino-pyrrolidine-1-carboxylic acid tert-butyl ester (0.236 mmol, 0.044 g) was added. The mixture was stirred at room temperature overnight. The solvent was then removed under reduced pressure and the residue was stirred in trifluoroacetic acid (1 mL) at room temperature for 3h. The solution was poured on to an SCX-2 cartridge (5 g), washed with methanol (10 mL) and then washed with ammonia (2N in methanol, 2 0mL). The ammonia washes were concentrated in vacuo to a brown residue that was purified by preparative HPLC (method A) to yield the title compound (0.016g). LCMS method: 1, RT:1.47 min, MI 323 [M+H]; 1H-NMR 300 MHz (1H d6-dmso) 8.81 (1H, s), 8.76 (2H, dd), 8.35 (1H, s), 8.32 (2H, dd), 8.23 (1H, d), 6.42 (1H, s), 4.98 (1H, m), 4.14 (3H, s), 3.19-3.07 (2H, m), 2.41-2.29 (2H, m), 2.07-1.95 (2H, m).

Synthesis of 2-(3-Fluoro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [A004]

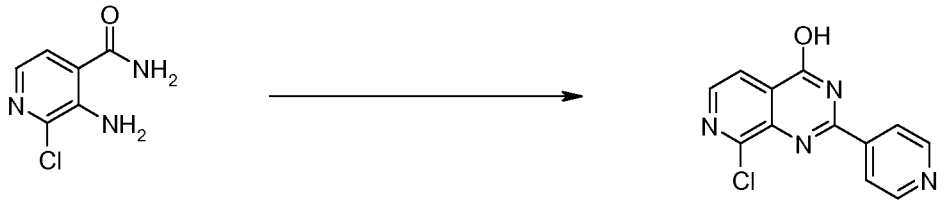
[A004]

2-(3-Fluoro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [A004]

3-Amino-2-chloro-isonicotinamide (0.5 g, 3.64 mmol), 3-Fluoroisonicotinaldehyde (0.54 g, 4.37 mmol), NaHSO3 (0.75 g, 7.29 mmol) and DMA (5 mL) were added successively to a microwave vial. The vial was sealed then heated at 160°C for 6min. Water (10 mL) was

added and the resulting solid was filtered and used without further purification. LCMS method: 1, RT:3.07 min, MI 243 [M+H]

Synthesis of 8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A005]

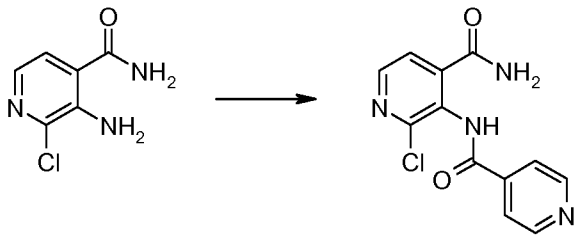


[A005]

8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A005]

A solution of 3-Amino-2-chloro-isonicotinamide (0.5 g, 2.91 mmol) and 4-Pyridinecarboxaldehyde (0.35 g, 3.32 mmol) in DMA (10mL) was heated under microwave (100°C, 2h). Sodium hydrogen sulfite (0.606 g, 5.83 mmol) was then added and the mixture was heated under microwave (150°C, 1h). Water was then added to the mixture and the resulting solid (0.34 g, 45%) was collected, washed with water and then by MeOH. LCMS method: 1, RT:3.89 min, MI 258 [M+H]

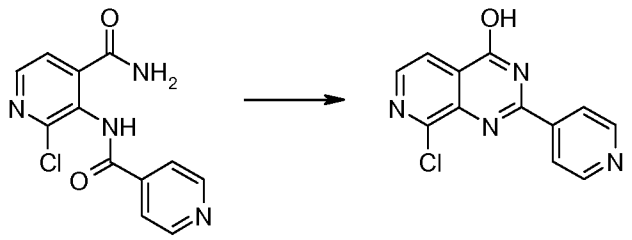
Synthesis of 8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A005]



[A006]

Synthesis of 2-Chloro-3-[(pyridine-4-carbonyl)-amino]-isonicotinamide [A006]

To a suspension of 3-Amino-2-chloro-isonicotinamide (0.5 g, 2.913 mmol) and K_2CO_3 (1g, 7.28mmol) in refluxing Et_2O (25 mL), Isonicotinoyl chloride hydrochloride (0.622 g, 3.5 mmol) was added portionwise. The mixture was stirred under reflux for 4h. The solvent was removed under reduced pressure and water (50 mL) was added. The resulting solid was filtered, washed with H_2O and then collected, dried with an azeotrope with toluene, to yield the title compound (0.78 g, 96 %) which was used without further purification. LCMS method: 1, RT:2.55 min, MI 277 [M+H]

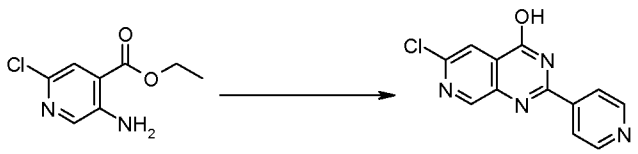


[A006] [A005]

Synthesis of 8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A004]

To a solution of 2-Chloro-3-[(pyridine-4-carbonyl)-amino]-isonicotinamide [A006] (0.2 g, 0.723 mmol) in MeOH (20 mL) was added a solution of cesium carbonate (0.47 g, 1.44 mmol) in H_2O (2 mL). The mixture was stirred at room temperature overnight. The MeOH was removed under reduced pressure and water (10 mL) was added. Acetic acid was added slowly and the resulting solid was collected, dried with a toluene azeotrope to yield the title compound which was used without further purification. LCMS method: 1, RT:3.43 min, MI 259 [M+H]

Synthesis of 6-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A007]

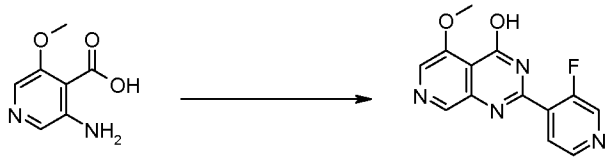


[A007]

6-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A007]

A solution of potassium pentoxide (2.6 mL, 5.1 mmol, 25% soln in Toluene) was added dropwise (~0.5mL/min) to a solution of 5-Amino-2-chloro-isonicotinic acid ethyl ester (0.4 g, 2 mmol) and 4-cyanopyridine (0.25 g, 2.4 mmol) in anhydrous THF (5 mL) cooled in an ice bath. The reaction was allowed to warm to RT and left to stir at room temperature overnight. Water (9 mL) was added and the mixture was stirred at RT for 20 mins. Acetic acid (~1mL) was then added and the mixture was left to stir at RT and the resulting yellow precipitate was filtered and the siolid washed with deionised water (2x 3mL). To give the title compound (0.43g, 83% yield). LCMS method: 1, RT: 2.21 min, MI 259 [M+H]

Synthesis of 2-(3-Fluoro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [A008]

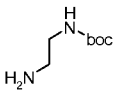
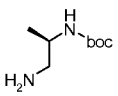
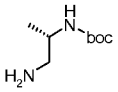
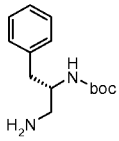


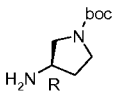
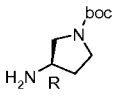
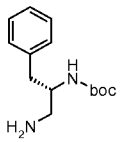
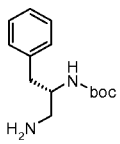
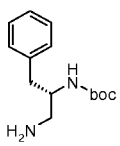
[A008]

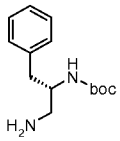
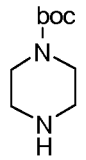
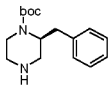
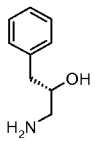
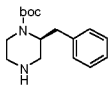
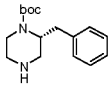
2-(3-Fluoro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [A008]

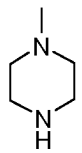
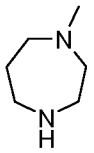
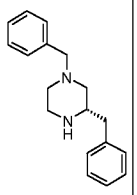
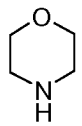
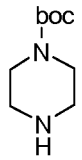
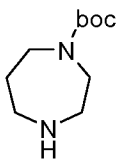
To a stirred solution of 3-Fluoroisonicotinonitrile (0.088 g, 0.71 mmol) in MeOH (5 mL) was added NaOMe (0.008 g, 0.15 mmol). After 1hr 3-amino-5-methoxy-isonicotinic acid (0.1 g, 0.54 mmol) was added and the RM heated to 85 °C for 18hr. The solution became yellow in colour. The reaction mixture was alloed to cool to RT and the white solid was collected by filtration and washed with MeOH to yield the title compound (0.07g, 43% yield). LCMS method: 1, RT:1.19 min, MI 271.24 [M+H]

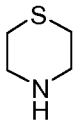
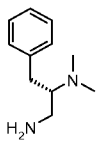
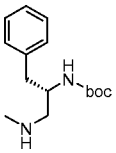
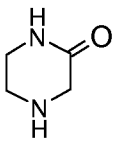
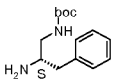
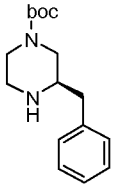
The following compounds were synthesised according to the general synthesis shown in scheme [A1]:

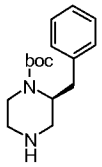
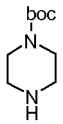
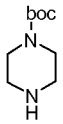
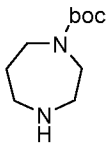
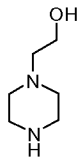
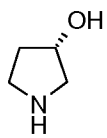
Ex	Pre-cursor	Met-hod	Amine [F-003]	Analysis		Name
				LCMS	NMR	
3	[A001]	A		Method 1: RT: 2.2 min, MI: 267 [M+H]		N-(2-aminoethyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
4	[A001	A		Method 1: RT:2.45 min, MI , 281 [M+H]		N-[(2R)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
5	[A001]	A		Method 1: RT: 2.52 min, MI, 281 [M+H]		N-[(2S)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
6	[A001]	B		Method 1: RT: 2.51 min, MI, 357 [M+H]	(1H, 300MHz, d6-dmso); 9.15ppm (1H, d), 8.70ppm (2H, d), 8.62ppm (2H, d), 8.20ppm (1H, d), 8.12ppm (2H, d), 7.35-7.26ppm	N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-

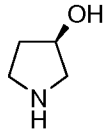
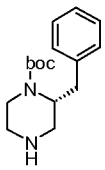
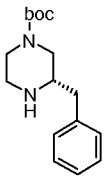
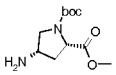
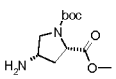
					(5H, m), 3.86ppm, (1H, d), 3.35ppm (2H, m), 2.27ppm (2H, m)	d]pyrimidin-4-amine
7	[A001]	B		Method 1: RT: 0.88 min, MI, 293 [M+H]	(1H, 300MHz, d6-dmso), 9.18 (1H, s), 8.94-8.90 (1H, m), 8.76 (2H, dd), 8.65 (1H, d), 8.35 (2H, dd), 4.94-4.85 (1H, m), 3.87-3.74 (3H, m), 3.19-3.07 (2H, m), 2.30-2.18 (2H, m), 2.02-1.92 (2H, m)	(3R)-N-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
8	[A004]	B		Method 1: RT: 0.5 min, MI, 311 [M+H]	(1H, 300MHz, d6-dmso), 9.47 (1H, brd), 9.15 (1H, s), 8.71 (1H, d), 8.66 (1H, d), 8.57 (1H, d), 8.47 (1H, s), 8.39 (1H, d), 8.08 (1H, dd), 4.92 (1H, br s), 3.46 (1H, dd), 3.34-3.22 (2H, m), 2.30-2.20 (1H, m), 2.18-2.08 (1H, m)	(3R)-N-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
9	[A003]	B		Method 1: RT: 2.92 min, MI, 387 [M+H]	(1H, 300MHz, d6-dmso); 8.72 (1H, s), 8.68 (2H, d), 8.28 (1H, s), 8.00 (2H, d), 7.39-7.30 (5H, m), 4.00 (3H, s), 3.96-3.91 (1H, m), 3.59 (2H, br s), 3.00 (1H, dd), 2.79 (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
10	[A004]	B		Method 1: RT: ,2.95 min MI, 375 [M+H]	(1H, 300MHz, d6-dmso), 9.12 (1H, s), 8.69 (1H, d), 8.53 (1H, d), 8.46 (1H, S), 8.21 (1H, d), 7.83 (1H, dd), 7.28-7.19 (5H, m), 3.81 (1H, dd), 3.66-3.49 (2H, m), 2.90 (1H, dd), 2.80 (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
11	[A005]	B		Method 1: RT: 2.98 min, MI: 392 [M+H]	(1H, 300MHz, d6-dmso), 8.70 (2H, d), 8.40 (1H, d), 8.36 (1H, br s), 7.98 (2H, d), 7.43-7.32 (5H, m), 3.97 (1H, d), 3.69-3.54 (2H, m), 3.06 (1H, dd), 2.84 (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

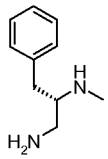
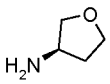
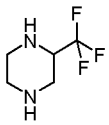
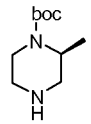
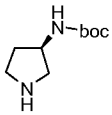
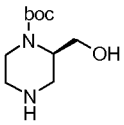
12	[A007]	A		Method 1: RT: 6.51 min , MI: 391 [M+H]	(1H, 300MHz, d6-dmso) 9.06 (1H, s), 8.69 (2H, dd), 7.98 (2H, dd), 7.87 (1H, s), 7.42-7.27 (5H, m), 4.54 (1H, dd), 4.37 (1H, d), 3.58-3.48 (1H, m), 3.04-2.93 (3H, m), 2.85-2.59 (3H, m)	N-[(2S)-2-amino-3-phenylpropyl]-6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
13	[A007]	A		Method 1: RT: 4.35 min , MI: 327 [M+H]	(300MHz, 1H, d6-dmso) 9.20 (1H, s), 8.79 (2H, d), 8.35 (2H, d), 8.13 (1H, s), 6.61 (1H, s), 4.15 (4H, br s), 3.33 (4H, br s)	1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
14	[A007]	A		Method 1: RT: 2.91 min, MI: 443.9 [M+H]	(300MHz, 1H, d6-dmso) 9.06 (1H, s), 8.69 (2H, dd), 7.98 (2H, dd), 7.87 (1H, s), 7.41-7.29 (5H, m), 4.54 (1H, dd), 4.37 (1H, d), 3.53 (1H, dt), 3.03-2.93 (3H, m), 2.85-2.57 (3H, m)	(3S)-3-benzyl-1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
15	[A001]	A		Method 1: RT: 4.30 min , MI: 358 [M+H]	(300MHz, 1H, d4-MeOH) 8.55 (d, 1H), 8.22 (dd, 2H), 8.03 (dd, 1H), 7.76 (m, 5H), 4.28 (m, 1H), 4.09 (1H, dd), 3.58 (1H, dd), 2.96 (1H, dd), 2.88 (1H, dd)	(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-ol
16	[A001]	A		Method 1: RT: 2.44 min , MI: 383 [M+H]	(1H, 300MHz, $CDCl_3$) 9.34 (s, 1H), 8.73 (d, 2H), 8.46 (d, 1H), 8.21 (d, 2H), 7.49 (d, 1H), 7.33 (m, 3H), 7.25 (d, 2H), 4.58 (d, 1H), 4.48 (d, 1H), 3.46 (t, 1H), 3.02 (m, 4H), 2.76 (m, 2H)	(3S)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
17	[A001]	A		Method 1: RT: 2.45 min , MI: 383 [M+H]	(1H, 300MHz, $CDCl_3$) 9.34 (s, 1H), 8.73 (d, 2H), 8.46 (d, 1H), 8.21 (d, 2H), 7.49 (d, 1H), 7.33 (m, 3H), 7.25 (d, 2H), 4.58 (d, 1H), 4.48 (d, 1H), 3.46 (t, 1H), 3.02 (m, 4H), 2.76 (m, 2H)	(3R)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

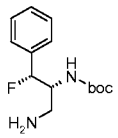
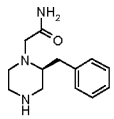
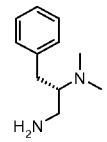
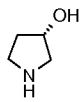
18	[A001]	A		Method 1: RT: 3.99 min , MI: 307 [M+H]	(1H, 300MHz, d6-dmso) 9.26 (1H, s), 8.75 (2H, dd), 8.58 (1H, d), 8.31 (2H, dd), 7.91 (1H, d), 3.98-3.96 (4H, m), 2.55-2.52 (4H, m), 2.25 (3H, s)	1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
19	[A001]	A		Method 1: RT: 4.00 min , MI: 321 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.75 (2H, dd), 8.52 (1H, d), 8.29 (2H, dd), 7.98 (1H, d), 4.13-4.06 (4H, m), 2.85-2.83 (2H, m), 2.55-2.51 (2H, m), 2.26 (3H, s), 2.10-2.03 (2H, m)	1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane
20	[A001]	A		Method 1: RT: 4.29 min , MI: 473 [M+H]	(1H, 300MHz, $CDCl_3$) 9.31 (s, 1H), 8.75 (d, 2H), 8.47 (d, 1H), 8.30 (d, 2H), 7.49 (d, 1H), 7.36 (m, 5H), 7.02 (m, 5H), 5.02 (s, 1H), 4.30 (d, 1H), 3.90 (td, 1H), 3.62 (d, 1H), 3.45 (d, 1H), 3.26 (m, 2H), 3.04 (d, 1H), 2.92 (d, 1H), 2.35 (m, 2H)	(2S)-2,4-dibenzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
21	[A001]	A		Method 1: RT: 2.86 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.76 (2H, d), 8.59 (1H, d), 8.33 (2H, d), 7.97 (1H, d), 4.02-3.99 (4H, t), 3.83-3.80 (4H, t)	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine
22	[A001]	A		Method 1: RT: 4.76 min , MI: 349 [M+H]	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.77 (2H, dd), 8.60 (1H, d), 8.34 (2H, dd), 7.97 (1H, d), 4.03-4.00 (4H, m), 3.61 (4H, br s), 1.43 (9H, s)	tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxylate
23	[A001]	A		Method 1: RT: 4.18 min , MI: 407 [M+H]	(1H, 300MHz, d6-dmso) 9.22 (1H, s), 8.76 (2H, dd), 8.56 (1H, d), 8.30 (2H, dd), 8.08-8.03 (1H, m), 4.28-4.22 (2H, m), 4.15-4.10 (2H, m), 3.72-3.65 (2H, m), 3.42 (2H, br s), 2.09-1.97 (2H, m), 1.11 (4H, s), 0.93 (5H, s)	tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane-1-carboxylate

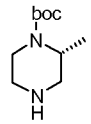
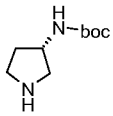
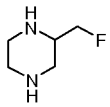
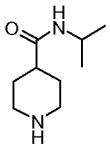
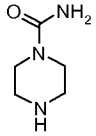
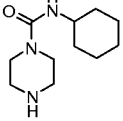
24	[A001]	A		Method 1: RT: 3.8 min , MI: 310 [M+H]	(1H, 300MHz, d6-dmso) 9.29 (1H, s), 8.76 (2H, dd), 8.60 (1H, d), 8.32 (2H, dd), 7.87 (1H, d), 4.23-4.20 (4H, m), 2.93-2.89 (4H, m)	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]thiomorpholine
25	[A001]	A	 [A009]	Method 1: RT: 2.34 min , MI: 385 [M+H]	(1H, 300MHz, d6-dmso) 9.13 (1H, s), 8.67 (2H, dd), 8.61 (1H, d), 8.15 (1H, d), 7.99 (2H, d), 7.37-7.26 (5H, m), 3.76 (2H, br s), 3.33-3.13 (1H, m), 3.07-2.88 (2H, m), 2.35 (6H, br s)	N,N-Dimethyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine
26	[A001]	A	 [A013]	Method 1: RT: 2.44 min , MI: 371 [M+H]	(1H, 300MHz, d6-dmso) 9.15 (1H, s), 8.77 – 8.75 (2H, m), 8.64 (1H, d), 8.30 – 8.28 (2H, m), 8.24 (1H, d), 7.32 – 7.29 (2H, m), 7.20 – 7.15 (2H, m), 7.09 – 7.04 (1H, m), 5.08 – 4.99 (1H, m), 3.11 – 2.87 (4H, m), 2.38 (3H, s).	N-[(2S)-2-amino-3-phenylpropyl]-N-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
27	[A001]	A		Method 1: RT: 2.21 min , MI: 307 [M+H]	1H NMR (d6-DMSO, 300MHz) 9.28 (1H, s), 8.77 (2H, d), 8.61 (1H, d), 8.34 (2H, d), 8.31 (1H, s), 8.03 (1H, d), 4.51 (2H, s), 4.18 (2H, t), 3.53-3.43 (2H, m).	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-one
28	[A001]	A		Method 1: RT: 2.44 min , MI: 357 [M+H]	-	N-[(2S)-1-amino-3-phenylpropan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
29	[A001]	A		Method 1: RT: 2.12 min, MI: 383.18 [M+H]	(1H, 300MHz, $CDCl_3$) 9.27 (s, 1H), 8.75 (d, 2H), 8.47 (d, 1H), 8.29 (d, 2H), 7.45 (d, 1H), 7.11 (m, 5H), 5.05 (m, 1H), 4.28 (d, 1H), 3.83 (dt, 1H), 3.23 (m, 3H), 3.09 (m, 2H), 3.01 (dt, 1H).	(2R)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

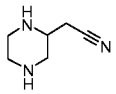
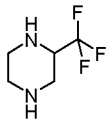
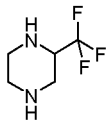
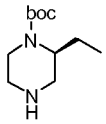
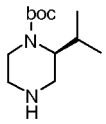
30	[A003]	B		Method 1: RT: 2.71 min, MI: 413.17 [M+H]	(1H, 500MHz, d6-dmso) 8.77 (s, 1H), 8.69 (d, 2H), 8.22 (s, 1H), 8.03 (d, 2H), 7.34 (m, 3H), 7.27 (d, 2H), 4.27 (m, 1H), 4.02 (m, 1H), 3.90 (s, 3H), 3.22 (t, 1H), 2.99 (m, 2H), 2.83 (t, 1H), 2.72 (dd, 1H), 2.63 (t, 1H), 2.62 (dd, 1H).	(3S)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
31	[A003]	B		Method 1: RT: 1.261 min , MI: 323.07 [M+H]	(1H, 300MHz, d6-dmso) 8.86 (1H, t), 8.78 – 8.76 (2H, m), 8.36 (1H, s), 8.32 – 8.30 (2H, m), 4.08 (3H, s), 3.75 (4H, m), 3.03 (4H, m).	1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
32	[A005]	B		Method 1: RT: 1.39 min , MI: 327 [M+H]	(1H, 300MHz, d6-dmso) 8.79 (d, 2H), 8.32-8.37 (m, 3H), 7.92 (d, 1H), 3.94 (brs, 4H), 2.95 (brs, 4H).	1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
33	[A001]	A		Method 1: RT: 3.92 min , MI: 307 [M+H]	(1H, 300MHz, d6-dmso) 9.21 (1H, s), 8.77 – 8.75 (2H, m), 8.54 (1H, d), 8.32 – 8.30 (2H, m), 8.00 (1H, d), 4.14 – 4.07 (4H, m), 3.15 – 3.12 (2H, m), 2.85 – 2.81 (2H, m), 2.04 – 1.97 (2H, m).	1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane
34	[A001]	A		Method 1: RT: 4.04 min , MI: 337 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.78 – 8.76 (2H, m), 8.60 (1H, d), 8.34 – 8.32 (2H, m), 7.94 (1H, d), 4.50 (1H, br m), 4.00 (4H, br m), 3.60 – 3.54 (2H, m), 2.67 (4H, br m), 2.49 – 2.46 (2H, m).	2-{4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}ethan-1-ol
35	[A001]	A		Method 1: RT: 2.35 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.77 – 8.74 (2H, m), 8.56 (1H, d), 8.34 – 8.32 (2H, m), 8.17 (1H, br m), 5.18 (1H, d), 4.49 (1H, br m), 4.08 (3H, br m), 3.88 (1H, br d), 2.05 (2H, br m).	(3S)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol

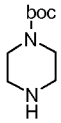
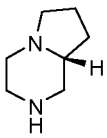
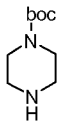
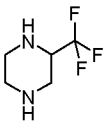
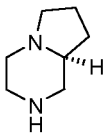
36	[A001]	A		Method 1: RT: 2.39 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.77 – 8.74 (2H, m), 8.56 (1H, d), 8.34 – 8.32 (2H, m), 8.17 (1H, br m), 5.18 (1H, d), 4.49 (1H, br m), 4.08 (3H, br m), 3.88 (1H, br d), 2.05 (2H, br m).	(3R)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol
37	[A003]	B		Method 1: RT: 2.74 min, MI: 413.17 [M+H]	(1H, 500MHz, d6-dmso) 8.79 (s, 1H), 8.70 (d, 2H), 8.23 (s, 1H), 8.05 (d, 2H), 7.33 (m, 3H), 7.27 (d, 2H), 3.21 (t, 1H), 3.17 (d, 2H), 3.00 (d, 1H), 2.92 (m, 1H), 2.82 (t, 1H), 2.76 (dd, 1H), 2.68 (d, 1H), 2.61 (dd, 1H).	(3R)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
38	[A001]	A		Method 1: RT: 2.06 min, MI: 383.17 [M+H]	(1H, 500MHz, $CDCl_3$) 9.29 (s, 1H), 8.75 (d, 2H), 8.47 (d, 1H), 8.28 (d, 2H), 7.45 (d, 1H), 7.09 (m, 5H), 5.04 (m, 1H), 4.25 (d, 1H), 3.83 (t, 1H), 3.28 (m, 2H), 3.22 (d, 1H), 3.09 (m, 2H), 3.02 (t, 1H).	(2S)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
39	[A001]	A	 [A015]	Method 1: RT: 1.04 min, MI: 351.25 [M+H]	(1H, 300MHz, d4-MeOH): 9.20 (s, 1H), 8.71 (dd, 2H), 8.59 (d, 1H), 8.48 (dd, 2H), 8.08 (d, 1H), 4.98 (m, 1H), 4.99 (m, 1H), 4.02 (dd, 1H), 3.74 (s, 3H), 3.42 (dd, 1H), 3.25 (dd, 1H), 2.78 (m, 2H), 2.21 (m, 1H).	methyl (2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-carboxylate
40	[A001]	A	 [A015]	Method 1: RT: 0.52 min , MI: 463 [M+H]	(1H, 300MHz, d4-MeOH): 9.21 (s, 1H), 8.71 (ss, 2H), 8.60 (d, 1H), 8.50 (dd, 2H), 8.09 (d, 1H), 4.99 (m, 1H), 4.29 (m, 1H), 3.86 (m, 2H), 3.73 (s, 3H), 3.47 (dd, 1H), 3.14 (m, 2H), 2.89 (dd, 1H), 2.74 (m, 1H), 2.49 (m, 1H), 2.12 (m, 1H), 1.88 (m, 1H).	methyl (2S,4S)-4-[(2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-amido]pyrrolidine-2-carboxylate

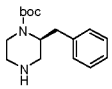
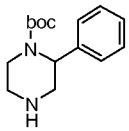
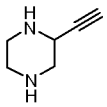
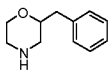
41	[A003]	A		Method 1: RT: 5.14 min , MI: 401 [M+H]	(1H, 300MHz, d6-dmso) 8.77 (s, 1H), 8.72 – 8.70 (2H, m), 8.33 (1H, s), 8.20 (1H, s), 8.12 – 8.10 (2H, m), 7.33 – 7.23 (5H, m), 4.12 (3H, s), 3.86 – 3.78 (1H, m), 3.62 – 3.53 (1H, m), 3.18 – 3.11 (1H, m), 2.98 – 2.92 (1H, m)2.71 – 2.64 (1H, m), 2.45 (3H, s).	[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl](methyl)amine
42	[A001]	A		Method 1: RT: 3.0 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.21 (1H, s), 8.81 – 8.77 (3H, m), 8.67 (1H, d), 8.37 – 8.33 (3H, m), 6.57 (2H, s), 5.00 – 4.90 (1H, m), 4.14 – 4.09 (1H, m), 4.01 – 3.94 (1H, m), 3.86 – 3.79 (2H, m), 2.42 – 2.33 (1H, m), 2.20 – 2.09 (1H, m).	N-[(3R)-oxolan-3-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
43	[A003]	B		Method 1: RT: 3.41 min, MI: 391.13 [M+H]	(1H, 300MHz, $CDCl_3$) 9.01 (s, 1H), 8.76 (d, 2H), 8.31 (d, 2H), 8.22 (s, 1H), 4.42 (d, 1H), 4.15 – 4.04 (m, 1H), 4.07 (s, 3H), 3.62 (br m, 1H), 3.33 – 3.12 (m, 3H), 3.00 (t, 1H).	1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
44	[A003]	B		3jdf138qc, 96%, 337.23, 1.37min, + [M+H] LC-MS17QC	(1H, 300MHz, $CDCl_3$) 8.95 (s, 1H), 8.74 (d, 2H), 8.31 (d, 2H), 8.16 (s, 1H), 4.20 (t, 2H), 4.05 (s, 3H), 3.16 (m, 2H), 2.99 (m, 2H), 2.81 (t, 1H), 1.14 (d, 3H).	(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine
45	[A003]	B		Method 1: RT: 1.52 min , MI: 323 [M+H]	(1H, 300MHz, d6-dmso) 8.80 (1H, s), 8.78 – 8.75 (2H, m), 8.34 (1H, s), 8.32 – 8.30 (2H, m), 4.07 (3H, s), 3.94 (2H, br s), 3.82 (1H, br s), 3.72 (1H, br s), 2.15 (1H, br s), 1.10 (1H, br s).	(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
46	[A003]	B		Method 1: RT: 1.32 min, MI:	(1H, 300MHz, d6-dmso): 8.84 (s, 1H), 8.76 (d, 2H), 8.34 (s, 1H), 8.29 (d, 2H), 4.87 (bs, 1H), 4.28 (dd,	[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-

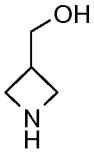
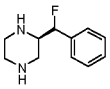
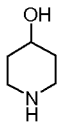
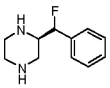
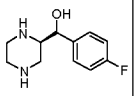
				353.2 [M+H]	2H), 4.06 (s, 3H), 3.43 (m, 1H), 3.07 (m, 3H), 2.82 (m, 3H).	d]pyrimidin-4-yl]piperazin-2-yl]methanol
47	[A003]	B	 [A018]	Method 1: RT: 2.79 min, MI: 405.22 [M+H]	(1H, 300MHz, $CDCl_3$): 8.90 (s, 1H), 8.72 (d, 2H), 8.22 (d, 2H), 8.14 (s, 1H), 7.40 (m, 5H), 5.43 (dd, 1H), 4.18 (m, 1H), 4.10 (s, 3H), 3.53 (m, 2H).	N-[(2R,3R)-2-amino-3-fluoro-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
48	[A003]	B		Method 1: RT: 3.76 min, MI: 470.24 [M+H]	(1H, 300MHz, $CDCl_3$): 8.94 (s, 1H), 8.70 (d, 2H), 8.12 (d, 2H), 8.05 (s, 1H), 7.28 (m, 2H), 7.08 (m, 3H), 4.04 (d, 1H), 3.84 (m, 4H), 3.65 (m, 1H), 3.56 (d, 1H), 3.29 (m, 1H), 3.06 (m, 3H), 2.89 (m, 1H), 2.66 (dt, 1H), 2.53 (dd, 1H).	2-[(2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl]acetamide
49	[A003]	A	 [A009]	Method 1: RT: 5.71 min , MI: 415 [M+H]	(1H, 300MHz, d4-MeOH) 8.63 (1H, s), 8.58 – 8.56 (2H, m), 8.10 (1H, s), 8.06 – 8.04 (2H, m), 7.31 – 7.19 (5H, m), 4.06 (3H, m), 3.98 – 3.91 (1H, m), 3.71 – 3.63 (1H, m), 3.59 – 3.47 (1H, m), 3.20 – 3.14 (1H, m), 2.67 – 2.60 (7H, m).	[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl]dimethylamine
50	[A003]	B		Method 1: RT: 3.69 min, MI: 324.19 [M+H]	(1H, 300MHz, $CDCl_3$) 8.92 (1H, s), 8.74 – 8.72 (2H, m), 8.36 – 8.34 (2H, m), 8.16 (1H, m), 4.62 (1H, br s), 4.26 – 4.16 (1H, m), 4.07 (3H, m), 3.82 – 3.75 (1H, m), 3.63 (1H, d), 2.12 – 2.20 (1H, m), 1.22 – 1.21 (2H, m).	(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol
51	[A003]	B		Method 1: RT: 0.63 min , MI: 351 [M+H]	(1H, 300MHz, $CDCl_3$): 8.97 (s, 1H), 8.78 (d, 2H), 8.31 (d, 2H), 8.19 (s, 1H), 4.23 (m, 2H), 4.07 (s, 3H), 3.08 (m, 2H), 2.75 (t, 2H), 1.16 (m, 6H).	1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3,5-cis-dimethylpiperaz

						ine
52	[A003]	B		Method 1: RT: 4.03 min, MI: 337.37 [M+H]	(1H, 300MHz, $CDCl_3$): 8.98 (s, 1H), 8.77 (d, 2H), 8.32 (d, 2H), 8.19 (s, 1H), 4.22 (t, 2H), 4.07 (s, 3H), 3.19 (m, 2H), 3.05 (m, 2H), 2.82 (m, 1H), 1.15 (d, 3H).	(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine
53	[A003]	B			(1H, 300 MHz, d_6-DMSO) 8.78 – 8.73 (3H, m), 8.30 – 8.28 (3H, m), 4.05 (3H, s), 3.92 (4H, m), 3.36 (3H, m)	(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
54	[A003]	B	 [A024]	Method 1: RT: 1.48 min, MI: 355.15 [M+H]	(1H, 300MHz, $CDCl_3$) 9.02 (1H, s), 8.80 – 8.78 (2H, m), 8.35 – 8.33 (2H, m), 8.22 (1H, m), 4.59 – 4.57 (1H, m), 4.44 – 4.41 (1H, m), 4.28 (1H, d), 4.22 – 4.16 (1H, m), 4.10 (3H, s), 3.25 – 3.20 (1H, m), 3.12 – 3.03 (1H, m).	3-(fluoromethyl)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
55	[A001]	A		Method 1: RT: 4.22 min, MI: 377.43 [M+H]	(1H, 300MHz, d6-dmso) 9.25 (1H, s), 8.75 (2H, dd), 8.58 (1H, d), 8.31 (2H, dd), 7.89 (1H, d), 7.74 (1H, d), 4.58 (2H, d), 3.86-3.79 (1H, m), 3.33 (3H, m), 1.94-1.78 (4H, m), 1.03 (6H, d).	N-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidine-4-carboxamide
56	[A001]	A		Method 1: RT: 2.42 min, MI: 336.18 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.76 (2H, dd), 8.60 (1H, d), 8.33 (2H, dd), 7.98 (1H, d), 6.11 (2H, s), 4.02-3.99 (4H, m), 3.60-3.56 (4H, m).	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide
57	[A001]	A		Method 1: RT: 4.8 min , MI: 418.47 [M+H]	(1H, 300MHz, d6-dmso) 9.25 (1H, s), 8.76 (2H, d), 8.58 (1H, d), 8.31 (2H, d), 7.96 (1H, d), 6.27 (1H, d), 4.00 (4H, m), 3.57 (4H, m), 3.47-3.38 (1H, m), 1.77-1.66 (4H, m), 1.56	N-cyclohexyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide

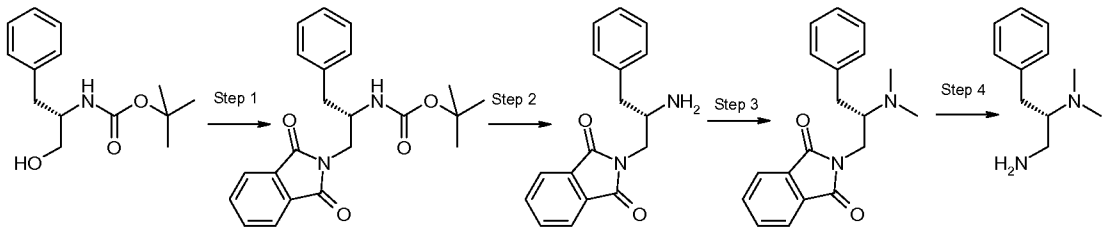
					(1H, d, br), 1.25-1.04 (5H, m).	
58	[A003]	B	 [A028]	Method 1: RT: 0.64 min, MI: 362.18 [M+H]	(1H, 300MHz, $CDCl_3$) 9.03 (1H, s), 8.81 – 7.79 (2H, m), 8.36 – 8.34 (1H, m), 8.24 (1H, s), 4.38 – 4.34 (1H, m), 4.16 – 4.12 (4H, m), 3.42 – 3.33 (1H, m), 3.28 – 3.19 (2H, m), 3.09 – 3.02 (2H, m), 2.60 – 2.58 (2H, m).	2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl}acetonitrile
59	[A001]	A		Method 1: RT: 3.3 min , MI: 361 [M+H]	(1H, 300MHz, d6-dmso) 9.31 (1H, s), 8.80 – 8.78 (2H, m), 8.63 (1H, d), 8.32 – 8.30 (2H, m), 7.97 (1H, d), 4.54 (1H, d), 4.25 (1H, d), 3.78 – 3.56 (3H, m), 3.18 – 3.06 (2H, m), 2.96 – 2.90 (2H, m).	1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
60	[A005]	B		Method 1: RT: 4.43 min , MI: 395 [M+H]		1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
61	[A001]	A		Method 1: RT: 1.30 min , MI: 321 [M+H]	(1H, 300MHz, d6-dmso) 9.33 (s, 1H), 8.78 (d, 2H), 8.65 (d, 1H), 8.33 (d, 2H), 8.01 (d, 1H), 4.55-4.66 (m, 1H), 3.73 (t, 1H), 3.28-3.47 (m, 4H), 1.66-1.75 (m, 2H), 1.04 (t, 3H).	(3S)-3-ethyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
62	[A001]	A		Method 1: RT: 1.76 min , MI: 335 [M+H]	(1H, 300MHz, d6-dmso) 9.21-9.25 (m, 1H), 8.71-8.77 (m, 2H), 8.54-8.60 (m, 1H), 8.22-8.29 (m, 2H), 7.82-7.89 (m, 1H), 4.44-4.62 (m, 2H), 3.31-3.44 (m, 2H), 3.01-3.15 (m, 2H), 2.90 (t, 1H), 2.73 (brs, 1H), 1.68-1.79 (m, 1H), 1.00 (d, 6H).	(3S)-3-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

63	[A008]	B		Method 1: RT: 2.19 min, MI: 341.14 [M+H]	(1H, 300MHz, d4-MeOH) 8.89 (1H, s), 8.61 (1H, d), 8.54 (1H, d), 8.43 (1H, s), 8.35 (1H, s), 8.20 (1H, dd), 4.16 (3H, s), 3.94 (4H, m), 3.36 (4H, m).	1-[2-(3-fluoropyridin-4-yl)-5-methoxypyrido[3,4-d]pyrimidin-4-yl]piperazine
64	[A001]	A		Method 1: RT: 0.66 min , MI: 333 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.78 – 8.76 (2H, m), 8.59 (1H, d), 8.33 – 8.31 (2H, m), 7.94 (1H, d), 4.67 (2H, dd), 3.47 – 3.39 (1H, m), 3.18 – 3.10 (2H, m), 3.08 – 3.04 (1H, m), 2.41 – 2.33 (1H, m), 2.21 – 2.09 (2H, m), 1.94 – 1.83 (1H, m), 1.80 – 1.65 (2H, m), 1.48 – 1.35 (1H, m).	4-{4-[(8aR)-octahydropyrrolo[1,2-a]piperazin-2-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine
65	[A004]	B		Method 1: RT: 1.89 min, MI: 311.15 [M+H]	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.73 (1H, d), 8.65 (1H, d), 8.60 (1H, d), 8.13 (1H, dd), 8.00 (1H, d), 4.06 (4H, m), 3.22 (4H, m), 2.97 (1H, s, br).	1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
66	[A004]	B		Method 1: RT: 4.02 min, MI: 379.15 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.73 (1H, d), 8.64 (1H, d), 8.60 (1H, d), 8.11 (1H, dd), 7.97 (1H, dd), 4.53 (1H, dd), 4.21 (1H, d), 3.75 (1H, m), 3.66 (1H, td), 3.51 (1H, dd), 3.15 (1H, d), 3.03 (1H, d), 2.88 (1H, t).	1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
67	[A001]	A		Method 1: RT: 4.32 min, MI: 333.18 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.78 – 8.76 (2H, m), 8.59 (1H, d), 8.33 – 8.31 (2H, m), 7.94 (1H, d), 4.64 (1H, dd), 3.46 (1H, br t), 3.20 – 3.03 (3H, m), 2.41 (1H, br m), 2.18 (2H, br m), 1.94 – 1.04 (1H, br m), 1.78 – 1.68 (2H, br m), 1.49 – 1.36 (1H, m).	4-{4-[(3aS)-octahydro-1H-pyrrolo[3,2-c]pyridin-5-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine

68	[A005]	B		Method 1: RT: 3.05 min , MI: 417 [M+H]	(1H, 300MHz, d6-dmso) 7.79 (d, 2H), 7.53 (brs, 1H), 7.39 (d, 1H), 7.26 (d, 2H), 6.83 (d, 1H), 6.57-6.67 (m, 5H), 3.83 (dd, 1H), 3.04 (t, 1H), 2.82-2.93 (m, 1H), 2.68 (d, 1H), 2.59 (d, 1H), 2.35 (dd, 1H), 2.14 (dd, 1H).	(3S)-3-benzyl-1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
69	[A001]	A		Method 1: RT: 2.32 min , MI: 369 [M+H]	(1H, 300MHz, d6-dmso) 9.23 (s, 1H), 8.74 (d, 2H), 8.56 (d, 1H), 8.26 (d, 2H), 7.89 (d, 1H), 7.51 (d, 2H), 7.25-7.40 (m, 3H), 4.51 (dd, 2H), 3.95 (d, 1H), 3.34-3.46 (m, 1H), 3.13-3.24 (m, 2H), 2.97-3.03 (m, 1H).	3-phenyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
70	[A003]	B		Method 1: RT: 2.47 min, MI: 324.18 [M+H] ;	(1H, 300MHz, $CDCl_3$) 9.00 (1H, s), 8.76 (2H, d), 8.33 (2H, d), 8.20 (1H, s), 4.08 (3H, s), 3.89 (4H, t), 3.77 (4H, t).	4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine
71	[A001]	A	 [A030]	Method 1: RT: 2.72 min, MI: 317.26 [M+H]	(1H, 300MHz, d4-MeOH) 9.24 (1H, s), 8.69 (2H, dd), 8.54 (1H, d), 8.42 (2H, dd), 7.97 (1H, dd), 4.20 (1H, dd), 4.07-3.92 (4H, m), 3.36-3.29 (1H, m), 3.00-2.94 (1H, m), 2.80 (1H, d), 2.65 (1H, s, br).	3-ethynyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
72	[A003]	B	 [A034]	Method 1: RT: 5.36 min, MI: 414.22 [M+H]	(1H, 300MHz, d6-dmso) 8.82 (1H, s), 8.71 (2H, dd), 8.27 (1H, s), 8.10 (2H, dd), 7.34-7.28 (5H, m), 4.27 (1H, d), 4.04 (1H, d), 3.95-3.91 (1H, m), 3.91 (3H, s), 3.81-3.73 (1H, m), 3.59-3.52 (1H, m), 3.38-3.33 (1H, m), 3.04-2.96 (1H, dd), 2.91-2.75 (2H, m).	2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine

73	[A005]	B		Method 1: RT: 3.33 min , MI: 330 [M+H]		{1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]azetidin-3-yl}methanol
74	[A003]	B	 [A036]	Method 1: RT: 1.88 min, MI: 431.18 [M+H]		(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
75	[A005]	B		Method 1: RT: 3.73 min , MI: 342 [M+H]	(1H, 300MHz, d6-dmso) 8.78 (d, 2H), 8.35 (d, 1H), 8.33 (d, 2H), 7.89 (d, 1H), 4.88 (d, 1H), 4.21-4.27 (m, 2H), 3.85-3.91 (m, 1H), 3.64-3.72 (m, 2H), 1.93-1.99 (m, 2H), 1.57-1.65 (m, 2H).	1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidin-4-ol
76	[A003]	B	 [A036]	Method 1: RT: 2.08 min, MI: 431.14 [M+H]	(1H, 500MHz, d6-dmso) 8.81 (1H, s), 8.71 (2H, d), 8.28 (1H, s), 8.10 (2H, d), 7.46-7.45 (5H, m), 5.51 (1H, dd), 4.41 (1H, d, br), 4.02 (1H, m, br), 3.98 (3H, s), 3.20 (2H, t, br), 3.08 (1H, d), 2.99 (1H, d), 2.68 (1H, t).	(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
77	[A003]	B	 [A043]	Method 1: RT: 2.08 min , MI: 447.08 [M+H] (3:1 mixture of diastereomers)	(1H, 500MHz, d6-dmso) 8.79 (0.25H, s), 8.77 (0.75H, s), 8.70 (2H, dd), 8.27 (0.25H, s), 8.22 (0.75H, s), 8.11 (0.75H, d), 8.08 (0.25H, d), 7.99 (1H, d, br), 7.43 (2H, t, br), 7.23 (1.5H, t), 7.20 (0.5H, t), 5.65 (0.75H, d), 5.54 (0.25H, d), 4.54 (0.25H, t), 4.43 (0.75H, t), 3.99 (0.75H, s), 3.93 (2.25H, s), 3.22 (0.75H, t), 3.14 (0.25H, t), 3.94-2.92 (2H, m), 2.85 (1H, t), 2.74 (1H, m), 2.65 (1H, t).	(4-fluorophenyl)[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl]methanol

Synthesis of (S)-N^2,N^2-Dimethyl-3-phenyl-propane-1,2-diamine [A009]



[A010] [A011] [A012] [A009]

Synthesis of [(S)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A010] A mixture of Boc-L-phenylalaninol (25 g, 99.5 mmol), triphenylphosphine (31.3 g, 119.4 mmol), phthalimide (16.1 mg, 109.5 mmol) and THF (300 mL) was chilled to 0°C. A solution of diisopropyl azodicarboxylate (19.5 mL, 99.5mmol) in THF (100 mL) was added over 15 mins. The resulting pale yellow solution was allowed to return to room temperature over night. The reaction mixture was concentrated to approximately 100 mL then partitioned between ethyl acetate and water. A white precipitate formed which was collected by filtration. The organic layer was washed with more water (x1) then brine (x1), dried ($MgSO_4$), filtered and evaporated to yield the title compound as a second white solid and this was material was used in further reactions, without further analysis.

Synthesis of ((S)-1-Aminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A011] A mixture of [(S)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A010] (2 g, 5.25 mmol), 4M HCl in dioxane (5 mL, 20 mmol) and methanol (50 mL) was stirred at room temperature. The reaction mixture was loaded straight on to a methanol conditioned SCX-2 cartridge. The cartridge was washed with methanol (2col cols) and then eluted with 2N ammonia in methanol (2CV). LCMS analysis showed the target material to be predominantly in the methanol wash but also partially in the NH3 elution. The collected fractions were left to stand for a 3 days. After this time, needle like crystals started to form in the methanol fraction. The crystals were collected by filtration and dried in the vac oven to yield the title compound [A011] (400mg): NMR: (1H, 300MHz, d6-DMSO) 8.08 (2H, br s), 7.04 (4H, s), 7.35-7.29 (4H, m), 7.26-7.17 (1H, m), 3.83-3.66 (2H, m), 3.61 (1H, dd), 3.06 (1H, dd), 2.86 (1H, dd); LCMS method: 1, RT:2.50 min, MI 281 [M+H]

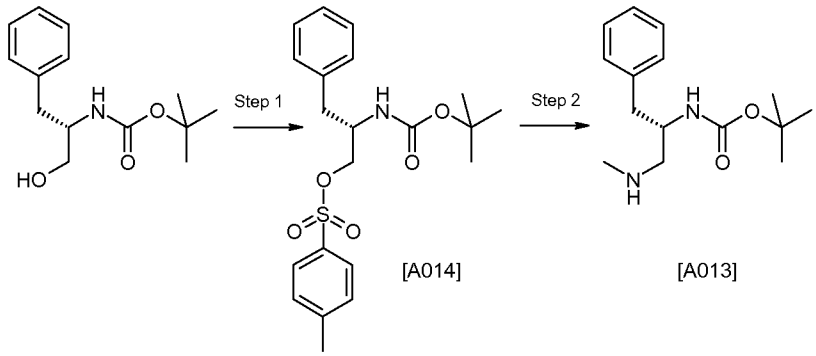
Synthesis of 2-((S)-2-Dimethylamino-3-phenyl-propyl)-isoindole-1,3-dione [A012]

A mixture of 2-((S)-2-Amino-3-phenyl-propyl)-isoindole-1,3-dione [A011] (200 mg, 0.71 mmol), formaldehyde (2 mL, xs) and formic acid (2 mL, xs) was heated to 100°C for 2 hours. The reaction mixture was concentrated under vacuum then partioned between 2M K_2CO_3 and DCM. The organic layer was washed with water then brine, passed through a phase separator and evaporated to yield the title compound [A012] (200mg) which was used without further purification: LCMS method: 1, RT: 2.42 min, MI 309 [M+H]

Synthesis of (S)-N^2,N^2-Dimethyl-3-phenyl-propane-1,2-diamine [A009]

A solution of 2-((S)-2-Dimethylamino-3-phenyl-propyl)-isoindole-1,3-dione [A012] (350mg), hydrazine monohydrate (66.1 ul, 1.36 mmol) and methanol (50 mL) was stirred at room temperature for 20 hours. The solvent was removed under vacuum to yield a white solid. This was then partitioned between 10% citric acid and isopropanol. The aqueous layer was filtered, basified with 2M NaOH, extracted into isoropanol, washed with brine, passed through a phase separator and evaporated to yield title compound [A009] (93mg): LCMS method: 1, RT:0.53 min, MI 179 [M+H]

Synthesis of ((S)-1-Methylaminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A013]



Synthesis of Synthesis of Toluene-4-sulfonicacid(S)-2-tert-butoxycarbonylamino-3-phenyl-propyl ester [A014]

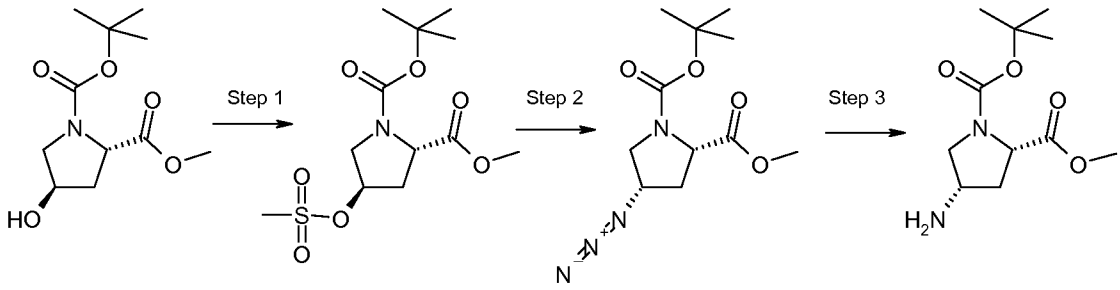
To a solution of Boc-L-phenylalaninol (0.5 g, 1.989 mmol) in DCM (10 mL) at 0°C was added triethylamine (0.83 mL, 5.968 mmol). The reaction mixture was stirred at this temperature for 5minutes. para-Toluenesufonyl chloride (2.188 mmol, 0.42 g) was added dropwise as a solution in DCM (5 mL), and the reaction mixture was allowed to warm up to

room temperature slowly. The reaction mixture stirred at room temperature for 4 hours. The reaction mixture was diluted with DCM (20 mL) and washed with water. Layers separated and the organic layer dried over anhydrous magnesium sulphate. The DCM was evaporated to dryness under reduced pressure to afford the title compound [A014] as a clear oil (0.8g). No further purification was carried out and the crude product was used immediately in the next step.

Synthesis of ((S)-1-Methylaminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A013]

Toluene-4-sulfonicacid(S)-2-tert-butoxycarbonylamino-3-phenyl-propyl ester [A014] (0.80 g, 1.973 mmol) was dissolved in THF (10 mL) and methyl amine (2N in THF, 10 mL) was added in one portion. The reaction mixture was stirred at 60°C overnight. The mixture was diluted with ethyl acetate and washed with brine. The layers were separated and the ethyl acetate dried over anhydrous magnesium sulphate. The solvent was removed under reduced pressure to afford the title compound [A013] as a clear oil. No further purification was carried out at this stage. Crude material was used directly in subsequent reactions without further purification.

Synthesis of (2S,4S)-4-Amino-2-hydroxymethyl-pyrrolidine-1-carboxylic acid tert-butyl ester [A015]



[A016] [A017] [A015]

Synthesis of (2S,4R)-4-Methanesulfonyloxy-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A016]

N-Boc-trans-4-hydroxy-L-proline methyl ester (12.28 mmol, 3 g), was dissolved in DCM (30 mL) and triethylamine (13.45 mmol, 1.87 mL) was added. The reaction was cooled to 0°C and methanesulfonyl chloride (24.46 mmol, 1.89mL) was added dropwise over 5 minutes. The reaction mixture was allowed to stir at this temperature for 45 minutes and then warmed

to room temperature for 2 hours. Brine was added and the layers were separated, the aqueous was extracted with dichloromethane (x2). The organics were washed with brine (x1), dried with $MgSO_4$, filtered and evaporated to yield the title compound as a clear oil (3.95g): NMR (1H, 300MHz, $CDCl_3$): 5.22 (m, 1H), 4.39 (m, 1H), 3.74 (s, 3H), 3.73 (m, 2H), 3.65 (s, 3H), 3.07 (s, 3H), 2.51 (m, 1H), 2.22 (m, 2H), 1.41 (d, 9H)

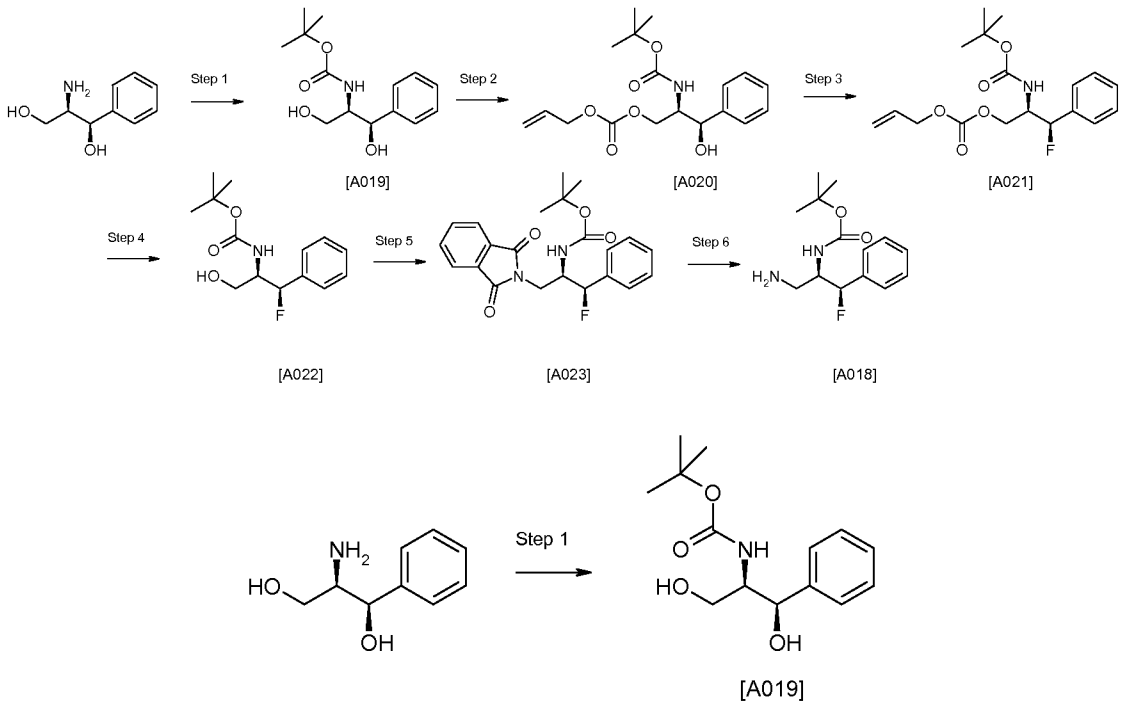
Step 2: Synthesis of (2S,4S)-4-Azido-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A017]

(2S,4R)-4-Methanesulfonyloxy-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A016] (12.28 mmol, 3.95 g), was dissoved in anhydrous DMF (20 mL) and sodium azide (61.14 mmol, 3.97 g) was added in one portion. The reaction was heated to 80°C for 3 hours. Upon cooling the reaction mixture was quenched with water and extracted with ethyl acetate (x3). The organics were washed with brine, dried with $MgSO_4$, filtered and evaporated to a colourless oil. Purified by flash column chromatography using 0 to 40% EtOAc / cyclohexane to yield the title compound [A017] (2.24g): NMR (1H, 300MHz, $CDCl_3$): 4.36 (m, 1H), 4.13 (m, 1H), 3.74 (s, 3H), 3.67 (m, 1H), 3.48 (dt, 1H), 2.47 (m, 1H), 2.14 (m, 2H), 1.43 (d, 9H)

Synthesis of (2S,4S)-4-Amino-2-hydroxymethyl-pyrrolidine-1-carboxylic acid tert-butyl ester [A015]

Water (5 mL) was added to a stirred solution of (2S,4S)-4-azido-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A017] (4.44 mmol, 1.2 g) and triphenylphosphine (9.32 mmol 2.45 g), in toluene (40 mL) and the reaction was heated to 60°C overnight. Upon cooling water was added and the layers separated. The aqueous was basified with 2M NaOH added and extracted twice with ethyl acetate, the organics combined, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to give the title compound (200 mg): NMR (1H, 300MHz, $CDCl_3$): 4.20 (m, 1H), 3.71 (s, 3H), 3.62 (m, 1H), 3.50 (m, 1H), 3.22 (m, 1H), 2.43 (m, 1H), 1.78 (m, 1H), 1.43 (d, 9H)

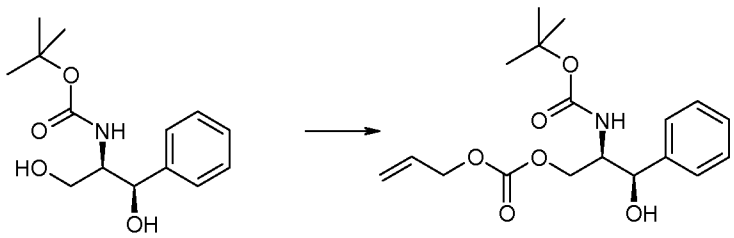
Synthesis of ((1R,2R)-1-Aminomethyl-2-fluoro-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A018]



Synthesis of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A019]

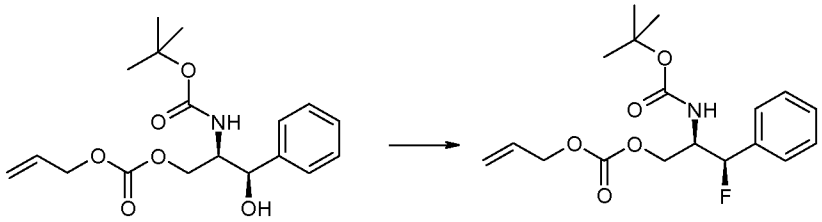
(1R,2R)-(-)-2-Amino-1-phenyl-propane-1,3-diol (5.98 mmol, 1.0 g) was dissolved in methanol (10 mL) and cooled to 0°C. A solution of di-tert-butyl dicarbonate in methanol (4mL) was added and the reaction was warmed to room temperature and stirred for 2 hours. The solvent was removed in vacuo and the product was purified by flash chromatography eluting with 0 to 70% EtOAc / cyclohexane to yield the title compound [A019] (1.20g): NMR (1H, 300MHz, $CDCl_3$): 7.29 (m, 5H), 5.19 (m, 1H), 4.96 (m, 1H), 3.35 (m, 1H), 2.66 (m, 1H), 1.33 (s, 9H); LCMS method: 1, RT:4.35 min, MI: no trace.

Synthesis of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A020]



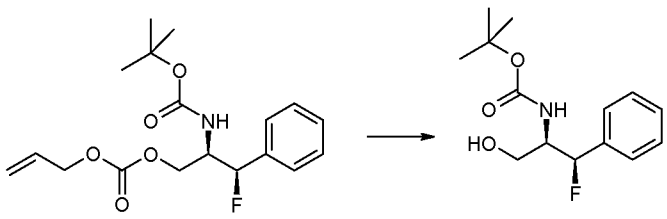
Allyl chloroformate (11.222 mmol, 1.35 g) was added dropwise to a strirred solution of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A019] (1.20 g, 4.48 mmol) and pyridine (15.711mmol, 1.27 mL) in DCM (50mL) at 0°C. The reaction was allowed to warm to room temperature and stirred for an hour. Water was added and the layers separated. The aqueous was extracted twice with DCM. The organics were combined, washed with brine, dried over anhydrous MgSO4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using 0 to 100% EtOAc / cyclohexane to yield the title compound [A020] (0.93g): NMR (1H, 300MHz, $CDCl_3$): 7.28 (m, 5H), 5.91 (m, 1H), 5.34 (d, 1H), 5.27 (d,1H), 4.99 (m, 1H), 4.84 (t, 1H), 4.61 (d, 2H), 4.27 (dd, 1H), 4.07 (dd, 1H), 4.01 (m, 1H), 3.09 (bs, 1H), 1.33 (s, 9H); LCMS: LC-MS17QC 94% 352+ [M+H] 5.17min

Synthesis of Carbonic acid allyl ester (2R,3R)-2-tert-butoxycarbonylamino-3-phenyl-3-(tetrahydro-pyran-2-yloxy)-propyl ester [A021]



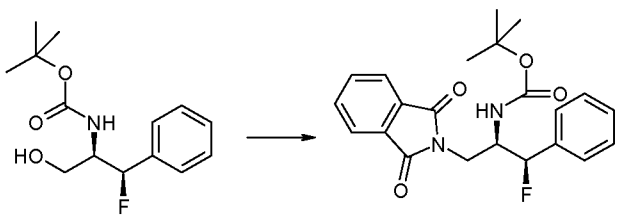
A solution of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A020] (1.42 mmol, 0.50 g) and DIPEA (4.97 mmol 0.865 mL) in DCM (20 mL) was added dropwise to a solution of (diethylamino)sulfur trifluoride (DAST) (4.97 mmol, 0.610 mL) at -78°C under nitrogen. The reaction was slowly warmed to room temperature and stirred for 2 hours. Water was added then extracted twice with DCM. The organics were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to yield the title compound [A021] which was was used directly in the next step without further purification: LCMS method: 1, RT:3.27 min, MI not seen.

Synthesis of ((1R,2R)-2-Fluoro-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A022]



To a solution of carbonic acid allyl ester (2R,3R)-2-tert-butoxycarbonylamino-3-fluoro-3-phenyl-propyl ester [A021] (2.0 mmol, 0.71 g) in anhydrous THF (15 mL) under nitrogen, was added tetrakis(triphenylphosphine)palladium(0) (0.08 mmol 0.093 g) and morpholine (3.014 mmol, 0.26 mL). The reaction was stirred at rt for 1h under a nitrogen atmosphere. Brine was added and the mixture extracted twice with ethyl acetate. The organics were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography using 0 to 10% MeOH / DCM to yield the the title compound [A022] (0.19g): NMR (1H, 300MHz, $CDCl_3$): 7.32 (m, 5H), 5.68 (d, 1H), 5.11 (m, 1H), 3.99 (m, 1H), 3.86 (m, 1H), 3.67 (m, 1H), 1.39 (s, 9H)

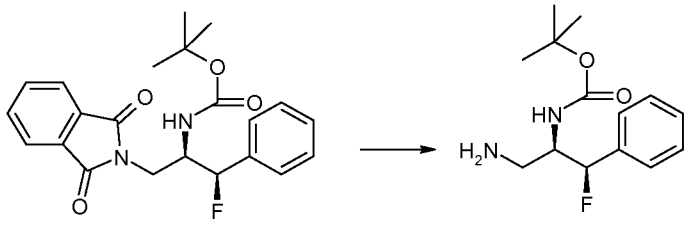
Synthesis of [(1R,2R)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-fluoro-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A023]



A solution of ((1R,2R)-2-Fluoro-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A022] (0.705 mmol, 0.19 g), triphenylphosphine (0.988 mmol, 0.259 g) and phthalimide (0.988 mmol, 0.145 g) was cooled to 0°C and diisopropyl azodicarboxylate (DIAD) (0.988 mmol, 0.193 mL) was added dropwise. The reaction was allowed to warm to room temperature and stirred for 1 hour. The solvent was removed in vacuo and the residue was dissolved in DCM. 2M NaOH (aqueous solution) was added and the layers separated using a phase separator. The organic was concentrated in vacuo. The product was purified by flash chromatography using 0 to 30% EtOAc / cyclohexane to yield the title compound [A023] (0.28g): 1LCMS1; 98%, 399.15+ $[M+H]^+$, 5.45min; NMR (1H, 300MHz, $CDCl_3$):

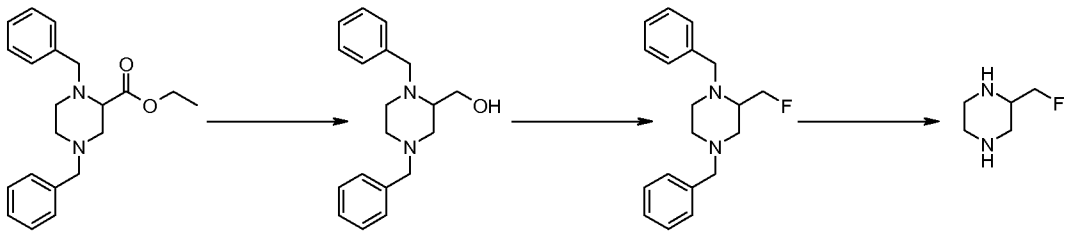
7.80 (m, 2H), 7.65 (m, 2H), 7.40 (m, 4H), 7.31 (m, 1H), 5.72 (dd, 1H), 5.06 (d, 1h), 4.47 (m, 1H), 3.83 (dd, 1H), 3.57 (dd, 1H), 1.20 (s, 9H)

Synthesis of ((1R,2R)-1-Aminomethyl-2-fluoro-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A018]



[(1R,2R)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-fluoro-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A023] (0.705 mmol, 0.28 g) was dissolved in methanol (5 mL) and Hydrazine monohydrate (0.916 mmol, 0.045 mL) was added. The reaction was stirred at room temperature for 1 hour then at 60°C overnight. Upon cooling the solvent was removed in vacuo and the residue dissolved in DCM. 2M NaOH (aqueous solution) was added and the mixture extracted twice. The organics were combined, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The product was purified using an SCX-2 cartridge, applying the crude material as a DCM solution and washing with methanol and DCM. The material was then washed off the SCX-2 cartridge by washing with ammonia (2N in methanol) and the ammonia washes concentrated in vacuo to yield thetitle compound [A018] (0.12g): NMR (1H, 300MHz, $CDCl_3$): 7.34 (m, 5H), 5.62 (d, 1H), 5.19 (d, 1H), 3.89 (m, 1H), 2.83 (m, 2H), 1.40 (s, 9H)

Synthesis of 2-Fluoromethyl-piperazine [A024]



[A025] [A026] [A027] [A024]

(1,4-Dibenzyl-piperazin-2-yl)-methanol [A026]

A solution of 1,4-Dibenzyl-piperazine-2-carboxylic acid ethyl ester [A025] (3.7 g, 10.9 mmol) in THF (10 mL) was added dropwise to a suspension of $LiAlH_4$ (2.24 g, 59 mmol) in THF (20 mL) at 0°C. The reaction was warmed to room temperature and stirred overnight. The reaction was diluted with ether, cooled to 0°C and quenched with water (2.25 mL) and 2M NaOH (4.5 ml) and water (4.5 mL). The suspension was stirred for 15mins and anhydrous MgSO4 was added and stirred for a further 15 mins. The white solid was filtered off (celite) and the solvent remoevd in vacuo. The product was purified by flash chromatography using 0 to 100% EtOAc / cyclohexane to give the title compound [A026] (3.03g, 94 % yield). LCMS method: 1, RT:2.16 min, MI 297.23 [M+H]; NMR (1H, 300MHz, $CDCl_3$): 3.43 (m, 3H), 2.63 (m, 3H), 2.95 (m, 1H), 3.49 (m, 3H), 3.61 (d, 1H), 4.04 (dd, 2H),7.31 (m, 10H)

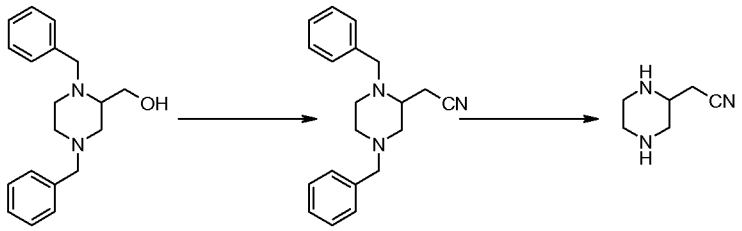
1,4-Dibenzyl-2-fluoromethyl-piperazine [A027]

(1,4-Dibenzyl-piperazin-2-yl)-methanol [A026] (1.09 g, 3.6 mmol) in DCM (5 mL) was added dropwise to a stirred solution of DAST (0.9 mL, 7.35 mmol) in DCM (10 mL) at 0°C. The reaction was warmed to room temperature and stirred overnight. Aqueous 2M NaOH (10 mL) was added the the layers seperated by phase seperator. The solvent was removed in vacuo and the product was purified by flash chromatography using 0 to 30% EtOAc / cyclohexane to give the title compound [A027] (0.42 g, 38% yield). LCMS method: 1, RT:5.88 min, MI 299.38 [M+H]; NMR (1H, 300MHz, $CDCl_3$): 2.28 (m, 3H), 2.50 (m, 2H), 2.70 (m, 2H), 2.83 (m, 1H), 3.49 (m, 3H), 4.11 (d, 1H), 4.53 (ddd, 1H), 4.68 (ddd, 1H), 7.25 (m, 10H)

2-Fluoromethyl-piperazine [A024]

1,4-Dibenzyl-2-fluoromethyl-piperazine [A027] (0.32g, 1.07 mmol) was dissolved in DCE (10 mL) and 1-Chloroethyl chloroformate (0.35 mL, 3.21 mmol) was added. The reaction was heated to reflux overnight. Upon cooling the solvent was removed in vacuo and the intermediate dicarabamate was purified by flash chromatpgraphy eluting with 0 to 50% EtOAc / cyclohexane. The residue was dissolved in methanol (10 mL) and heated to reflux for 1 hour. The solvent was rmoved in vacuo to give the title compound [A024] which was used in the next step and used without further purification

Synthesis of Piperazin-2-yl-acetonitrile [A028]



[A026] [A029] [A028]

(1,4-Dibenzyl-piperazin-2-yl)-acetonitrile [A029]

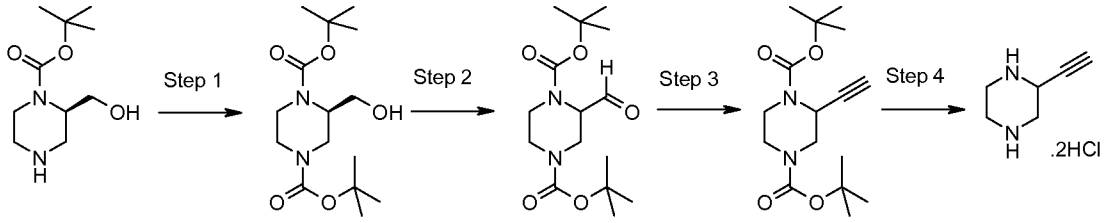
A solution of (1,4-Dibenzyl-piperazin-2-yl)-methanol [A026] (1g, 3.37 mmol) in DCM (10 mL) was added dropwise to a solution of thionyl chloride (0.32 mL, 4.4 mmol) in DCM (5 mL) and the reaction was stirred at room temperature ovenight. The solvent was removed in vacuo and water was added. The aqeous was extracted with ether then bascified with saturated Na2CO3. This was extracted twice with DCM, dried over anhydrous MgSO4, filtered and concentrated in vacuo and used crude in the next step and used without further purification.

To a refluxing solution of KCN (0.244g, 3.7 mmol) in water (10 mL) was added 1,4-Dibenzyl-2-chloromethyl-piperazine (0.91g, 2.9 mmol) in ethanol (10 mL) dropwise. The reaction was heated to reflux for 3 hours. Upon cooling the solvent was removed in vacuo and the residue was was taken up in DCM, washed with water, dried over MgSO4, filtered and concentrated in vacuo. The product was purified by flash chromatography using 0 to 40% EtOAc / cyclohexane, to give the title compound [A029] (0.52 g, 59 % yield). LCMS method: 1, RT:2.87 min, MI 306.26 [M+H]; NMR (1H, 300MHz, $CDCl_3$): 2.43 (m, 3H), 2.58 (m, 4H), 2.87 (dd, 1H), 3.00 (m, 1H), 3.48 (m, 3H), 3.80 (d, 1H), 7.28 (m, 10H).

Piperazin-2-yl-acetonitrile [A028]

(1,4-Dibenzyl-piperazin-2-yl)-acetonitrile [A029] (0.52 g, 1.7 mmol) was dissolved in DCE (10 mL) and 1-Chloroethyl chloroformate (0.55 mL, 5.1 mmol) was added. The reaction was heated to reflux for 2 days. Upon cooling the solvent was removed in vacuo and the intermediate dicarabamate was purified by flash chromatography eluting with 0 to 40% EtOAc / cyclohexane. The residue was dissolved in methanol (10 ml) and heated to reflux for an hour. The solvent was removed in vacuo to give clean product. NMR (1H, 300MHz, d6-dmso): 3.16 (m, 3H), 3.03 (t, 1H), 3.49 (m, 4H), 3.89 (m, 1H), 10.06 (m, 2H)

Synthesis of 2-Ethynyl-piperazine [A030]



[A031] [A032] [A033] [A030]

Synthesis of (R)-2-Hydroxymethyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A031].

To a stirred solution of (R)-1-Boc-2-Hydroxymethyl-piperazine (1 g, 4.62 mmol) and Na_2CO_3 (990 mg, 9.25 mmol) in a mixture of dioxane (8 ml) and water (2 ml) at 0 °C was added Di-tert-butyl dicarbonate and the reaction mixture warmed to room temperature. After 18 hours all solvents were removed *in vacuo* and the resulting residue partitioned between DCM and water. The DCM phase was passed through phase separation cartridge and evaporated to provide a white solid. Purification by column chromatography (0-50% EtOAc:cyclohexane) gave the title compound [A031] as a white solid (1.26g, 86%). 1H-NMR (1H, 300MHz, $CDCl_3$): 4.17 (2H, s, br), 3.93 (1H, s, br), 3.84 (1H, d, br), 3.59 (2H, s, br), 2.95 (3H, s, br), 1.46 (18H, s).

Synthesis of 2-Formyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A032]

A solution of oxalyl chloride (165 µl, 1.90 mmol) in DCM (5 ml) was cooled to -78 °C. DMSO (270 µl, 3.79 mmol) was added dropwise and the reaction mixture stirred for 15mins. A solution of (R)-2-Hydroxymethyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A031] (500 mg, 0.58 mmol) in DCM (1 ml) was added dropwise and the reaction mixture stirred for 1 hour. Triethylamine (1.1 ml, 7.90 mmol) was added and the reaction mixture warmed to room temperature. Saturated $NaHCO_3$ was added, the layers separated and the organic phase collected and evaporated to give the title compound [A032] as a white powder (480mg, 97%). 1H-NMR (1H, 300MHz, $CDCl_3$): 9.58 (1H, s), 4.63-4.45 (2H, m, br), 3.95-3.79 (2H, m, br), 3.15-3.11 (2H, m, br), 2.88 (1H, d, br), 1.44 (18H, s).

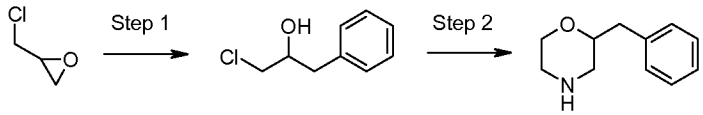
Synthesis of 2-Ethynyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A033]

To a stirred solution of 2-Formyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A032] (480 mg, 0.530 mmol) and K_2CO_3 (425 mg, 3.06 mmol) in MeOH (20 ml) was added Dimethyl (1-diazo-2-oxopropyl)phosphonate (350 mg, 1.83 mmol). After 18 hours the solvent was removed *in vacuo* and the resulting residue partitioned (DCM:water). The organic phase was separated and concentrated to provide the title compound [A033] as a white solid (430mg, 91%).1H-NMR (1H, 300MHz, $CDCl_3$): 4.88 (1H, s, br), 4.25-4.01 (2H, m, br), 3.80 (1H, d, br), 3.18 (1H, t, br), 3.02-2.74 (2H, m), 2.23 (1H, d), 1.47 (18H, s).

Synthesis of 2-Ethynyl-piperazine [A030]

2-Ethynyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A033] (430 mg, 1.39 mmol) was stirred in 4N HCl:dioxane (1 ml) for 4 hours. A pale yellow solid (226 mg, 89%) was collected by filtration and washed with Et_2O then dried in a vacuum oven at 40 °C to yield the title compound [A030]: 1H-NMR (1H, 300MHz, d6-dmso): 4.57 (1H, dt), 4.04 (1H, d), 3.63 (1H, dd), 3.42-3.23 (5H, m).

Synthesis of 2-Benzyl-morpholine [A034]



[A035] [A034]

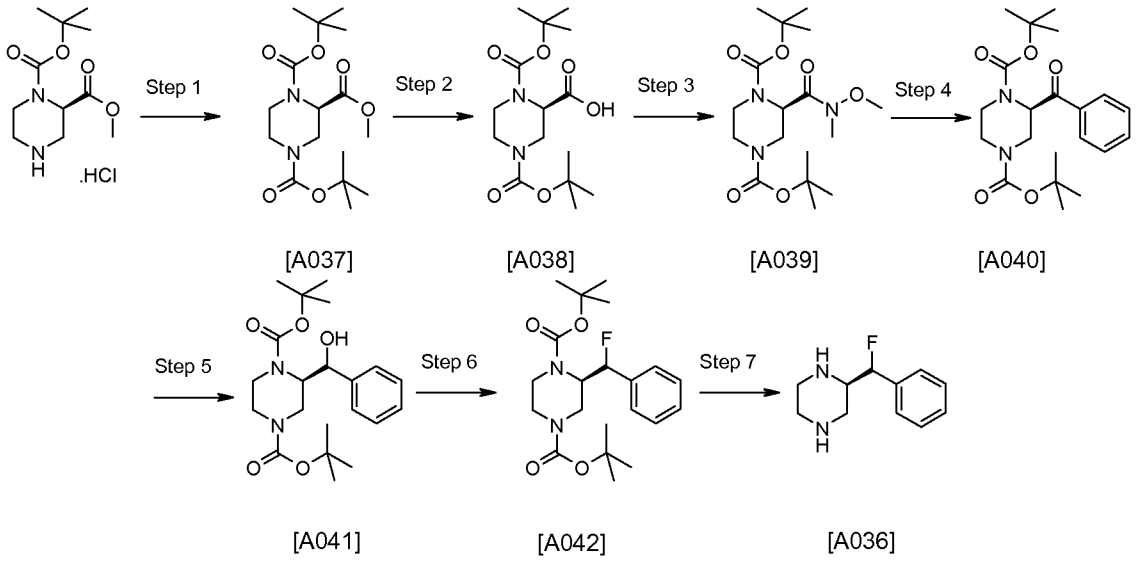
Synthesis of 1-Chloro-3-phenyl-propan-2-ol [A035]

To a stirred solution of Phenyl magnesium bromide (3M in Et_2O, 4.4ml, 13mmol) in Et_2O (14 ml) at 0 °C was added CuI (210mg, 1.08 mmol). Epichlorohydrin (1g, 10.8mmol) in Et_2O (14 ml) was then added and the reaction mixture allowed to warm to room temperature then stirred for 2 hours. Sat. NH_4Cl was added and the solution diluted with water then extracted with EtOAc (x2). The combined organics were washed with brine, dried over $MgSO_4$ and concentrated. Purification by column chromatography (0-20% Et_2O:cyclohexane) provided the title compound [A035] as a colourless oil (1.66g, 90%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.36-7.22 (5H, m), 4.11-4.01 (1H, m), 3.59 (1H, dd), 3.50 (1H, dd), 2.90 (2H, d), 2.18 (1H, d).

Synthesis of 2-Benzyl-morpholine [A034]

To a stirred solution of NaOH (1.63 g, 40.8 mmol) in water3.5 ml) was added 1-Chloro-3-phenyl-propan-2-ol [A035] (1.16 g, 6.8 mmol) in MeOH (7 ml). After 5 min 2-Aminoethane hydrogen sulphate (3.84 g, 27.2mmol) was added and the reaction mixture stirred at 40 °C for 2 hours. NaOH (powdered, 1.63g, 40.8mmol) and PhMe (18 ml) were then added and the reaction heated to 65 °C for 18 hours. Dilution with water (10 ml), was followed by extraction with PhMe (x2). The combined organics were washed (water then brine), dried and concentrated. Purification by column chromatography (0-10% MeOH:DCM) provided the title compound as a colourless oil (360 mg, 30%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.31-7.19 (5H, m), 3.86 (1H, dd), 3.70-3.54 (2H, m), 2.92-2.77 (4H, m), 2.67-2.55 (2H, m).

Synthesis of (R)-2-(Fluoro-phenyl-methyl)-piperazine [A036]



Synthesis of (R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester 2-methyl ester [A037]

To a stirred suspension of (R)-1-N-Boc-piperazine-2-carboxylic acid methyl ester hydrochloride (2 g, 7.12 mmol) and Na_2CO_3 (2.26 g, 21.4 mmol) in dioxane (16ml) and water (4 ml) at 0 °C was added Di-tert-butyl-dicarbonate (1.55 g, 7.12 mmol). After 18 hours all solvents were removed *in vacuo* and the resulting residue partitioned between DCM and water. The organic phase was collected and evaporated to give a colourless oil. Purification by column chromatography (0-30% EtOAc:cyclohexane) gave the title compound [A037] as

a white powder (2.33 g, 95%). 1H-NMR (1H, 300MHz, $CDCl_3$): 5.30 (1H, s), 4.72 (1H, s, br), 4.54 (1H, t, br), 4.08-3.80 (1H, m), 3.73 (3H, s), 3.27-2.73 (3H, m), 1.44 (18H, s).

Synthesis of (R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester [A038]

(R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester 2-methyl ester [A037] (2.33 g, 6.77 mmol) and KOH (1.14 g, 20.3 mmol) were heated to reflux in EtOH (50 ml) for 18 hours. Having cooled to room temperature, solvents were removed *in vacuo* and the residue purified by column chromatography (0-10% MeOH:DCM; 0.1% TEA) to provide the title compound [A038] as a pale orange foam (2.1 g, 94%). 1H-NMR (1H, 300MHz, $CDCl_3$): 4.66-4.50 (2H, m, br), 3.96-3.74 (2H, m, br), 3.47 (1H, s), 3.23 (1H, s, br), 2.85 (1H, s, br), 1.42 (18H, s).

Synthesis of (R)-2-(Methoxy-methyl-carbamoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A039]

(R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester [A038] (2.10 g, 6.36 mmol), O-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (2.9 g, 7.63 mmol), N,O-Dimethylhydroxylamine hydrochloride (750 mg, 7.6 3mmol) and TEA (2.2 ml, 15.3 mmol) were stirred in DMA for 18 hours. The reaction mixture was then partitioned between EtOAc and NaOH (1M), and the aqueous phase re-extracted with EtOAc. The combined organics were dried over $MgSO_4$ and concentrated. Purification by column chromatography (0-50% EtOAc:cyclohexane) gave the title compound [A039] as a viscous pale yellow oil (2.15 g, 91%). 1H-NMR (1H, 300MHz, $CDCl_3$): 5.30 (1H, s), 4.86-4.71 (1H, m), 4.47-4.32 (1H, m), 4.06-3.75 (2H, m), 3.85 (3H, s), 3.18 (3H, s), 3.18-2.85 (2H, m), 1.45 (9H, s), 1.42 (9H, s). LCMS method: 1, RT:3.46 min, MI 374.26 [M+H].

Synthesis of (R)-2-Benzoyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A040]

To a stirred solution of (R)-2-(Methoxy-methyl-carbamoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A039] (500 mg, 1.34 mmol) in THF at 0 °C was added Phenylmagnesium chloride solution (3.4 ml, 6.7mmol, 2.0 M in THF) and the reaction mixture allowed to warm to room temperature. Having stirred for 4 hours the solution was quenched (1N NaOH) and solvents removed *in vacuo*. The residue was partitioned between DCM and Rochelles salt (10% aq.) and the organic phase separated and aqueous re-extracted with DCM. The combined organics were then dried ($MgSO_4$) and concentrated. Purification by column chromatography (0-50% EtOAc:cyclohexane) provided the title compound [A040] as a white

solid (416 mg, 80%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.89 (2H, s, br), 7.57 (1H, s, br), 7.47 (2H, s, br), 5.53 (0.6H, s, br), 5.35 (0.4H, s, br), 4.53-4.38 (1H, m, br), 4.06 (0.6H, m, br), 3.87-3.80 (1.4H, m, br), 3.67-3.53 (1H, m, br), 3.41-3.29 (1H, m, br), 2.94-2.81 (1H, m, br), 1.55-1.12 (19H, m, br); LCMS method: 1, RT:3.75 min, MI 391.32 [M+H]

Synthesis of (R)-2-(Hydroxy-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A041]

To a stirred suspension of (R)-2-Benzoyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A040] (220 mg, 0.553mmol) in MeOH (4 ml) was added sodium borohydride (41 mg, 1.11 mmol). After 2 hours the reaction mixture was partitioned between EtOAc and water, the organic phase separated and concentrated *in vacuo* to give the title compound [A041] as a white crystalline solid (210 mg, 97%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.43-7.26 (5H, m), 4.74 (1H, s, br), 4.31-3.65 (4H, m), 3.25-2.81 (3H, m), 1.55-1.46 (18H, m), 1.13 (1H, s, br); LCMS method: 1, RT:3.86 min, MI 393.32 [M+H]

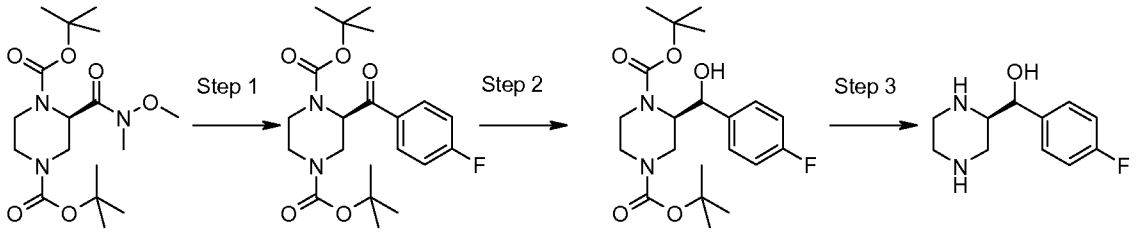
Synthesis of (R)-2-(Fluoro-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A042]

To a stirred solution of (R)-2-(Hydroxy-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A041] (210 mg, 0.535 mmol) in $CHCl_3$ (3 ml) at 0 °C was added (Diethylamino)sulfur trifluoride (330 µl, 2.68 mmol). After 2 hours the reaction mixture was quenched with ice, basified with $NaHCO_3$ (to pH8), then the product extracted into DCM, which was evaporated to give a colourless oil. Purification was achieved by column chromatography (0-50% EtOAc:cyclohexane) to provide the title compound [A042] as a white solid (85mg, 40%). 1H- NMR (1H, 300MHz, $CDCl_3$): 7.34 (5H, m, br), 5.53 (1H, d, br), 4.38-3.84 (4H, m, br), 3.08-2.84 (3H, m, br), 1.49 (9H, s, br), 1.25 (9H, s, br); LCMS method: 1, RT:3.68 min, MI 295.21 [M+H]

Synthesis of (R)-2-(Fluoro-phenyl-methyl)-piperazine [A036]

(R)-2-(Fluoro-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A042] (85 mg, 0.215 mmol) was stirred in 4N HCl:dioxane (2 ml). After 2 hours the solution was dissolved in MeOH and loaded onto an SCX cartridge which was washed with MeOH followed by 2N NH_3:MeOH. Evaporation provided the title compound [A036] as a yellow gum (35mg, 83%). 1H-NMR (1H, 300MHz, d4-MeOH): 7.49-7.43 (5H, m), 5.25 (1H, d), 3.85 (1H, dd), 3.79-3.726(1H, m), 3.20-3.14 (2H, m), 3.00-2.82 (3H, m).

Synthesis of (4-Fluoro-phenyl)-(R)-piperazin-2-yl-methanol [A043]



[A039] [A044] [A045] [A043]

Synthesis of (R)-2-(4-Fluoro-benzoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A044]

To a stirred solution of (R)-2-(Methoxy-methyl-carbamoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A043] (1.15 g, 3.08 mmol) in THF (24 ml) was added 4-Fluorophenylmagnesium bromide solution (2.0M in Et_2O, 7.7 ml, 15.4 mmol) and the reaction mixture allowed to warm to room temperature. Having stirred for 4 hours the reaction was quenched (1N NaOH) and solvents removed *in vacuo*. The residue was partitioned between DCM and Rochelles salt (10% aq). The organic phase was separated and aqueous phase re-extracted with DCM. Evaporation of the combined organics followed by purification by column chromatography (0-50% EtOAc:cyclohexane) gave the title compound [A044] as a pale yellow oil (800mg, 64%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.94 (2H, s, br), 7.15 (2H, s, br), 5.47 (1H, m, br), 4.48-4.32 (1H, m, br), 4.07-4.03 (1H, m, br), 3.91-3.76 (1H, m, br), 3.61-3.51 (1H, m, br), 3.43-3.31 (1H, m, br), 3.18-3.24 (1H, m, br), 1.56-1.17 (18H, m, br); LCMS method: 1, RT:3.79 min, MI 409.32 [M+H]

Synthesis of (R)-2-[(4-Fluoro-phenyl)-hydroxy-methyl]-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A045]

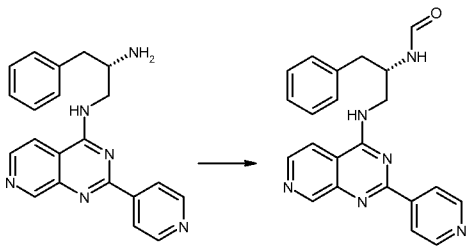
To a stirred solution of (R)-2-(4-Fluoro-benzoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A044] (520 mg, 1.28 mmol) in MeOH (8 ml) was added sodium borohydride at 0 °C and the reaction mixture allowed to warm to room temperature. After 2 hours the reaction mixture was partitioned between EtOAc and water, the organic phase separated and concentrated *in vacuo* to give a pale yellow oil. Purification by column chromatography (0-50% EtOAc:cyclohexane) provided the title compound [A045] as a white crystalline solid

(330mg, 63%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.41-7.08 (5H, m), 4.74 (1H, m), 4.27-3.93 (3H, m), 3.64 (1H, m), 3.23-2.84 (1H, m), 1.45 (18H, m), 1.18 (1H, s, br).

Synthesis of (4-Fluoro-phenyl)-(R)-piperazin-2-yl-methanol [A043]

(R)-2-[(4-Fluoro-phenyl)-hydroxy-methyl]-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A045] (330 mg, 0.808 mmol) was stirred in 4N HCl:dioxane (2 ml). After 2 hours the solution was dissolved in MeOH and loaded onto an SCX cartridge which was washed with MeOH followed by 2N NH_3:MeOH. Evaporation provided the title compound [A043] as a yellow gum which was used without further purification (170mg, 100%).

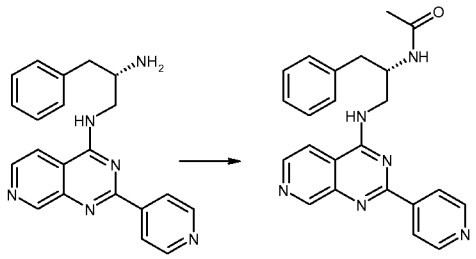
Synthesis of N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide [78]



[6] [78]

A mixture of (S)-3-Phenyl-N^1-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [6] (70 mg, 0.21 mmol) and ethylformate (1.5 mL, 18.6 mmol) was heated in the microwave at 100°C for 1 hour. The reaction mixture was concentrated under vacuum, redissolved in methanol then loaded onto a methanol conditioned SCX-2 cartridge (5g). The cartridge was washed with methanol (2ColVols) then eluted with 2N NH3 in methanol (2CV). The ammonia washes were evaporated to yield the title compound [78]: LCMS method: 1, RT:3.87 min, MI 385 [M+H]; NMR: (1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.90-8.87 (1H, br t), 8.73 (2H, d), 8.63 (1H, d), 8.25 (2H, dd), 8.14 (1H, d), 8.04 (1H, br d), 7.97 (1H, br s), 7.327.20 (5H, m), 4.55-4.46 (1H, m), 3.98-3.90 (1H, m), 3.70-3.62 (1H, m), 3.00-2.93 (1H, dd), 2.85-2.77 (1H, dd)

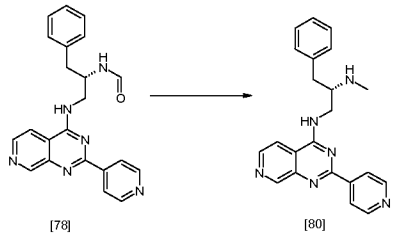
Synthesis of N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-acetamide [79]



[6] [79]

To a stirred solution of (S)-3-Phenyl-N^1-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [6] (70 mg, 0.21 mmol), DIPEA (73 ul, 0.42mmol) and anhydrous DCM (5 mL) at room temperature was added acetic anhydride (29 µl, 0.31 mmol). The reaction mixture was concentrated under vacuum then redissolved in methanol plus formic acid (2 drops) and loaded onto a methanol conditioned SCX-2 cartridge (5 g). The cartridge was washed with methanol (2CV) then eluted with 2N NH_3 in methanol (2CV). The ammonia washes were evaporated to yield the title compound [79]: LCMS method: 1, RT:3.92 min, MI 399 [M+H]; NMR: (1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.85 (1H, br t), 8.72 (2H, dd), 8.63 (1H, d), 7.85 (1H, dd), 7.30-7.17 (5H, m), 4.43-4,33 (1H, m), 4.01-3.92 (1H, m), 3.63-3.55 (1H, m), 2.90 (1H, dd), 2.80 (1H, dd), 1.70 (3H, s)

Synthesis of methyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine [80]

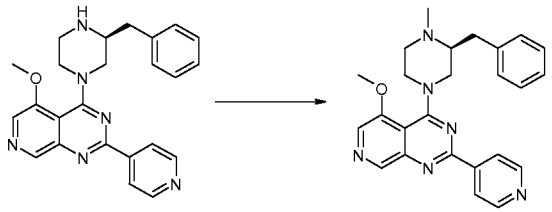


[78] [80]

A stirred suspension of lithium aluminium hydride (19 mg, 0.5 mmol) in anhydrous THF (2.5 mL) was chilled to 0 °C. N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide [78] (40 mg, 0.1 mmol) in THF (2.5 mL) was added over five minutes. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. A further portion of lithium aluminium hydride (10.5mg, 0.28mmol) was added to the reaction mixture and stirring continued at room temperature for 18 hours. Another portion of lithium aluminium hydride (30mg, 0.79mmol) was added to the reaction mixture and stirring continued at room temperature for a further 18 hours. This procedure was repeated on a

second batch of N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide [78] (40 mg, 0.234 mmol) and the crude reaction mixture combined and diluted with ether (20 mL), cooled to 0 °C and quenched by drop-wise addition of water (approx 150 µL), NaOH (approx 300 µL of a 2M solution) and water (approx 300 µL of a 2M solution) again. $MgSO_4$ was added and the mixture filtered and concentrated by rotary evaporation. The crude residue was purified by preparative HPLC (method A). The appropriate fractions were combined, the solvent evaporated and the residue was dissolved in MeOD resulting in precipitation of an impurity which was removed by filtration to give the title compound [80] (2.5 mg). LCMS method: 1, RT:2.39 min, MI 371 [M+H]. ^{1}H NMR (1H, 300MHz, d6-dmso) 9.13 (1H, s), 8.64 – 8.62 (2H, m), 8.54 (1H, d), 8.21 – 8.19 (2H, m), 7.99 (1H, d), 7.32 – 7.21 (5H, m), 3.97 – 3.91 (1H, m), 3.78 – 3.71 (1H, m), 3.29 – 3.22 (1H, m), 3.05 – 2.99 (1H, m), 2.77 – 2.70 (1H, m).

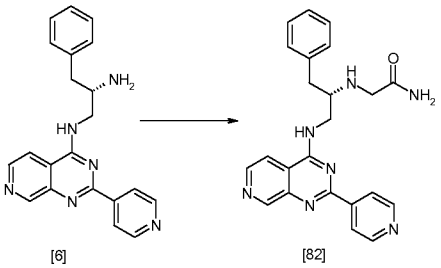
Synthesis of (2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1-methylpiperazine; formic acid [81]



[30] [81]

A stirred solution of 4-((S)-3-Benzyl-piperazin-1-yl)-5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [30] in CH_2Cl_2 (2 mL) was prepared. Paraformaldehyde (55 mg), acetic acid (6 mL, 0.121 mmol) and $CNBH_3$ (180 mg of MP-$CNBH_3$ with 2 mmol/g loading, 0.360 mmol) were added and the reaction was shaken at room temperature overnight. The resin was filtered off and the product was loaded onto a CSX cartridge, washing with methanol and eluting with ammonia in methanol. The ammonia fraction was concentrated and the residue purified then by prep LCMS. The appropriate fractions were combined and concentrated to give the title compound [81]. LCMS method: 1, RT:2.74 min, MI 427.22 [M+H]; ^{1}H NMR (1H, 300MHz, $CDCl_3$) 8.95 (s, 1H), 8.73 – 8.71 (d, 2H), 8.29 (s, 1H), 8.13 - 8.11 (d, 2H), 8.06 (s, 1H), 7.37 – 7.35 (m, 3H), 7.22 – 7.19 (m, 2H), 4.28 (d, 1H), 4.07 (d, 1H), 3.82 (s, 3H), 3.72 – 3.63 (m, 1H), 3.34 (dd, 1H), 3.23 – 3.15 (m, 2H), 2.76 – 2.69 (m, 1H), 2.63 (s, 3H), 2.60 – 2.51 (m, 2H).

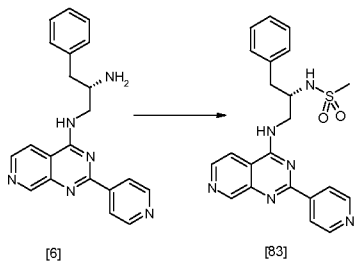
Synthesis of 2-{[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amino}acetamide [82]



[6] [82]

A mixture of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol), 2-Bromoacetamide (38.5 mg, 0.28 mmol), and potassium carbonate (77.5 mg, 0.56 mmol) in DMF (5 mL) was stirred at room temperature for 3 days. A further portion of 2-Bromoacetamide (38.5 mg, 0.28 mmol) was added and the reaction mixture stirred for a further 24 h. The solvent was removed by rotary evaporation and the residue dissolved in methanol (2 mL), filtered then purified by preparative HPLC (method B). The appropriate fractions were combined, evaporated, triturated with diethyl ether and dried in the vac oven to give the title compound [82]: LCMS method: 1, RT:4.49 min, MI 414 [M+H]; ^{1}H NMR (1H, 300MHz, d6-dmso) 9.16 (1H, s), 9.00 (1H, br m), 8.72 – 8.70 (2H, m), 8.64 – 8.62 (1H, m), 8.23 – 8.21 (1H, m), 8.10 – 8.08 (2H, m), 7.32 – 7.26 (5H, m), 7.03 (1H, br s), 3.89 – 3.81 (1H, m), 3.53 – 3.45 (1H, m).

Synthesis of N-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)methanesulfonamide [83]

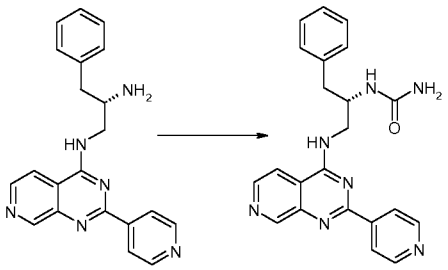


[6] [83]

To a solution of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol) and DIPEA (98 mL, 0.56 mmol) in CH_2Cl_2 (10 mL) at room temperature was added methane sulfonyl chloride (22 mL, 0.28 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with water and the organic phase separated, dried over $MgSO_4$ and purified by column chromatography on silica, eluting with

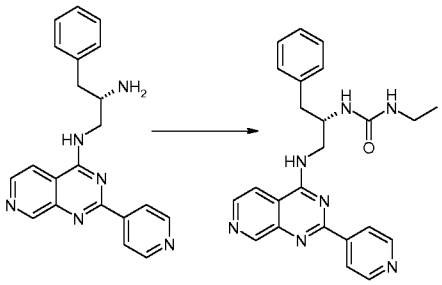
CH_2Cl_2 containing 0 – 10% Methanol. The appropriate fractions were combined and concentrated to give the title compound [83]: LCMS method: 1, RT: 4.04 min, MI 435 [M+H]; ^{1}H NMR (1H, 300MHz, d6-dmso) 9.18 (1H, s), 8.92 (1H, br t), 8.73 – 8.71 (2H, m), 8.65 (1H, d), 8.22 – 8.20 (2H, m), 8.16 (1H, d), 7.39 (1H, br s), 7.33 – 7.31 (4H, m), 7.30 – 7.24 (1H, m), 3.93 – 3.88 (2H, m), 3.69 – 3.61 (1H, m), 2.99 – 2.92 (1H, m), 2.83 – 2.76 (1H, m), 2.35 (3H, s).

Synthesis of (1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea [84]



A mixture of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol), potassium cyanate (227 mg, 2.8 mmol), and acetic acid (4 mL) in water (4 mL) was stirred at 50 °C for 3 hours. A further portion of potassium cyanate (227 mg, 2.8 mmol) was added and the reaction mixture heated in a sealed tube in the microwave at 100 °C for 30 min. The reaction mixture was concentrated under vacuum then partitioned between ethyl acetate and water. The target material was found to partially precipitate on the internal surface of the seperating funnel. This solid was collected and combined with the organic layer which was evaporated to dryness then dissolved in DMSO / Methanol (1 mL), the target material started to precipitate, water (2 mL) was added and the solid was collected by filtration then dried in the vac oven to give (the title compound [84]: LCMS method: 1, RT:4.54 min, MI 398 [M+H];. ^{1}H NMR (1H, 300MHz, d6-dmso) 9.18 (1H, s), 8.99 (1H, br t), 8.74 – 8.72 (2H, m), 8.64 (1H, d), 8.28 – 8.25 (2H, m), 8.12 (1H, d), 7.32– 7.19 (5H, m), 6.05 (1H, d), 5.48 (2H, s), 4.29 – 4.23 (1H, m), 3.88 – 3.80 (1H, m), 3.69 – 3.60 (1H, m), 2.94 – 2.88 (1H, m), 2.83 – 2.76 (1H, m).

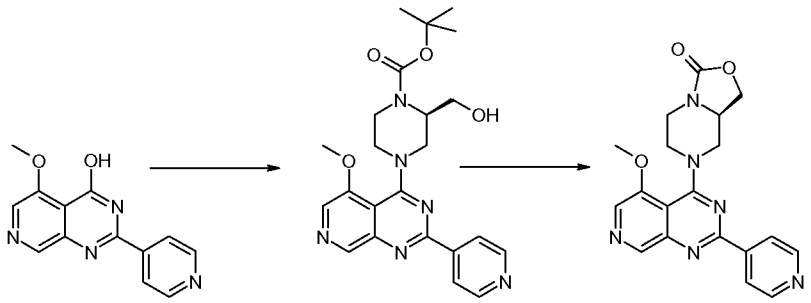
Synthesis of 3-ethyl-1-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea [85]



[6] [85]

A solution of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol) and ethyl isocyanate (19 mg, 0.27 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 1 h. The reaction mixture was concentrated by rotary evaporation and the residue purified by column chromatography on silica, eluting with CH_2Cl_2 containing 0 – 10% MeOH. The appropriate fractions were combined, evaporated and the residue triturated with diethyl ether then dried in the vacuum oven to give the title compound [85]. LCMS method: 1, RT:4.20 min, MI 428 [M+H]; ^{1}H NMR (1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.94 (1H, br t), 8.74 – 8.72 (2H, m), 8.64 (1H, d), 8.28 – 8.24 (2H, m), 8.13 (1H, d), 7.32– 7.20 (5H, m), 5.86 (1H, d), 5.79 (1H, t), 4.29 – 4.22 (1H, m), 3.90 – 3.83 (1H, m), 3.70 – 3.61 (1H, m), 2.94 – 2.77 (2H, m), 0.84 (3H, t).

Synthesis of (3aR)-5-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-1H-[1,3]oxazolo[3,4-a]piperazin-1-one [86]



[A003] [A046] [86]

(R)-2-Benzyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A046]

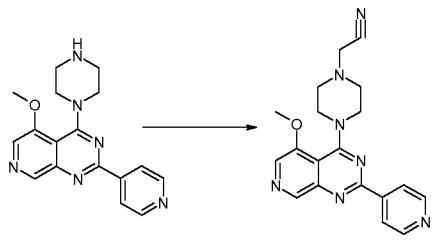
To a solution of 2-Pyridin-4-yl-pyrido[2,3-d]pyrimidin-4-ol [A003] (0.2g, 0.78 mmol) in DMA 93 mL), 2,4,6-Triisopropylbenzenesulfonyl chloride (0.26 g, 0.86 mmol), Et_3N (0.22 mL, 1.57 mmol) and DMAP (10 mg) were added successively. The mixture was stirred at rt

for 2h and (R)-2-Hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (0.2g, 0.94 mmol) was added. The reaction was stirred overnight and the solvent was removed under reduced pressure. The product was purified by flash chromatography using 0 to 8% MeOH / DCM to give the title compound [A046] (0.14g, 39% yield). LCMS method: 1, RT:4.41 min, MI 453.27 [M+H].

(3aR)-5-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-1H-[1,3]oxazolo[3,4-a]piperazin-1-one [86]

A solution of (R)-2-Hydroxymethyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A046] (20 mg, 0.044 mmol) in CH_2Cl_2 was added drop-wise to a stirred solution of DAST (11 mL, 0.088 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred overnight. Aqueous $NaHCO_3$ was added the organic phase separated, loaded onto a SCX cartridge, washed with MeOH and eluted with ammonia in methanol. The product was purified purified by preparative HPLC (method A) . The appropriate fractions were combined and concentrated to give the title compound [86]: LCMS method: 1, RT:2.95 min, MI 379 [M+H]; ^1H, NMR (1H, 300MHz, $CDCl_3$): 9.03 (s, 1H), 8.60 (d, 2H), 8.29 (d, 2H), 8.24 (s, 1H), 4.50 (m, 2H), 4.18 (d, 1H), 4.09 (m, 4H), 3.97 (dd, 1H), 3.31 (td, 1H), 3.16 (td, 1H), 3.10 (dd, 1H).

Example [87]: Synthesis of 2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}acetonitrile [87]



[31] [87]

To a stirred mixture of 1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [31] (90 mg, 0.28 mmol) and NEt_3 (78 mL, 0.56 mmol) in DMA (2 mL) was added Chloroacetonitrile (26 mL, 0.42 mmol) and the mixture was stirred at room temperature overnight. The crude reaction mixture was diluted with water and extracted with CH_2Cl_2 (2 x 5 mL), the organic extracts were combined washed with sat $NaHCO_3$ (2 x 10 mL) brine (10 mL) dried $MgSO_4$ filtered and evaporated to give a brown oil which was purified by SXC-2

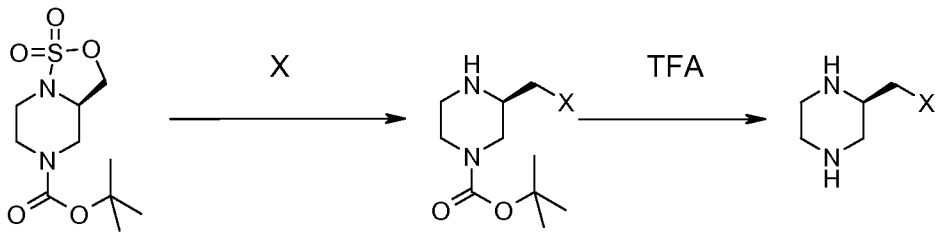
ion exchange (1 g) to give the title compound [87] as a pale yellow solid (0.085 g, 90% yield). LCMS method: 1, RT:4.90 min, MI 362 [M+H]; ^{1}H NMR (1H, 300MHz, $CDCl_3$): 9.02 (1H, s), 8.97 – 8.77 (2H, m), 8.36 – 8.34 (2H, m), 8.22 (s, 1H), 4.11 (3H, s), 3.81 (4H, br t), 3.65 (2H, s), 2.83 (4H, br t).

General synthesis of 2-substituted-piperazine derivatives of general formula [F-008b]

Scheme A2

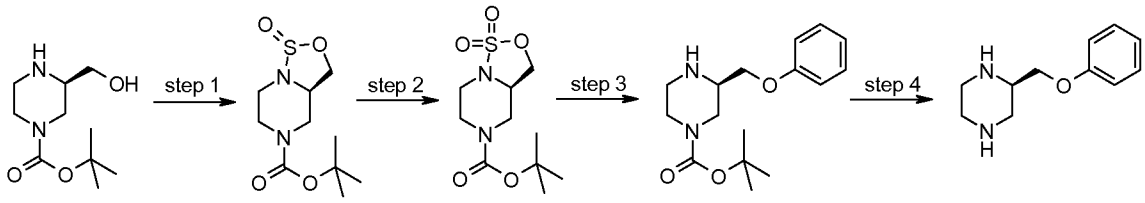
2-substituted piperazine derivatives of general formula [F-008b] were prepared by the reaction of (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A049] with a phenol in the presence of a strong base such as sodium hydride or potassium cyanide in a polar aprotic solvent such as DMF to give the 2-substituted piperazine derivatives of general formula [F-008a]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release resin, followed by chromatographic purification. The N-Boc derivatives of general formula [F-008a] were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC to give the 2-substituted-piperazine derivatives of general formula [F-008b].

Scheme A2



[A049] [F-008a] [F-008b]

Syntheisis of (R)-2-Phenoxymethyl-piperazine [A047]



[A048] [A049] [A050] [A047]

(R)-1-Oxo-tetrahydro-2-oxa-1λ^4-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048]

A solution of (R)-3-Hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (5.00 g, 23.118 mmol) in CH_2Cl_2 (330 mL) was prepared and cooled to 0 °C. Imidazole (6.295 g, 92.472 mmol) and triethylamine (7.06 mL, 50.860 mmol) were added followed drop-wise addition of thionyl chloride (1.94 mL, 26.586 mmol) as a solution in CH_2Cl_2 (20 mL) over 20 min. The reaction mixture was allowed to warm to room temperature (ice bath not removed) and the reaction mixture stirred at room temperature for 3 days. The reaction mixture was diluted with water (250 mL) and the organic phase separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic portions dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by chromatography on silica, eluting with cyclohexane containing 0 - 50% EtOAc. The appropriate fractions were combined and concentrated to give the title compound [A048] (5.196 g, 86%) as a pale yellow oil that solidified on standing. ^{1}H NMR (1H, 400MHz, d6-dmso) 4.81 (1H, dd), 4.58 (1H, dd), 4.44 (1H, dd), 4.28 (1H, br d), 4.12 (1H, br d), 4.02 (1H, br d), 3.93 – 3.87 (2H, m), 3.67 – 3.56 (2H, m), 3.46 – 3.34 (2H, m), 3.14 – 3.06 (1H, d), 3.01 – 2.69 (4H, br m), 2.55 (1H, dt), 1.42 (s, 9H), 1.41 (s, 9H).

(R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A049]

A stirred solution of (R)-1-Oxo-tetrahydro-2-oxa-1λ^4-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048] (2.99 g, 11.409 mmol) in anhydrous MeCN (25 mL) was prepared under nitrogen and cooled to 0 °C. Sodium (meta)periodate (2.464 g, 11.523 mmol) was added followed by ruthenium (III) chloride hydrate (24 mg, 0.114 mmol) (reaction mixture turns brown) and water (25 mL). The reaction mixture was stirred at 0 °C for 10 min

and then removed from ice bath and stirred at room temperature for 10 min. TLC shows complete conversion to a new, slightly more polar spot. The reaction mixture was diluted with sat. $NaHCO_3$ (aq) (100 mL) and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic extracts were dried and concentrated by rotary evapoartion. The residue was purified by chromatography on silica, eluting with cyclohexane containing 0 - 50% EtOAc to give the title compound [A049] (1.72 g, 54%) as a pale yellow solid. ^{1}H NMR (1H, 500MHz, $CDCl_3$) 4.63 (1H, dd,), 4.25 - 4.07 (3H, overlapping t and broad m), 3.67 - 3.61 (1H, m), 3.45 (1H, br. d, J = 11.2 Hz), 3.13 (1H, br. s), 2.98 - 2.94 (2H, br. m), 1.47 (9H, s).

(R)-3-Phenoxymethyl-piperazine-1-carboxylic acid tert-butyl ester [A050]

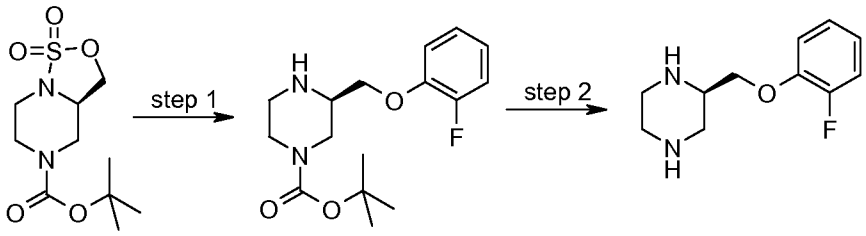
A solution of (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A049] (200 mg, 0.719 mmol) in anhydrous DMF (5 mL) was prepared under nitrogen. Sodium phenolate (88 mg, 0.754 mmol) was added and the reaction mixture heated to 50 °C overnight. A further 0.25 equivalents of sodium phenolate was added and heating continued for a further 5 hours. The reaction mixture was cooled to room temperature and 2 mL of 2M HCl (aq) was added. The mixture was stirred at room temperature for 1 hour. The reaction mixture was loaded onto a 10 g SCX cartridge, washing with methanol and eluting with 7N ammonia in MeOH. The ammonia fractions were combined and concentrated under reduced pressure. The residue was purified by chromatography on silica, eluting with CH_2Cl_2 containing 0 - 10% MeOH. The appropriate fractions were combined and concentrated to give the title compound [A00?] (75 mg, 36%) as a colourless oil. LCMS method: 1, RT:2.85 min, MI 293 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.31 – 7.24 (2H, m), 6.97 (1H, t), 6.91 (2H, d), 4.05 (1H, br s), 3.97 – 3.95 (2H, m), 3.88 – 3.85 (1H, m), 3.09 (1H, br s), 3.04 – 3.01 (1H, br m), 2.96 – 2.91 (1H, br m), 2.83 – 2.74 (1H, br m), 2.74 (1H, br s), 2.14 (1H, br s)1.48 (9H, s).

(R)-2-Phenoxymethyl-piperazine [A047]

A solution of (R)-3-Phenoxymethyl-piperazine-1-carboxylic acid tert-butyl ester [A050] (98 mg, 0.332 mmol) in anhydrous dioxane (1 mL) was prepared and 4M HCl in dioxane (5 mL) was added. The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated by rotary evaporation to give a pale pink solid. The product was dissolved in MeOH and loaded onto a SCX cartridge, washing with MeOH and eluting with 7N ammonia in MeOH. The ammonia fraction was concentrated by rotary evaporation to

give the title compound [A047] (58 mg, 91%) as a pale oil that crystalised on standing. LCMS method: 1, RT:0.56 min, MI 193 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.30 – 7.27 (2H, m), 6.97 – 6.94 (1H, m), 6.91 – 6.90 (2H, m), 3.92 – 3.90 (1H, m), 3.83 – 3.83 (1H, m), 3.17 – 3.12 (1H, m), 3.07 – 3.03 (2H, m), 2.99 – 2.96 (1H, m), 2.92 – 2.87 (1H, m), 2.84 – 2.79 (1H, m) 2.63 (1H, dd).

Synthesis of (R)-2-(2-Fluoro-phenoxymethyl)-piperazine [A051]



[A048] [A052] [A051]

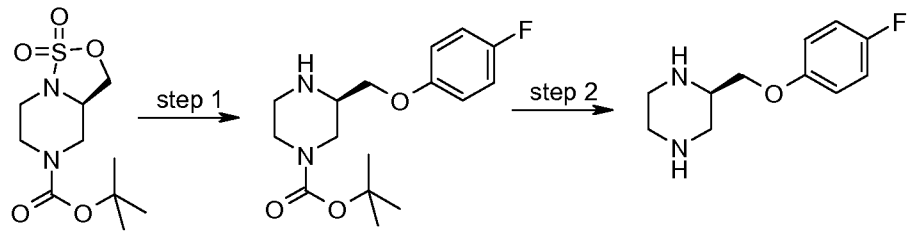
(R)-3-(2-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A052]

A suspension of sodium hydride (69 mg, 1.726 mmol) in anhydrous DMF (5 mL) was prepared and 2-fluorophenol (0.15 mL, 1.726 mmol) added dropwise. The reaction mixture was stirred at room temperature for 10 min then (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A051] (400 mg, 1.438 mmol) was added. The reaction mixture was heated to 50 °C overnight. The reaction mixture was cooled to room temperature and 2M HCl (aq) (1.4 mL, 2.875 mmol) was added. The reaction mixture was stirred at room temperature for 1.5 h. The reaction mixture was loaded onto a SCX cartridge, washing with methanol and eluting with 7N ammonia in MeOH. The ammonia fractions were combined and concentrated by rotary evaporation. The residue was purified by chromatography on silica, eluting with CH_2Cl_2 containing 0 - 10% MeOH. The appropriate fractions were combined and concentrated to give the title compound [A052] (318 mg, 71%) as a colourless oil. LCMS method: 1, RT:2.92 min, MI 311 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.10 – 7.04 (2H, m), 6.99 – 6.91 (2H, m), 4.04 – 3.89 (4H, m and overlapping br s), 3.14 – 3.11 (1H, m), 3.03 (1H, br d), 2.96 (1H, br t), 2.83 – 2.79 (1H, m), 2.75 (1H, br s), 2.23 (1H, br s), 1.48 (9H, s).

(R)-2-(2-Fluoro-phenoxymethyl)-piperazine [A051]

Following the procedure described in scheme A2, (R)-3-(2-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A052] (310 mg, 1.00 mmol) was treated with 4M HCl in dioxane (2 mL) to give the title compound [A051] (196 mg, 93%) as a pale yellow oil. LCMS method: 1, RT:0.75 min, MI 211 [M+H];LCMS method 1LCMS5, RT: 0.75 min, MI: 211 [M+1]. ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.10 – 7.03 (2H, m), 6.98 – 6.89 (2H, m), 4.00 – 3.97 (1H, m), 3.91 – 3.88 (1H, m), 3.23 – 3.18 (1H, m), 3.08 – 3.03 (2H, m), 3.00 – 2.98 (1H, m), 2.94 – 2.89 (1H, m), 2.85 – 2.80 (1H, m), 2.66 – 2.61 (1H, m).

Synthesis of (R)-2-(4-Fluoro-phenoxymethyl)-piperazine [A053]



[A048] [A054] [A053]

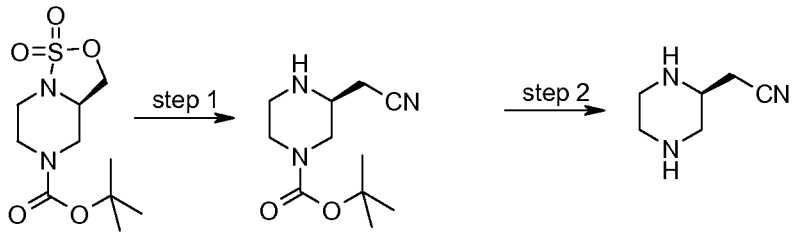
(R)-3-(4-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A054]

Following the procedure described in Scheme A2 step 1, (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048] (400 mg, 1.438 mmol) was reacted with 4-fluorophenol (193 mg, 1.726 mmol) to give the title compound [A054] (100 mg, 22%) as a colourless oil. LCMS method: 1, RT:3.00 min, MI 311 [M+H];. ^{1}H NMR (1H, 500MHz, $CDCl_3$) 6.99 – 6.96 (2H, m), 6.85 – 6.83 (2H, m), 4.06 (1H, br s), 3.95 (1H, br s), 3.95 – 3.90 (1H, m), 3.84 – 3.80 (1H, m), 3.10 – 3.05 (1H, m), 3.03 (1H, br d), 2.93 (1H, br t), 2.83 – 2.78 (1H, m), 2.72 (1H, br s), 2.10 (1H, br s), 1.48 (9H, s).

(R)-2-(4-Fluoro-phenoxymethyl)-piperazine [A053]

Following the procedure described in example Scheme A2, step 4, (R)-3-(4-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A054] (100 mg, 0.322 mmol) was treated with 4M HCl in dioxane (2 mL) to give the title compound [A053] (68 mg, 100%) as a colourless oil that solidified on standing. LCMS method: 1, RT:0.59 min, MI 211 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 6.99 – 6.95 (2H, m), 6.85 – 6.82 (2H, m), 3.88 – 3.86 (1H, m), 3.81 – 3.78 (1H, m), 3.15 – 3.10 (1H, m), 3.05 – 3.02 (2H, m), 2.98 – 2.96 (1H, m), 2.91 – 2.86 (1H, m), 2.83 – 2.78 (1H, m), 2.63 – 2.58 (1H, m).

Synthesis of (S)-Piperazin-2-yl-acetonitrile [A055]



[A048] [A056] [A055]

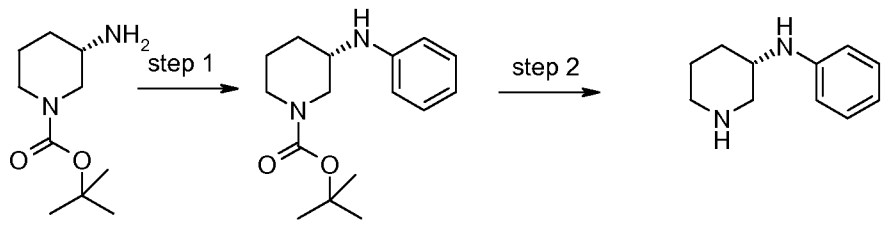
(S)-3-Cyanomethyl-piperazine-1-carboxylic acid tert-butyl ester [A056]

Following the procedure described in Scheme A1, step 3, (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048] (1.52 g, 5.46 mmol) was reacted with KCN (356 mg, 5.46 mmol) to give the title compound [A056] (850 mg, 69%). ^{1}H NMR (1H, 500MHz, $CDCl_3$) 3.95 (1H, br s), 3.84 (1H, br d), 3.03 – 2.92 (3H, m), 2.82 – 2.75 (1H, m), 2.70 (1H, br s), 2.51 – 2.41 (2H, m), 1.49 (9H, s). LCMS method: 1, RT:1.39 min, MI 226 [M+H].

(S)-Piperazin-2-yl-acetonitrile [A055]

Following the procedure described in example Scheme A2, step 4, (S)-3-Cyanomethyl-piperazine-1-carboxylic acid tert-butyl ester [A056] (800 mg, 3.55 mmol) was treated with 4M HCl in dioxane to give the title compound [A055] (434 mg, 98%) as a pale orange solid. LCMS method: 1, RT:0.49 min, MI 126 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 3.06 – 2.99 (3H, m), 2.93 – 2.90 (1H, m), 2.87 – 2.82 (1H, m), 2.77 – 2.72 (1H, m), 2.56 – 2.51 (1H, m), 2.44 – 2.42 (2H, m).

Syntheiss of Phenyl-(S)-piperidin-3-yl-amine [A057]



[A058] [A057]

(S)-3-Phenylamino-piperidine-1-carboxylic acid tert-butyl ester [A058]

A solution of (S)-3-Amino-piperidine-1-carboxylic acid tert-butyl ester (500 mg, 2.497 mmol), Pd2(dba)3 (95 mg, 0.104 mmol) and 2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (61 mg, 0.156 mmol) in toluene (5 mL) was prepared under nitrogen. The solvent was degasses and sodium tert-butoxide (280 mg, 2.912 mmol) was added followed by bromobenzene (0.22 mL, 2.080 mmol). The reaction mixture was heated to 100 °C for 24 h. The reaction mixture was cooled to room temperature and concentrated by rotary evaporation. The residue was filtered through a plug of silica, eluting with CH_2Cl_2. The eluent was concentrated by rotary evaporation. The crude residue was purified by chromatography on silica, eluting with cyclohexane containing 5 - 50% EtOAc. The appropriate fractions were combined and concentrated to give the title compound [A058] (535 mg, 78%) as a pale yellow oil that solidified on standing. LCMS method: 1, RT:5.51 min, MI 227 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.20 – 7.17 (2H, m), 6.71 (1H, t), 6.64 (2H, d), 4.02 (1H, br s), 3.74 – 3.70 (1H, m), 3.63 (1H, br s), 3.39 (1H, br m), 3.09 (1H, br m), 2.89 (1H, br s), 2.02 – 1.99 (1H, m), 1.78 – 1.73 (1H, m), 1.59 – 1.51 (2H, m), 1.46 (9H, s).

Phenyl-(S)-piperidin-3-yl-amine [A057]

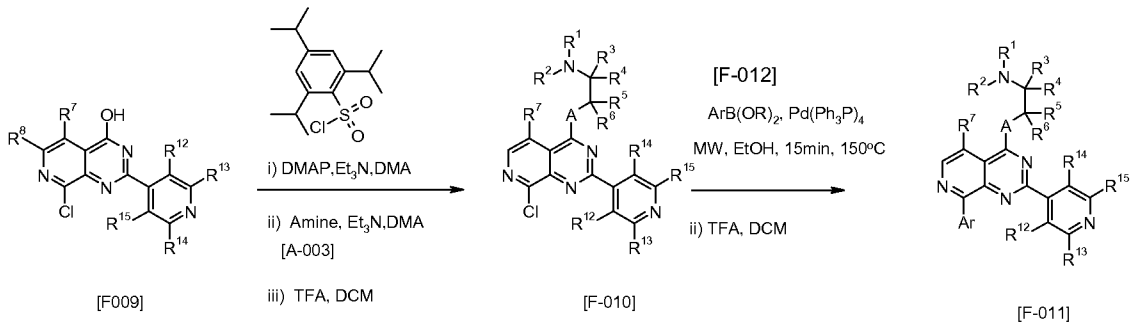
Following the procedure described in Scheme A2, step 4, (S)-3-phenylamino-piperidine-1-carboxylic acid tert-butyl ester [A058] (138 mg, 0.5 mmol) was treated with 4 HCl in dioxane (2 mL) to give the title compound [A057] (85 mg, 97%) as a pale yellow oil. LCMS method: 1, RT:0.96 min, MI 177 [M+H].

General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-011] Scheme A3

4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] were prepared by the reaction of a 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [F-009] with with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidini-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-003], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature.

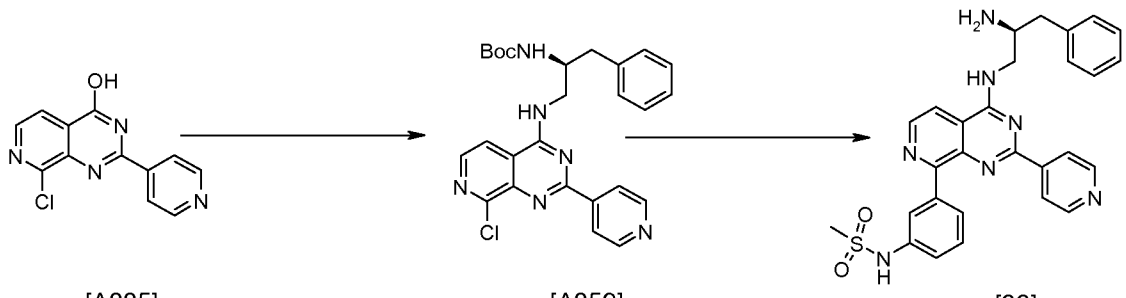
After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC. The 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] were reacted in a Suzuki type reaction utilising a suitable boronic acid or boronic ester, of general formula [F-012], a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ a base such as Et_3N, KOH, Na_2CO_3 or NaOH in a polar solvent such as EtOH, THF, DMA or dioxane at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme A3



[F009] [F-010] [F-011]

Synthesis of N-{3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-8-yl]-phenyl}-methanesulfonamide [88]



[A005] [A059] [88]

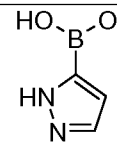
[(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059]

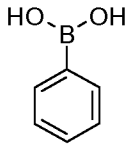
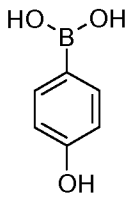
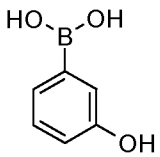
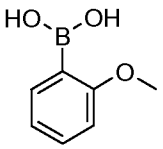
To a solution of 2-Pyridin-4-yl-pyrido[2,3-d]pyrimidin-4-ol [A005] (1 g, 3.8 mmol) in DMA (15 mL), 2,4,6-Triisopropylbenzenesulfonyl chloride (1.3g, 4.25 mmol), Et_3N (1.1 mL, 7.73 mmol) and DMAP (0.1 g) were added successively. The mixture was stirred at rt for 1h then ((S)-2-Amino-1-benzyl-ethyl)-carbamic acid tert-butyl ester (1.16 g, 4.64 mmol) was added. The reaction was stirred overnight and the solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography (SP1 [eluent: DCM/MeOH: 1/0 then 95/5 then 9/1]) to give the title compound: LCMS method: 1, RT:5.76 min, MI 492 [M+H]

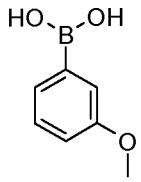
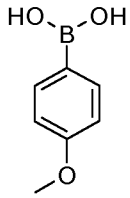
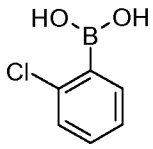
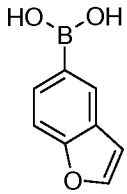
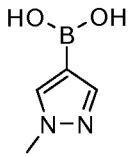
N-{3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-8-yl]-phenyl}-methanesulfonamide [88]

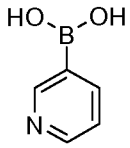
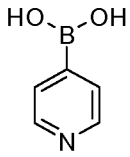
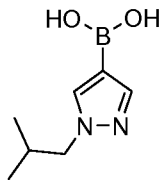
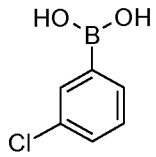
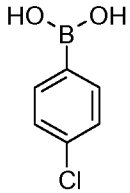
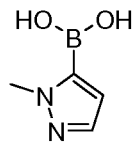
A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07g, 0.142mmol), 3-(methanesulfonylamino)phenylboronic acid pinacol ester (0.06g, 0.2mmol), Pd(Ph3P)4 (0.017g, 0.014mmol), aq K3PO4 (0.5M, 0.57mL, 0.28mmol) and DMA (1mL). The vial was heated under microwave irradiations (150°C, 10min). The solvent was removed under reduced pressure. The crude was purified by Column chromatography (Eluent: DCM/MeOH: 1:0 to 9/1). The purified compound was solubilised in DCM (2mL) and TFA (0.5mL) was added. The solution was stirred 3h and then was poured onto SCX2 column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M which was used without further purification to give the title compound [88]: LCMS method: 1, RT:3.01 min, MI 526 [M+H]; NMR 1H (1H, 300MHz, d6-dmso) 8.70 (d, 2H), 8.68 (d, 1H), 8.25 (d, 2H), 8.14 (d, 1H), 8.04 (d, 2H), 7.37-7.24 (m, 7H), 3.91-3.86 (m, 1H), 3.46-3.33 (m, 2H), 3.10 (s, 3H), 2.77-2.69 (m, 2H).

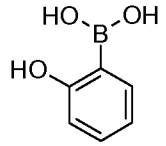
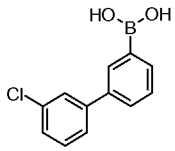
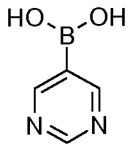
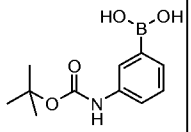
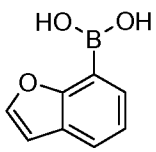
The following compounds were synthesised according to the general synthesis shown in scheme [A3]:

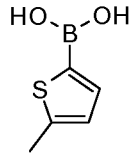
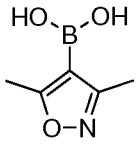
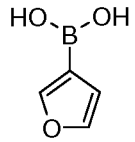
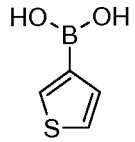
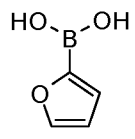
Ex	SM	Boronic acid	Analysis		Name
89	[A059]		Method 1: RT: 3.01 min,	(1H, 300MHz, d6-dmso) 8.76ppm (2H, dd), 8.67ppm (1H,d), 8.29ppm (1H, s), 8.15ppm (1H, d), 8.08ppm	N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-pyrazol-5-yl)-2-(pyridin-4-

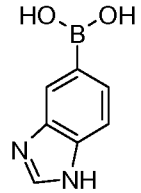
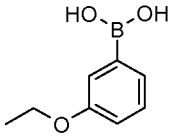
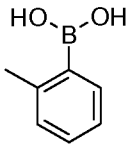
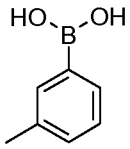
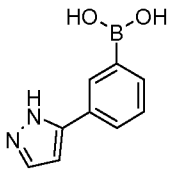
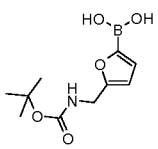
			MI: 423 [M+H]	(2H, dd), 7.71ppm (1H, d), 7.61ppm (1H, d), 7.41-7.30ppm (5H, m), 3.97ppm, (1H, d), 3.58ppm (2H, br s), 3.35ppm (2H, m), 2.97-2.80ppm (2H, m)	yl)pyrido[3,4-d]pyrimidin-4-amine
90	[A059]		Method 1: RT: 3.62 min, MI: 433 [M+H]	(1H, 300MHz, d6-dmso) 9.47ppm (1H, br s), 8.70ppm (1H, d), 8.67ppm (2H, dd), 8.42ppm (1H, br s), 8.18-8.14ppm (3H, m), 7.90ppm (2H, dd), 7.57-7.46ppm (3H, m), 7.42-7.31ppm (5H, m), 3.99ppm (1H, d), 3.67-3.51ppm (2H, m), 3.01ppm (1H, dd), 2.83ppm (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-8-phenyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
91	[A059]		Method 1: RT: 2.93 min, MI: 449 [M+H]	(1H, 300MHz, d6-dmso) 8.85-8.85ppm (1H, br s), 8.70ppm (2H, d), 8.62ppm (1H, d), 8.12ppm (2H, d), 8.04ppm (1H, d), 8.00ppm (2H, d), 7.39-7.27ppm (5H, m), 6.91ppm (2H, d), 3.97-3.86ppm (1H, m), 3.54-3.44ppm (2H, m), 2.83ppm (2H, br s)	4-(4-{[(2S)-2-amino-3-phenylpropyl]-amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol
92	[A059]		Method 1: RT: 3.00 min, MI: 449 [M+H]	(1H, 300MHz, d6-dmso) 8.73-8.69ppm (3H, t), 8.16ppm (1H, d), 8.04ppm (2H, d), 7.64-7.62ppm (2H, m), 7.36-7.23ppm (5H, m), 6.88ppm (1H, dd), 3.88ppm (1H, d), 3.46-3.30ppm (2H, m), 2.77-2.74ppm (2H, m)	3-(4-{[(2S)-2-amino-3-phenylpropyl]-amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol
93	[A059]		Method 1: RT: 3.16 min, MI: 463 [M+H]	(1H, 300MHz, d6-dmso) 8.65-8.63ppm (3H, t), 8.19ppm (1H, d), 7.87ppm (2H, d), 7.48ppm (1H, dt), 7.36-7.24ppm (5H, m), 7.17ppm (1H, d), 7.07ppm (1H, t), 3.92-3.84ppm (1H, dd), 3.61ppm (3H, s), 3.44-3.29ppm (2H, m), 2.77-	N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

				2.75ppm (2H, m)	
94	[A059]		Method 1: RT: 3.54 min, MI: 463 [M+H]	(1H, 300MHz, d6-dmso) 8.70ppm (3H, d), 8.18ppm (1H, d), 8.02ppm (2H, d), 7.80-7.76ppm (2H, m), 7.45ppm (1H, t), 7.34-7.24ppm (5H, m), 7.07ppm (1H, dd), 3.88ppm (1H, d), 3.83ppm (3H, s), 3.43-3.33ppm (2H, m), 2.77-2.73ppm (2H, m)	N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
95	[A059]		Method 1: RT: 3.56 min, MI: 463 [M+H]	(1H, 300MHz, d6-dmso) 8.70ppm (2H, d), 8.65ppm (1H, d), 8.24 (2H, d), 8.10ppm (1H, d), 8.04ppm (2H, d), 7.36-7.23ppm (5H, m), 7.09ppm (2H, d), 3.89-3.84ppm (1H, m), 3.85ppm (3H, s), 3.44-3.30ppm (2H, m), 2.74ppm (2H, t)	N-[(2S)-2-amino-3-phenylpropyl]-8-(4-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
96	[A059]		Method 1: RT: 3.46 min, MI: 467 [M+H]	(1H, 300MHz, d6-dmso) 8.69ppm (2H, d), 8.63ppm (2H, dd), 8.28ppm (1H, d), 8.19-8.16ppm (1H, m), 8.01ppm (1H, d), 7.84ppm (2H, dd), 7.64-7.60ppm (1H, m), 7.36-7.23ppm (5H, m), 3.92-3.84ppm (1H, m), 3.44-3.25ppm (2H, m), 2.76-2.74ppm (2H, m)	N-[(2S)-2-amino-3-phenylpropyl]-8-(2-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
97	[A059]		Method 1: RT: 3.69 min, MI: 473 [M+H]	(1H, 300MHz, d6-dmso) 8.68 (d, 3H), 8.48 (d, 1H), 8.18-8.15 (m, 2H), 8.06 (d. 1H), 8.01 (d, 1H), 7.73 (d, 1H), 7.36-7.26 (m, 5H), 7.10 (d, 1H), 3.88 (d, 1H), 3.45-3.37 (m, 2H), 2.77-2.73 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
98	[A059]		Method 1: RT: 2.98 min, MI: 437 [M+H]	(1H, 300MHz, d6-dmso) 8.77 (s, 1H), 8.75 (d, 2H), 8.54 (d, 1H), 8.44 (s, 1H), 8.12 (d, 2H), 7.97 (d, 1H), 7.36-7.27 (m,5H), 3.99 (s, 3H), 3.87 (d, 1H), 3.43-3.35 (m, 2H), 2.77-2.74 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

99	[A059]		Method 1: RT: 2.58 min, MI: 434 [M+H]	(1H, 300MHz, d6-dmso) 9.33 (d, 1H), 8.73-8.66 (m, 3H), 8.51 (td, 1H), 8.21 (d, 1H), 7.98 (d, 2H), 7.57 (dd, 1H), 7.37-7.27 (m, 5H), 3.92-3.84 (m, 1H), 3.47-3.38 (m, 2H), 2.78-2.76 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(pyridin-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
100	[A059]		Method 1: RT: 2.41 min, MI: 434 [M+H]	(1H, 300MHz, d6-dmso) 8.77-2.75 (m, 3H), 8.71 (d, 2H), 8.28 (d, 1H), 8.15 (d, 2H), 8.02 (d, 2H), 7.36-7.26 (m, 5H), 3.91-3.86 (m, 1H), 3.46-3.36 (m, 2H), 2.78-2.73 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-2,8-bis(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
101	[A059]		Method 1: RT: 3.90 min, MI: 479 [M+H]	(1H, 300MHz, d6-dmso) 8.75-8.73 (m, 3H), 8.54 (d, 1H), 8.49 (s, 1H), 8.11 (d, 2H), 7.98 (d, 1H), 7.35-7.25 (m, 5H), 4.07 (d, 2H), 3.88-3.84 (m, 1H), 3.43-3.36 (m, 2H), 2.74-2.70 (m, 2H), 2.23-2.14 (m, 1H), 0.91 (d, 6H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
102	[A059]		Method 1: RT: 4.05 min, MI: 466 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
103	[A059]		Method 1: RT: 4.08 min, MI: 467 [M+H]	(1H, 300MHz, d6-dmso) 8.72-8.62 (m, 3H), 8.35 (s, 1H), 8.23 (d, 2H), 8.19 (d, 1H), 7.94 (d, 2H), 7.62 (d, 2H), 7.39-7.32 (m, 5H), 4.02-3.94 (m, 1H), 3.59-3.50 (m, 2H), 3.00-2.92 (m, 1H), 2.85-2.80 (m, 1H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(4-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
104	[A059]		Method 1: RT: 2.72 min, MI: 437 [M+H]	(1H, 300MHz, d6-dmso) 8.72 (d, 2H), 8.72 (d, 1H), 8.22 (d, 1H), 8.04 (d, 2H), 7.61 (d, 1H), 7.35-7.23 (m, 5H), 7.09 (d, 1H), 4.02 (s, 3H), 3.90-3.85 (m, 1H), 3.44-3.33 (m, 2H), 2.75-2.71 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-

					amine
105	[A059]			(1H, 300MHz, d6-dmso) 8.68-8.74 (m, 3H), 8.38 (d, 1H), 8.35 (s, 1H), 8.22 (d, 1H), 7.96 (d, 2H), 7.32-7.40 (m, 6H), 6.98-7.04 (m, 2H), 3.98 (d, 1H), 3.50-3.58 (m, 2H), 2.95 (dd, 1H), 2.85 (dd, 1H).	2-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol
106	[A059]		Method 1: RT: 4.74 min, MI: 543 [M+H]	(1H, 300MHz, d6-dmso) 8.75 (d, 1H), 8.66 (d, 2H), 8.52 (s, 1H), 8.26-8.18 (m, 2H), 7.99 (d, 2H), 7.83 (d, 1H), 7.80 (s, 1H), 7.72 (d, 1H), 7.67 (t, 1H), 7.52 (t, 1H), 7.46 (d, 1H), 7.38-7.30 (m, 5H), 4.00-3.92 (m, 1H), 3.58-3.52 (m, 2H), 2.91-2.86 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(3-chlorophenyl)-phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
107	[A059]		Method 1: RT: 4.73 min, MI: 543 [M+H]	(1H, 300MHz, d6-dmso) 8.74 (d, 1H), 8.70 (d, 2H), 8.34)d, 2H), 8.27 (d, 2H), 8.18 (d, 1H), 8.01 (d, 2H), 7.88 (d, 2H), 7.83 (d, 2H), 7.57 (d, 2H), 7.40-7.31 (m, 5H), 3.99-3.93 (m, 1H), 3.60-3.53 (m, 2H), 2.89-2.82 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[4-(4-chlorophenyl)-phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
108	[A059]		Method 1: RT: 2.83 min, MI: 435 [M+H]	(1H, 300MHz, d6-dmso) 9.50 (s, 2H), 9.27 (s, 1H), 8.71 (d, 1H), 8.69 (d, 2H), 8.22 (d, 1H), 7.93 (d, 2H), 7.37-7.28 (m, 5H), 3.92-3.85 (m, 1H), 3.47-3.38 (m, 2H), 2.79-2.76 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(pyrimidin-5-yl)pyrido[3,4-d]pyrimidin-4-amine
109	[A059]		Method 1: RT: 2.43 min, MI: 448 [M+H]	(1H, 300MHz, d6-dmso) 8.69 (d, 2H), 8.65 (d, 1H), 8.13 (d, 1H), 8.04 (d, 2H), 7.38-7.26 (m, 7H), 7.17 (t, 1H), 6.68 (d, 1H), 5.16 (brs, 2H), 3.91-3.85 (m, 1H), 3.45-3.35 (m, 2H), 2.77-2.75 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(3-aminophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
110	[A059]		Method 1: RT: 4.07 min, MI:	(1H, 300MHz, d6-dmso) 8.78 (d, 2H), 8.72 (d, 1H), 8.53 (s, 1H), 8.16 (d, 3H), 7.90 (d, 1H), 7.71 (d, 1H), 7.43 (t, 1H), 7.36-7.26 (m, 6H), 3.92-	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-7-yl)-2-(pyridin-4-yl)pyrido[3,4-

			473 [M+H]	3.84 (m, 1H), 3.52-3.45 (m, 2H), 2.83-2.79 (m, 2H).	d]pyrimidin-4-amine
111	[A059]		Method 1: RT: 1.81 min, MI: 453 [M+H]	(1H, d6-DMSO, 500MHz) 8.67 (d, 2H), 8.30-8.16 (m, 1H), 8.01 (d, 2H), 7.36-7.24 (m, 7H), 6.82 (d, 1H), 3.86-3.73 (m, 1H), 2.75-2.72 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(5-methylthiophen-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
112	[A059]		Method 1: RT: 3.02 min, MI: 452 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(dimethyl-1,2-oxazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
113	[A059]		Method 1: RT: 3.42 min, MI: 426 [M+H] C	(1H, 300MHz, d6-dmso) 8.99 (d, 1H), 8.71 (d, 2H), 8.58 (d, 1H), 8.44 (s, 1H), 8.03 (d, 1H), 7.96 (d, 2H), 7.82 (t, 1H), 7.39-7.29 (m, 5H), 4.00-3.94 (m, 1H), 3.68-3.48 (m, 2H), 303 (dd, 1H), 2.84 (dd, 1H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
114	[A059]		Method 1: RT: 3.55 min, MI: 439 [M+H]	(1H, 300MHz, d6-dmso) 8.96 (d, 1H), 8.74 (d, 2H), 8.63 (d, 1H), 8.13-8.09 (m, 4H), 7.64 (dd, 1H), 7.36-7.25 (m, 5H), 3.92-3.85 (m, 1H), 3.45-3.36 (m, 2H), 2.76-2.71 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(thiophen-3-yl)pyrido[3,4-d]pyrimidin-4-amine
115	[A059]		Method 1: RT: 3.26 min, MI: 423 [M+H]	(1H, 300MHz, d6-dmso) 8.76 (d, 2H), 8.61 (d, 1H), 8.12-8.06 (m, 3H), 7.95 (s, 1H), 7.36-7.26 (m, 5H), 6.80-6.78 (m, 1H), 3.92-3.85 (m, 1H), 3.46-3.39 (m, 2H), 2.78-2.75 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

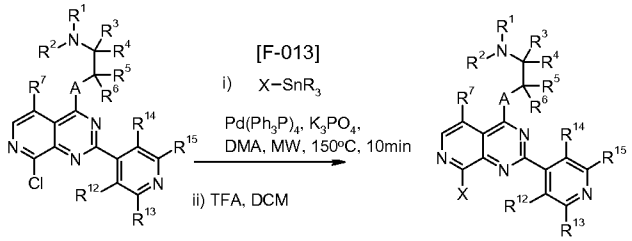
116	[A059]		Method 1: RT: 2.23 min, MI: 473 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-1,3-benzodiazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
117	[A059]		Method 1: RT: 3.72 min, MI: 477 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(3-ethoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
118	[A059]				N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
119	[A059]				N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
120	[A059]		Method 1: RT: 3.55 min, MI: 499 [M+H]	(1H, 300MHz, d6-dmso) 8.87 (brs, 1H), 8.70 (d, 1H), 8.67 (d, 2H), 8.18 (d, 1H), 8.14-8.09 (m, 3H), 7.91 (d, 1H), 7.77 (brs, 1H), 7.56 (t, 1H), 7.36-7.26 (m, 5H), 6.74 (d, 1H), 3.94-3.85 (m, 1H), 3.44-3.39 (m, 2H), 2.77-2.74 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(1H-pyrazol-5-yl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
121	[A059]				N-[(2S)-2-amino-3-phenylpropyl]-8-[5-(aminomethyl)-furan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-

					d]pyrimidin-4-amine

General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F011] Scheme A4

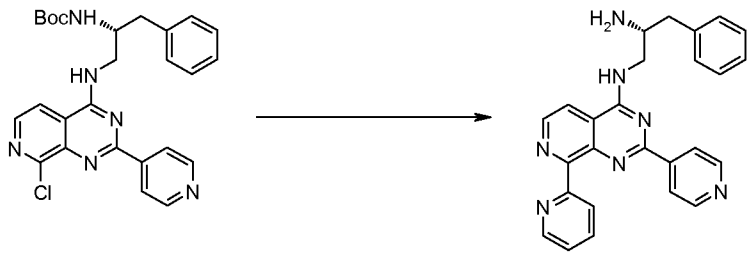
8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F011] were prepared by reaction of a 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] in a Stille type reaction utilising a suitable stannane of general formula [F013], a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ a base such as K_3PO_4, in a polar solvent such as DMA or dioxane at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme A4



[F-010] [F-011]

Synthesis of (R)-3-Phenyl-N^1-(2-pyridin-4-yl-8-pyridin-2-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [122]



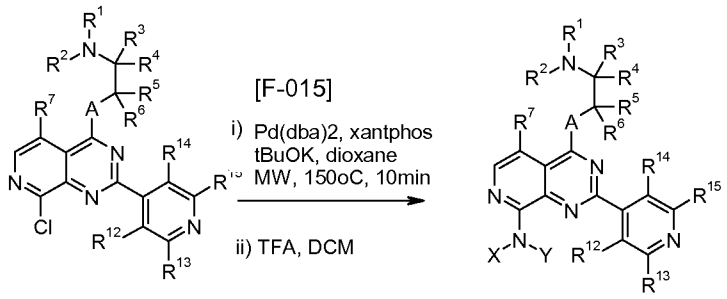
[A059] [122]

(R)-3-Phenyl-N^1-(2-pyridin-4-yl-8-pyridin-2-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [122]

A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07g, 0.142mmol), 2-(Tributylstannyl)pyridine (0.068g, 0.185mmol), $Pd(Ph_3P)_4$ (0.016g, 0.014mmol), LiCl (0.018 g, 0.428mmol) and DMA (1.5 mL). The mixture was heated under microwave irradiation (150oC, 10min) and the solvent was removed under reduced pressure. The crude was purified by Column chromatography (Eluent: DCM/MeOH: 1:0 to 9:1). The purified compound was solubilised in DCM and 0.5mL of TFA was added. The solution was stirred 3h and then was poured on a SCX column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M, the basic solvent was concentrated under reduced pressure to yield the title compound as a yellow solid which was was used without further purification: LCMS method: 1, RT:2.34 min, MI 434 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$); 8.70-8.76 (m, 2H), 8.63 (d, 2H), 8.42 (brs, 1H), 8.27 (d, 1H), 7.96 (dd, 1H), 7.93 (m, 1H), 7.81 (d, 2H), 7.50 (td, 1H), 7.32-7.52 (m, 5H), 4.00 (d, 1H), 3.51-3.60 (m, 2H), 3.01 (dd, 1H), 2.83 (dd, 1H).

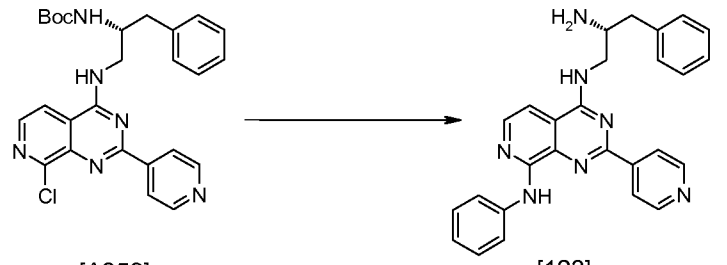
General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] Scheme A5

8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] were prepared by reaction of a 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] in a Buchwald type reaction utilising a suitable amine, of general formula [F-015], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.



[F-010] [F-014]

Synthesis of N^4-((R)-2-Amino-3-phenyl-propyl)-N^8-phenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine [123]

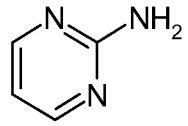
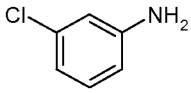
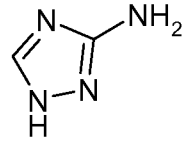


[A059] [123]

N^4-((R)-2-Amino-3-phenyl-propyl)-N^8-phenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine [123]

In a microwave vial, [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.05g 0.1 mmol) Aniline (0.015 g, 0.15 mmol), $Pd(dba)_2$ (0.003 g, 0.005mmol), Xantphos (0.006 g, 0.01 mmol), Sodium tert butoxide (0.02 g, 0. 2mmol) and dioxane (1.3 mL) were added successively. The microwave vial was heated under microwaves (150°C, 10min). The solvent was then removed under reduced pressure, DCM (2 mL) and TFA (0.5 mL) were added successively and the solution was stirred 3h. The solution was poured on a SCX2 column and was washed with MeOH. The compound was released using a 2M NH3/MeOH solution, and then was concentrated under reduce pressure. The crude was purified by preparative HPLC (method A) to yield the title compound [123]: LCMS method: 1, RT:3.53 min, MI 448 [M+H]; NMR (1H, 300MHz, d6-dmso): peaks might be underneath solvent peaks at 2.5 and 3.3 ppm. 9.35 (s, 1H), 8.71 (d, 2H), 8.35 (d, 2H), 8.03-8.08 (m, 3H), 7.46 (d, 1H), 7.27-7.38 (m, 7H), 7.02 (t, 1H), 3.86 (d, 1H), 2.70-2.78 (m, 2H).

The following compounds were synthesised according to the general synthesis shown in scheme [A5]:

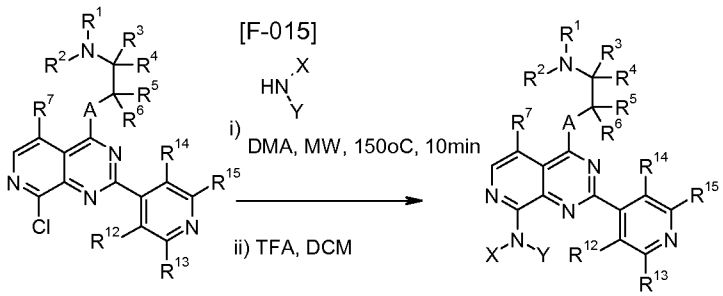
Ex	SM	Amine	Analysis		Name
124	[A059]		Method 1: RT: 2.16 min, MI: 450 [M+H]	(1H, 300MHz, d6-dmso): 8.70 (d, 2H), 8.64 (d, 2H), 8.34 (s, 1H), 8.25 (d, 1H), 8.04 (d, 2H), 7.70 (d, 1H), 7.40-7.33 (m, 5H), 7.10 (t, 1H), 3.97-3.92 (m, 1H), 3.58-3.50 (m, 2H), 2.99-2.93 (m, 1H), 2.87-2.80 (m, 1H).	4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(pyrimidin-2-yl)pyrido[3,4-d]pyrimidine-4,8-diamine
125	[A059]		Method 1: RT: 2.16 min, MI: 482 [M+H]		4-N-[(2S)-2-amino-3-phenylpropyl]-8-N-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidine-4,8-diamine
126	[A059]		Method 1: RT: 2.69 min, MI: 439 [M+H]		4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(1H-1,2,4-triazol-3-yl)pyrido[3,4-d]pyrimidine-4,8-diamine

General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] Scheme A6

8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] were prepared by reaction of a 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivative of general formula [F-010] in a nucleophilic aromatic substitution type reaction utilising a suitable amine [method A], thiol [method B] or phenol [method C] of general formula [F-015], and a base such as NaH in a polar aprotic solvent such as DMA or DMF at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

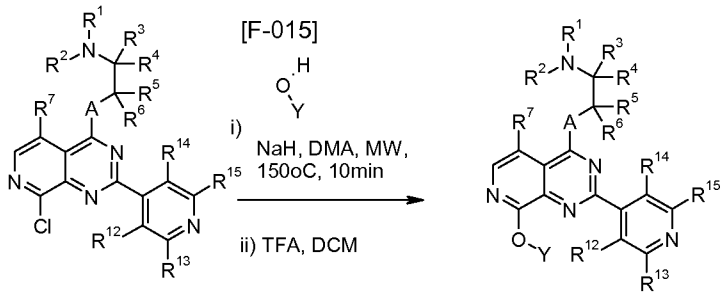
Scheme A6

Method A



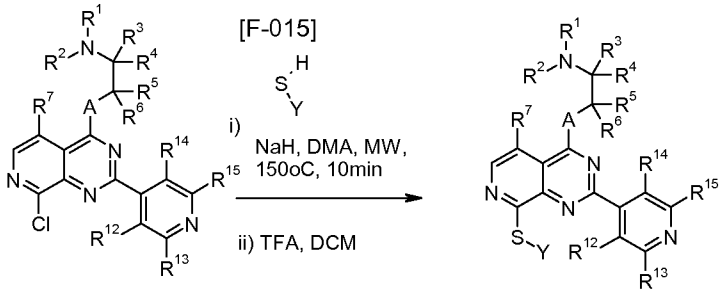
[F-010] [F-014]

Method B



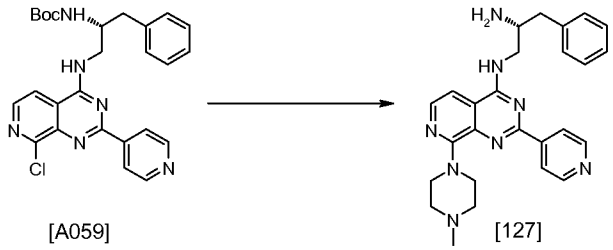
[F-010] [F-014]

Method C



[F-010] [F-014]

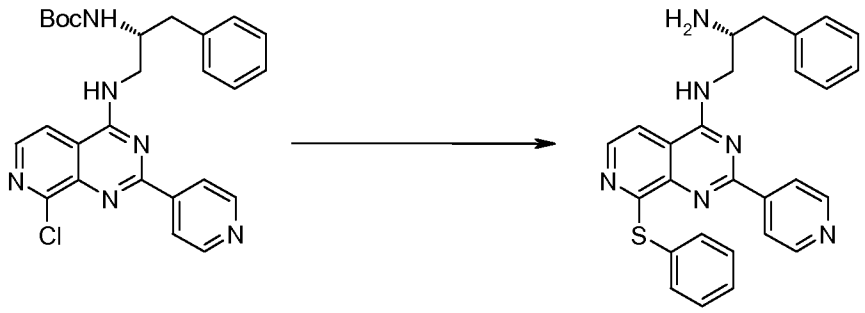
Synthesis of (R)-N^1-[8-(4-Methyl-piperazin-1-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine [127]



(R)-N^1-[8-(4-Methyl-piperazin-1-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine [127]

A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07 g, 0.142 mmol), N-methylpiperazine (0.031 mL, 0.285 mmol) and DMA (2 mL). The solution was heated under microwaves (150°C, 10min). 2 other equivalent of N-methylpiperazine (0.031 mL, 0.285 mmol) was added and the vial was heated again under microwaves (150°C, 10 min). The solvent was removed under reduced pressure and DCM (2 mL) and TFA (0.5 mL) were added successively. The solution was stirred 3h and then was poured on a SCX-2 column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M. The crude was then purified by preparative HPLC (method A) to yield the title compound [127]: LCMS method: 1, RT:1.55 min, MI 455 [M+H]; NMR (1H, 300MHz, d6-dmso): 9.17 (brs, 1H), 8.86 (d, 2H), 8.30 (s, 3H), 8.10 (d, 1H), 7.86 (d, 2H), 7.48 (d, 1H), 7.35-7.41 (m, 5H), 3.83-4.04 (m, 5H), 3.66-3.76 (m, 1H), 3.54-3.64 (m, 1H), 3.12 (dd, 1H), 2.86 (dd, 1H), 2.67-2.72 (m, 4H), 2.53 (s, 3H).

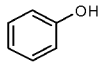
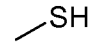
Synthesis of (R)-3-Phenyl-N^1-(8-phenylsulfanyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [128]



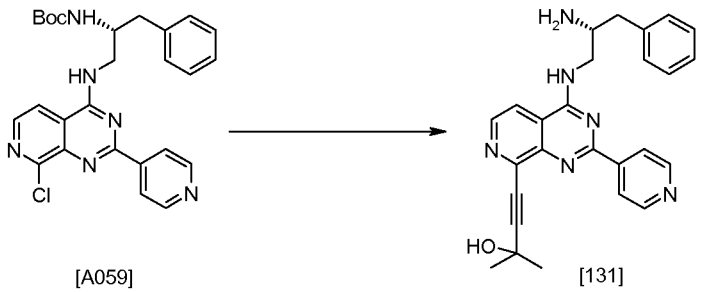
(R)-3-Phenyl-N^1-(8-phenylsulfanyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [128]

To a suspension of NaH (60% in mineral oil, 0.008 g, 0.2mmol) in DMF (2 mL), Thiophenol (0.02 g, 0.185 mmol) was added. The mixture was stirred 1h and [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07 g, 0.142 mmol) was added. The mixture was stirred overnight and water (0.3 mL) was added. The solvent were removed under reduced pressure and DCM (2 mL) and TFA (0.5mL) were added successively. The solution was stirred 3h and then was poured on a SCX-2 column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M. The crude was then purified by preparative HPLC (method A). To yield the title compound [128]: LCMS method: 1, RT:4.06 min, MI 465 [M+H]; NMR (1H, 300MHz, d6-dmso): 9.38 (brs, 1H), 8.72 (d, 2H), 8.23 (s, 3H), 8.03 (d, 2H), 7.89 (d, 1H), 7.58-7.61 (m, 2H), 7.36-7.47 (m, 6H), 3.98 (d, 1H), 3.56-3.73 (m, 2H), 3.05 (dd, 1H), 2.87 (dd, 1H).

The following compounds were synthesised according to the general synthesis shown in scheme [A6]:

Ex	Met-hod	SM	Nuc	Analysis		Name
129	B	[A059]		Method 1: RT: 3.39 min, MI: 449 [M+H]	(1H, 300MHz, d6-dmso): 9.43 (brs, 1H), 8.68 (d, 2H), 8.29 (s, 2H), 8.03 (d, 1H), 7.99 (d, 2H), 7.85 (d, 1H), 7.36-7.48 (m, 6H), 7.21-7.28 (m, 3H), 4.00 (d, 1H), 3.58-3.55 (m, 2H), 3.06 (dd, 1H), 2.81 -2.93 (m, 1H),	N-[(2S)-2-amino-3-phenylpropyl]-8-phenoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
130	C	[A059]		Method 1: RT: 3.43 min, MI: 403 [M+H]	(1H, 300MHz, d6-dmso): 9.58 (brs, 1H), 8.69 (d, 2H), 8.42 (d, 1H), 8.32 (s, 2H), 7.94 (d, 2H), 7.81 (d, 1H), 7.36-7.45 (m, 5H), 3.99 (d, 1H), 3.59-3.70 (m, 2H), 3.07 (dd, 1H), 2.81 (dd, 1H), 2.53 (s, 3H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(methylsulfanyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

Synthesis of 4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)-2-methylbut-3-yn-2-ol [131]



4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)-2-methylbut-3-yn-2-ol [131]

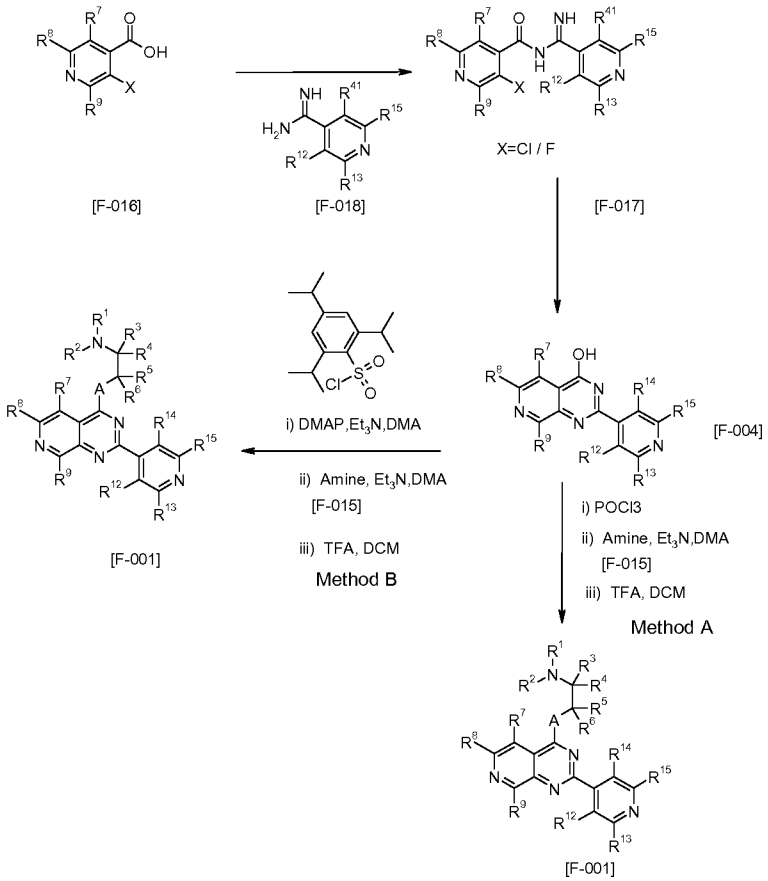
A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.05 g, 0.1 mmol), $Pd(PPh_3)_2Cl_2$ (0.007 g, 0.01 mmol), CuI (0.002 g, 0.01mmol), 2-methyl-3-butyn-2-ol (0.035 g, 0.037 mmol), Triphenylphosphine (0.005g, 0.02 mmol), Triethylamine (0.2 mL) and DMF (0.8 mL). The vial was heated under microwave (150°C, 10min). The solvent was removed under reduced pressure and DCM (2 mL) and TFA (1 mL) were added and the mixture was stirred 3h. The solution was poured on a SCX2 column and was washed with MeOH. The compound was released using a 2M NH3/MeOH solution, and then was concentrated under reduce pressure. The crude was purified by preparative HPLC (method A) to yield the title compound [131]: LCMS method: 1, RT:3.12 min, MI 439 [M+H]; NMR (1H, 300MHz, d6-dmso): 8.71 (d, 2H), 8.56 (d, 1H), 8.31 (brs, 1H), 8.15 (d, 1H), 8.08 (d, 2H), 7.41-7.31 (m, 5H), 3.97-3.92 (m, 1H), 3.59-3.50 (m, 2H), 2.99-2.90 (m, 1H), 2.86-2.79 (m, 1H), 1.59 (s, 6H).

General synthesis of substituted 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A7

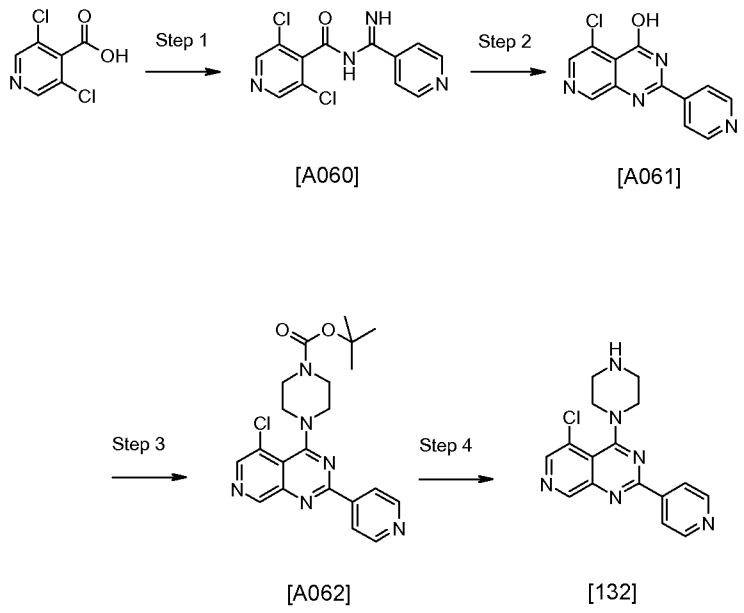
2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] were prepared by coupling of a ortho-halo-isonicotinic acid derivative of general formula [F-016] with an appropriately substituted 4-carbamimidoyl-pyridines of general formula [F-018] with a suitable coupling agent such as O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) in a polar aprotic solvent such as DMA or DMF. The isonicotinoyl-amidine derivative of general formula [F-017] were then cyclised to displace the relevant halogen group to yield the desired 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004]. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-

d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride and the intermediate 4-chloro derivative was then reacted with primary or secondary amino derivative of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A7



Synthesis of 5-Chloro-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [132]



Synthesis of 3,5-Dichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A060]

3,5-Dichloro-isonicotinic acid (10.4mmol, 1.997g), was dissolved in anhydrous DMF (50mL) at room temperature and HATU (10.4mmol, 3.95g), added in one portion and the mixture stirred for 5mins. Then DIPEA (28.6mmol, 5.0mL) was added in one portion and reaction stirred for 40 minutes. Pyridine-4-carboximidamide hydrochloride (9.52mmol, 1.5g) was added in one portion and reaction stirred at room temperature for 18 hours.

The reaction mixture was then poured into water (~250mL in total including rinses of reaction vessel) in a conical flask. The resultant mixture was stirred at room temperature for 90 minutes and the precipitate formed was filtered, washed with water (x2) and ether (x2). Then the solid was dried in vac oven for 4hrs to yield the title compound [A060] (2.359g), as a pale brown powder. LCMS method: 1, RT:3.31 min, MI 295 [M+H].

Synthesis of 5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061]

In a 25mL Biotage microwave vessel, under nitrogen, was added 3,5-Dichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A060] (1.5mmol, 0.443g), cesium carbonate (3.0mmol, 0.978g) and N,N'-Dibenzylethylenediamine (0.3mmol, 0.071mL). The mixture was stirred in anhydrous DMA (10mL), vigorously and iron (III) chloride (0.15mmol, 0.024g) added in one portion. Then the mixture was heated in the microwave at 120°C for 90mins. The reaction was allowed to cool to room temperature and acetic acid (12.0mmol, 0.69mL), added dropwise over about 5 minutes and the resulting mixture diluted with MeOH (10mL) and stirred at RT for 30mins. The mixture was added to a 10g SCX-2 cartridge and washed with methanol (~25-30mL). The cartridge was then washed with ammonia (2N in MeOH, 40mL) and the ammonia washes concentrated in vacuo to yield 5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one (130mg). The non-basic methanol washes of the SCX-2 cartridge were left standing overnight, forming a precipitate. This was filtered, washed with methanol (x1), and dried in a vacuum oven overnight to yield the title compound [A061] (13mg) as an off-white solid. LCMS method: 1, RT:2.12 min, MI 259 [M+H].

Synthesis of 4-(5-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A062]

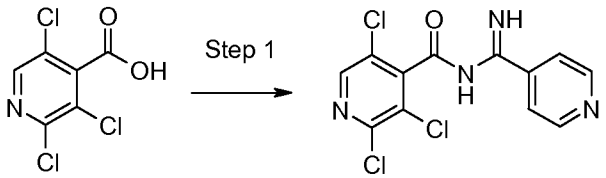
5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061] (0.553mmol, 0.143g), was suspended in anhydrous DCM (14mL) at RT under nitrogen and triethylamine (1.38mmol, 0.193mL), DMAP (approximately 0.005g) and 2,4,6-triisopropylbenzene sulfonyl chloride (0.663mmol, 0.201g) were added sequentially. The reaction was stirred at room temperature

as an off-white suspension for 2hrs. Slowly the mixture becomes a pale green suspension, that was left stirring overnight. Then pyridine (4mL) was added and the reaction vessel sonicated for 5minutes to try to improve the dissolution causing the reaction to change colour from green to brown suspension. The resultant mixture was stirred at room temperature for 1 hour. Boc-piperazine (0.608mmol, 0.113g) was added in one portion and the mixture left stirring for 18 hours.

The reaction was diluted with water and extracted with DCM (x3). Combined organics washed with brine (x1), dried ($MgSO_4$), filtered and concentrated in vacuo. To yield the title compound [A062] which was used in the next reaction without further purification: LCMS method: 1, RT:5.69 min, MI 427 [M+H].

Synthesis of 5-Chloro-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [132] To a solution of 4-(5-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A062] (0.47mmol, 0.201g), in anhydrous DCM (8mL), at room temperature was added HCl (4.0N in dioxane, 2mL) to yield an orange suspension that was stirred at room temperature for 3 hours. The mixture was then concentrated in vacuo, redissolved in DCM/MeOH (1:1, 6mL total) and added to an SCX-2 10g cartridge. The cartridge was washed with DCM and MeOH (~35mL total ~2:3 ratio respectively). Then the cartridge was washed with ammonia in methanol (2N, 40mL) and the ammonia washes were concentrated in vacuo to yield 92mg brown oil. The crude material was purified by column chromatography (SP1 4g VWR column with 0-20% MeOH/DCM 15 volumes) to yield the title compound [138] (0.044g) as an orangey-yellow foam. LCMS method: 1, RT:1.60 min, MI 327 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.15 (1H, s), 8.77 (2H, d), 8.61 (1H, s), 8.29 (2H, d), 3.69 (4H, br s), 2.85 (4H, br s)

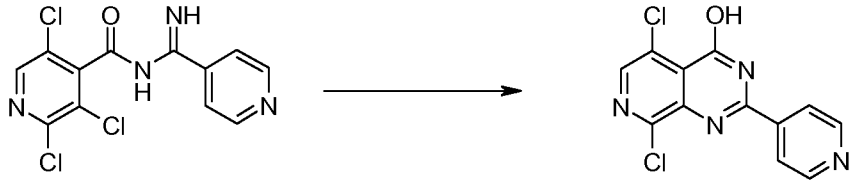
Synthesis of 5,8-Dichloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A063]



[A064]

2,3,5-Trichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A064] was prepared by reaction of 2,3,5-Trichloro-isonicotinic acid, pyridine-4-carboximidamide hydrochloride,

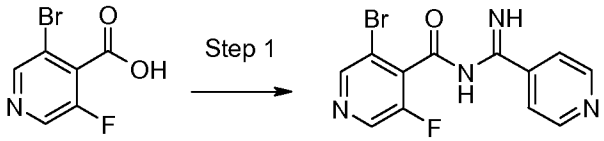
HATU, DIPEA and DMF at room temperature to give the title compound. LCMS method: 1, RT:4.37 min, MI 330 [M+H]; NMR: (1H, 300MHz, d6-dmso); 10.24 (1H, br s), 10.14 (1H, br s), 8.75 (2H, d), 8.60 (1H, s), 7.89 (2H, d).



[A064] [A063]

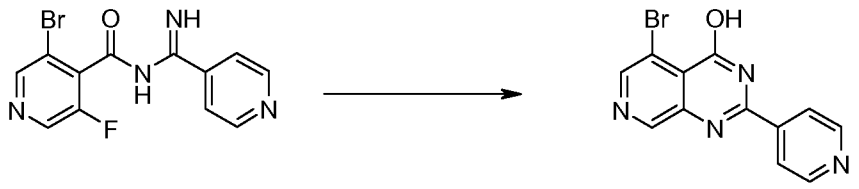
5,8-Dichloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A063] was prepared by reaction of 2,3,5-Trichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide[A064], $FeCl_3$, Ce_2CO_3, HCl (4N in dioxane) and DMA in a in μwave for 2hrs at 120°C The reaction mixture was cooled and water (0.5mL) was added followed by MeOH (2mL) and HCl (4eq wrt carbonate, 2.4mmol, 0.6mL 4N HCl in dioxane) and the mixture was stirred for 10mins. The yellow precipitate was collected by filtration and the solid was washed with MeOH (2x, 2mL) then dried in vac oven to give the title compound as a yellow solid (51 mg, 56% yield): LCMS method: 1, RT:4.80 min, MI 293 [M+H]; NMR: (1H, 300MHz, d6-dmso); 13.36 (1H, br s), 8.92 (2H, d), 8.49 (1H, s), 8.14 (2H, br d).

Synthesis of 3-Bromo-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A065]



[A066]

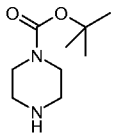
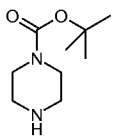
2-Bromo-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A066] was prepare by reaction of 3-Bromo-4-carboxy-5-fluoro-pyridinium; chloride, pyridine-4-carboximidamide hydrochloride, HATU, DIPEA and DMF at room temperature to give the title compound. LCMS method: 1, RT:3.20 min, MI 325 [M+H].



[A066] [A065]

2-Bromo-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A066] (0.05g, 0.155 mmol), DMA (0.5 mL), K_2CO_3 (0.022g, 0.16 mmol), DIPEA (0.28 mL, 0.16 mmol) and DBA (0.024 mL, 0.16 mmol) wa heated at 150°C in μwave for 45mins. The crude reaction mixture was evapourated under reduced pressure and the crude material was purified by column chromatography (SP1 4g VWR column in 0.5%Et3N / DCM / 0-20% MeOH) to yield the title compound [A065] (0.044g, 80% yield) as an orangey-yellow foam: LCMS method: 1, RT:11.57 min, MI 304 [M+H].

The following compounds were synthesised according to the general synthesis shown in scheme [A7]:

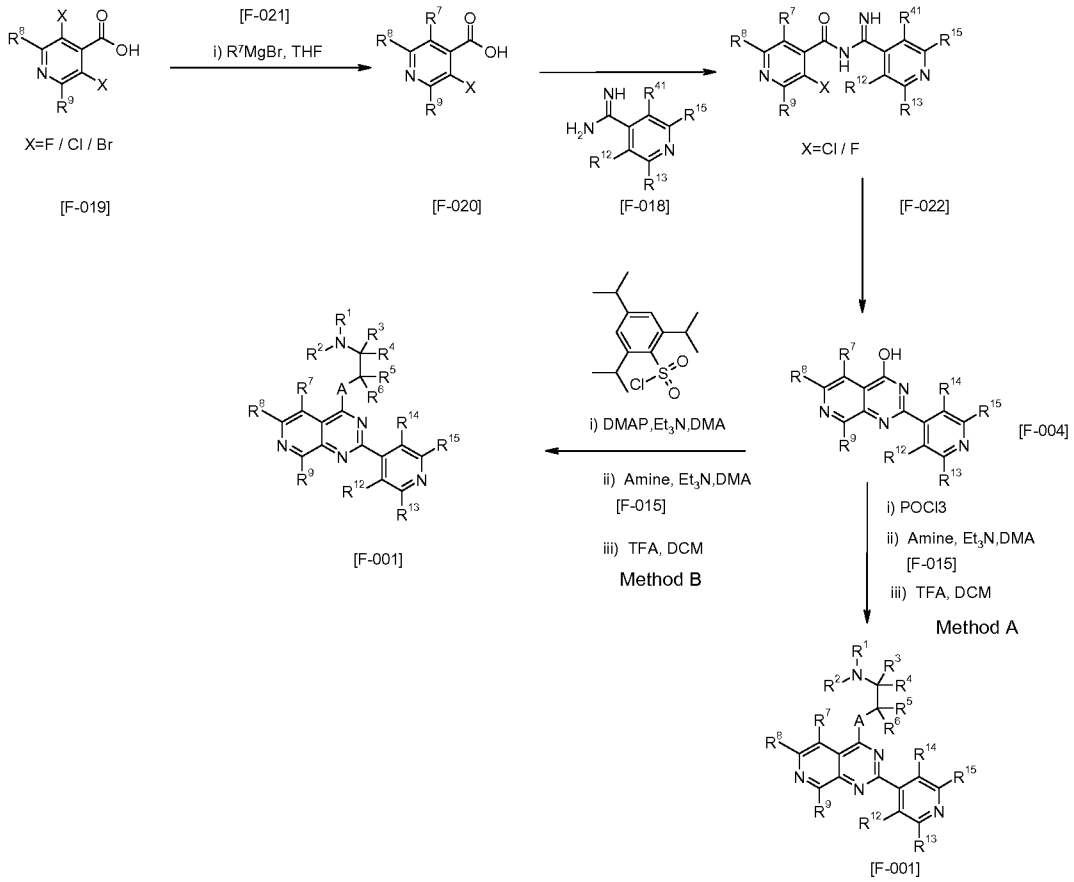
Ex	SM	Met - hod	Amine [F-015]	Analysis		Name
133	[A065]	A		Method 1: RT: 1.77 min, MI: 373 [M+H]	(1H, 500MHz, d6-dmso), 9.17 (1H, s), 8.77 (2H, dd), 8.72 (1H, s), 8.29 (2H, dd), 3.78-3.61 (4H, m), 2.94 (2H, br s), 2.82-2.71 (2H, m)	1-[5-bromo-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
134	[A063]	A		Method 1: RT: 5.02 min, MI: 361 [M+H]	(1H, 500MHz, d6-dmso) 8.79 (2H, dd), 8.41 (1H, s), 8.30 (2H, dd), 3.74 (4H, br s), 2.98-2.75 (4H, m)	1-[5,8-dichloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

General synthesis of substituted 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A8

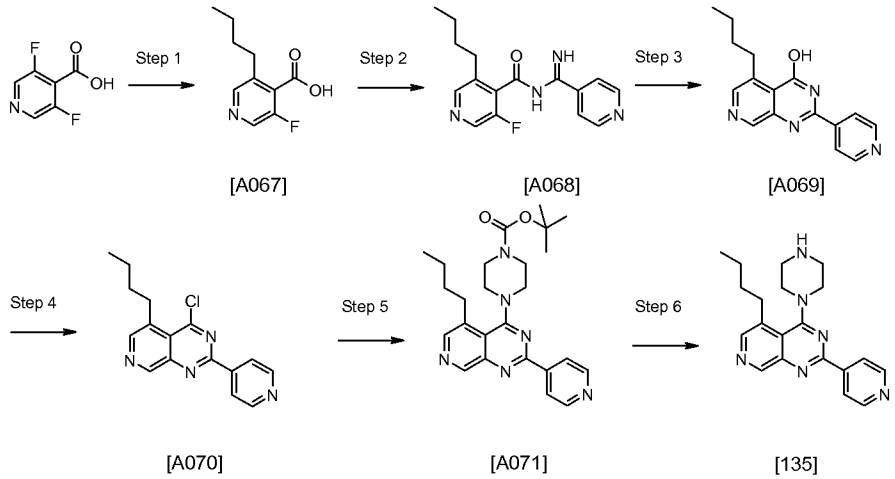
Ortho-halo-isonicotinic acid derivatives of general formula [F-020] were prepared by reaction of a dihalo isoinicotinic acid derivative of general formula [F-019] with a grindard reagent of general formula [F-021] in a polar aprotic solvent such as THF or Et_2O. 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] were prepared by

coupling of a ortho-halo-isonicotinic acid derivative of general formula [F-020] with an appropriately substituted 4-carbamimidoyl-pyridines of general formula [F-018] with a suitable coupling agent such as O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) in a polar aprotic solvent such as DMA or DMF. The isonicotinoyl-amidine derivative of general formula [F-022] were cyclised to displace the relevant halogen group to yield the desired -Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004]. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride and the intermediate 4-chloro derivative was then reacted with primary or secondary amino derivative of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A8



Synthesis of 5-Butyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [135]



Synthesis of 3-Butyl-5-fluoro-isonicotinic acid [A067]

3,5-Difluoro-isonicotinic acid (0.557 g, 3.5 mmol) was suspended in anhydrous THF (8 mL) at 0°C, under an atmosphere of nitrogen. To this was added butyl magnesium chloride (2.0 M in diethyl ether, 5.25 mL, 10.5 mmol) dropwise over 10 minutes. The suspension slowly

changed form during the slow addition with preliminary agglomeration of solid then the solid started to dissolve slowly, achieving full solution around completion of addition of reagent. The reaction mixture was allowed to warm to room temperature and stirred over 72 hours to form a thick yellow suspension. Diluted with water and transferred into a single neck flask and concentrated in vacuo. The yellow solid was diluted with water (10 mL) and EtOAc (10 mL). The pH was adjusted pH~2, by dropwise addition of HCl (conc.) and extracted with EtOAc (x3 - some of the yellow colour goes into organics). Combined organics were washed with brine (x1), dried ($MgSO_4$) and concentrated in vacuo to yield the title compound [A067] as an orange gum/solid (0.402g) that solidifies slowly: NMR: (1H, 300MHz, d6-dmso); 8.52 (1H, s), 8.42 (1H, s), 2.67 (2H, t), 1.58-1.48 (2H, m), 1.35-1.22 (2H, m), 0.87 (3H, t); LCMS method: 1, RT:1.22 min, MI 198 [M+H].

Synthesis of 3-Butyl-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A068]

3-Butyl-5-fluoro-isonicotinic acid [A067] (2.05 mmol, 0.402 g) was dissolved in anhydrous DMF (8 mL) and diisopropylethylamine (DIPEA) (5.95 mmol, 1.04 mL) was added and the mixture stirred at room temperature for 5 minutes. Then O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) (2.0 5mmol, 0.78 g) was added in one portion and the resultant mixture stirred for 1 hour. pyridine-4-carboximidamide hydrochloride (1.95 mmol, 0.307 g) was then added portionwise over 5 minutes to the reaction. The resultant solution was stirred at room temperature for 18 hours. The reaction mixture was poured into water (85 mL) and stirred for 30 minutes and then extracted with EtOAc (x3). The combined organics washed with water (x4), brine (x1), dried ($MgSO_4$), filtered and concentrated in vacuo to yield the title compound [A068] (480mg) as a brown solid. The material was used crude in next reaction: NMR: (1H, 300MHz, d6-dmso); 10.28 (1H, br s), 9.93 (1H, br s), 8.74 (2H, d), 8.45 (1H, s), 8.37 (1H, s), 7.90 (2H, d), 2.72-2.66 (2H, m), 1.58-1.48 (2H, m), 1.28-1.15 (2H, m), 0.79 (3H, t); LCMS method: 1, RT:3.90 min, MI 301 [M+H].

Synthesis of 5-Butyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A069]

3-butyl-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A068] was placed into 25mL Biotage microwave vessel in solution in anhydrous DMA (5 mL) and heated at 150°C in the microwave for 45mins. The reaction mixture was filtered material through an SCX-2 25g cartridge. The cartridge was washed with methanol (50 mL). Then the cartridge was

washed with ammonia (2N, 40 mL) and the ammonia washes concentrated in vacuo to yield the title compound [A069] (390mg) as a pale brown solid, : NMR: (1H, 300MHz, d6-dmso); 8.95 (1H, s), 8.79 (2H, dd), 8.46 (1H, s), 8.10 (2H, dd), 3.21 (2H, t), 1.63-1.50 (2H, m), 1.43-1.27 (2H, m), 0.91 (3H, t) – also shows one equivalent of DMA; LCMS method: 1, RT:3.29 min, MI 281 [M+H].

Synthesis of 5-Butyl-4-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [A070]

5-Butyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A069] (1.35 mmol, 0.378 g) was suspended in anhydrous 1,2-dichloroethane (DCE) (10 mL) and phosphorus oxychloride ($POCl_3$) (1.4 mmol, 0.131 mL) was added dropwise over 2-3 minutes. Finally DIPEA (2.0 mmol, 0.348 mL) was added and the mixture stirred at RT under nitrogen overnight. The brown solid slowly to change appearance after $POCl_3$ addition, then darkens further on addition of DIPEA to become a dark brown apparent solution. The reaction was left stirring at room temperature overnight under nitrogen. After 20 hours $POCl_3$ (65 μL) was added and stirred at room temperature overnight. The crude mixture was concentrated in vacuo, then azeotroped with toluene (x2) to dryness. The residue was diluted with sodium carbonate (aq. soln., 2N, 20mL) and extracted with DCM (x2), EtOAc (x1). Combined organics washed with brine (x1), dried ($MgSO_4$), filtered through a pad of silica and concentrated in vacuo to yield the title compound [A070] (180mg) as a of a pale brown solid which was used in the next reaction without further purification: LCMS method: 1, RT:5.66 min, MI 299 [M+H].

Synthesis of 4-(5-Butyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A071]

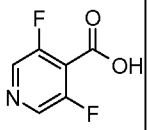
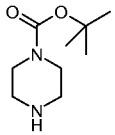
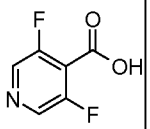
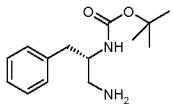
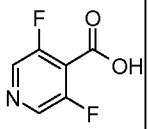
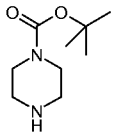
5-Butyl-4-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [A070] (0.615 mmol, 0.180 g), was dissolved in anhydrous DCM (5 mL), under nitrogen at room temperature and treated with triethylamine (0.868 mmol, 0.121 mL) and N-Boc-piperazine (0.682 mmol, 0.127 g) in one portion. The resulting mixture was stirred at room temperature for 2 hours. Then sodium carbonate (1N aq. soln, 20 mL) was added and extracted with DCM (x2) and EtOAc (x1). Combined organics washed with brine (x1), dried ($MgSO_4$), filtered and concentrated in vacuo to a dark brown solid, which was purified by column chromatography (SP1 on 25g VWR cartridge in 0-10% MeOH/DCM, 15col vols) to yield the title compound [A071] as a brown gum (0.092g) which was used in the next reaction without further purification: NMR:

(1H, 300MHz, d6-dmso); 9.24 (1H, s), 8.79 (2H, d), 8.49 (1H, s), 8.36 (2H, d), 3.77-3.48 (8H, m), 3.19-3.07 (2H, m), 1.64-1.23 (4H, m), 1.48 (9H, s), 0.96-0.87 (3H, t)

Synthesis of 5-Butyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [135]

4-(5-Butyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A071] (0.20mmol, 0.09g) was dissolved in anhydrous DCM (4 mL) and treated with hydrogen chloride (4N in dioxane, 4 mL) at room temperature and stirred for 2 hours. The reaction was diluted with methanol and poured onto SCX-2 cartridge (5 g), washing with MeOH/DCM (20mL). The cartridge was then washed with ammonia (2N, 20 mL) and the ammonia washes concentrated in vacuo to yield a brown gum (0.059 g). The residue was purified by column chromatography (SP1 4 g column, in a gradient 5-20% MeOH/DCM 15col vols) to yield the title compound [133] as an orangey-brown gum (0.020g).; NMR: (1H, 300MHz, d6-dmso); 9.09 (1H, s), 8.76 (2H, d), 8.51 (1H, s), 8.31 (2H, d), 3.73-3.58 (2H, br s), 3.50-3.37 (2H, br s), 3.07 (2H, t), 2.90-2.79 (4H, br s), 1.51-1.38 (2H, m), 1.28-1.15pm (2H, m), 0.84 (3H, t); LCMS method: 1, RT:2.58 min, MI 349 [M+H].

The following compounds were synthesised according to the general synthesis shown in scheme [A8]:

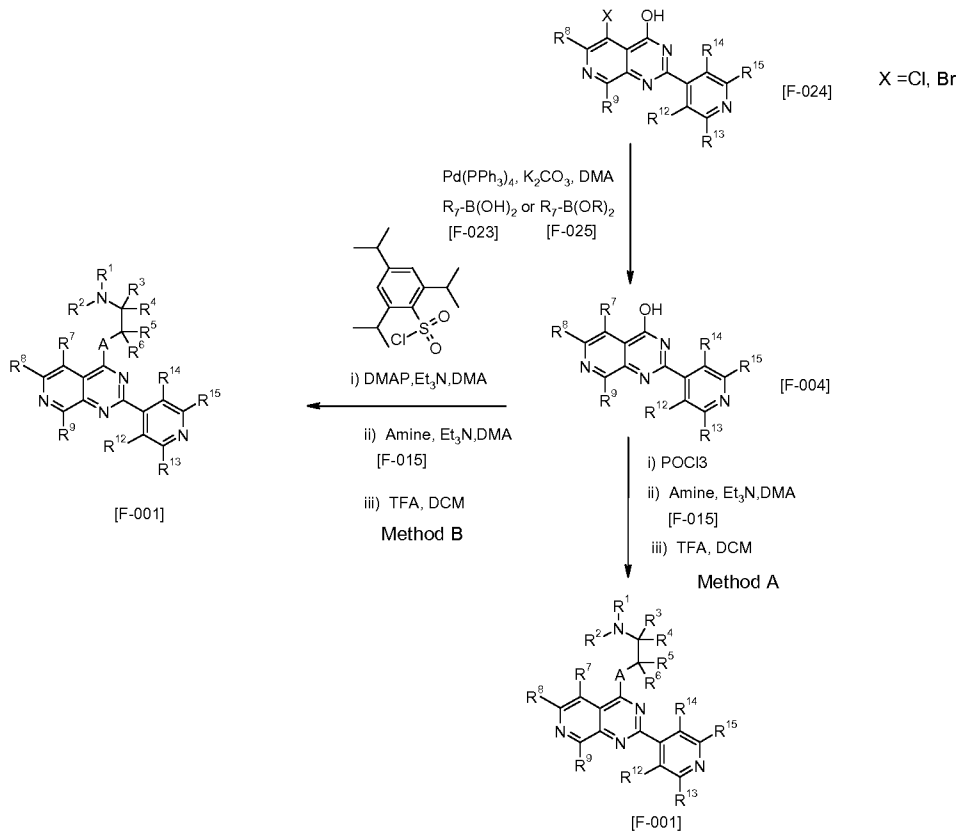
Ex	SM [F-019]	Grig-nard [F-021]	Amine [F-015]	Analysis		Name
136		EtMg Br		Method 1: RT: 1.64 min, MI: 321 [M+H]	(1H, 300MHz, d6-dmso) 9.08 (1H, s), 8.76 (2H, dd), 8.54 (1H, s), 8.30 (2H, dd), 3.72-3.58 (2H, br s), 3.55-3.45 (2H, br s), 3.10 (2H, dd), 2.89-2.77 (4H, br s), 1.17 (3H, t)	1-[5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
137		EtMg Br		Method 1: RT: 2.90 min, MI: 385 [M+H]	(1H, 300MHz, d6-dmso) 9.02 (1H, s), 8.72 (2H, dd), 8.42 (1H, s), 8.16 (2H, dd), 7.35-7.24 (5H, m), 3.91 (1H, dd), 3.43 (1H, dd), 3.37-3.29 (1H, m), 3.21 (2H, dd), 2.83-2.70 (2H, m), 1.33 (3H, t)	N-[(2S)-2-amino-3-phenylpropyl]-5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
138		MeMg Br		Method 1: RT: 3.93 min, MI: 307 [M+H]	(1H, 300MHz, d6-dmso) 9.06 (1H, s), 8.76 (2H, dd), 8.43 (1H, s), 8.30 (2H, dd), 3.57 (4H, br s), 2.84 (4H, br s), 2.65 (3H, s)	1-[5-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

General synthesis of substituted 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A9

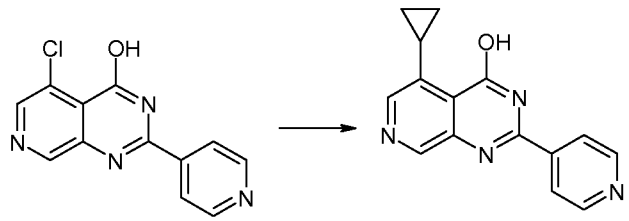
5-Substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] were prepared by reaction of a 5-halo substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-024] (prepared in scheme A7) in a palladium catalysed cross coupling reaction with a boronic acid or boronate ester derivative of general formula [F-023] in the presence of a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(OAc)_2$, and a base such as K_2CO_3 or Cs_2CO_3 in a polar solvent such as

dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor, or a palladium catalysed cross coupling reaction of a 5-halo substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-024] (prepared in scheme A7) with a fluoroborate derivative of general formula [F-025] in the presence of a catalyst such as $Pd(PPh_3)_4$ or $Pd(OAc)_2$, a ligand such as RuPhos and a base such as K_2CO_3 or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 5-substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride and the intermediated 4-chloro derivative was then reacted with primary or secondary amino derivative of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC

Scheme A9



Synthesis of 1-[5-cyclopropyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [139]

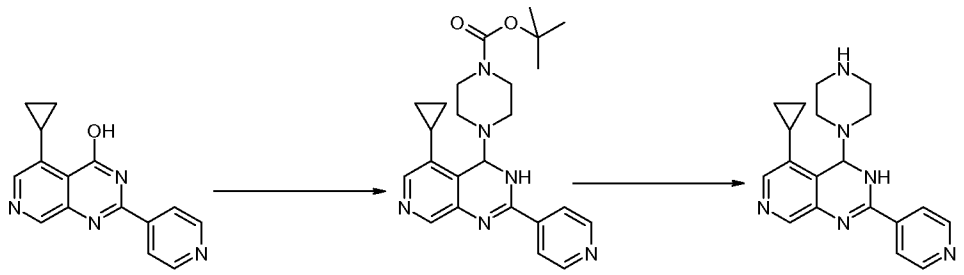


[A061] [A072]

5-Cyclopropyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A060]

5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061] (0.670mmol, 0.173g), potassium carbonate (2.01mmol, 0.278g) and cyclopropyl boronic acid (1.34mmol, 0.115g) was suspended in anhydrous DMA (3mL) and then subjected to vacuum/argon balloon sparge (x3). Then tetrakis(triphenylphosphine)palladium (0.067mmol, 0.077g) was added in one portion and the reaction vessel sealed and heated in a microwave at 150°C for 1hr. The reaction was cooled to room temperature, under nitrogen. Potassium carbonate (2.01mmol, 0.278g) and cyclopropyl boronic acid (1.34mmol, 0.115g) were

added and the reaction mixture subjected to vacuum/argon balloon sparge (x3). Then tetrakis(triphenylphosphine)palladium (0.067mmol, 0.077g) was added in one portion and the reaction vessel sealed and heated in a microwave at 180°C for 1hr. The reaction was cooled to room temperature under air and left standing over 48 hours. The reaction mixture was then poured on to an SCX-2 cartridge (10g) and washed with methanol (~40mL total). Then the cartridge was washed with ammonia (2N in MeOH, ~ 40mL) and the ammonia washes concentrated in vacuo to yield the title compound [A072] (78mg) as a yellow solid which was taken through to next reaction without purification.



[A072] [A073] [139]

4-(5-Cyclopropyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A073]

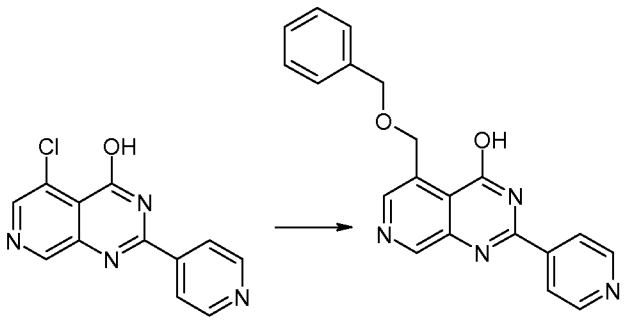
A mixture of 5-Cyclopropyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A072] (0.08 g, 0.3 mmol), DIPEA (0.16 mL, 0.9 mmol), 2,4,6-triisopropylbenzene sulfonyl chloride (0.11 g, 0.36 mmol), DMAP (3 mg) and DMA (2 mL) was stirred at room temperature under nitrogen and left to stir at at RT for 2hrs. Boc-piperazine (0.062 g, 0.33 mmol) was added and the mixture was left to stir at RT overnight. Water was added and the mixture was extracted with EtOAc (x4). The extracts were combined washed with water (x4), brine, dried (MgSO4) and concentrated in vacuo. The crude reaction product was purified by flash column chromatography (SP1, EtOAc:cyclohexane elution) to yield the title compound [A073]: , method: 1, RT:5.57 min, MI 433 [M+H].

1-[5-cyclopropyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [139]

A mixture of 4-(5-Cyclopropyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A073] (0.9 g, 0.2 mmol) in DCM (3 mL) and 4N HCl dioxane (1 mL) was stirred at RT overnight. The crude reaction mixture was evapourated under reduced pressure then dissolved in MeOH and washed onto SCX-2 (5g) cartridge and washed with MeOH/DCM (1:1, ~ 4 mL) then MeOH (10 mL). Then eluted with ammonia (2N in MeOH, 15mL). The Ammonia elutent was concentrated in vacuo and the

crude product was purified by normal phase chromatography (SiO2, SP1 in MeOH (0-15%)/CHCl3) to give the title compound [139] (30 mg, 43% yield): LCMS method: 1, RT:1.65 min, MI 333 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.99 (1H, s), 8.76 (2H, dd), 8.30 (2H, dd), 8.09 (1H, s), 3.87-3.54 (4H, m), 2.87 (4H, br s), 2.63-2.57 (1H, m), 1.24 (2H, ddd), 1.01 (2H, ddd)

Synthesis of 5-Benzyloxymethyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A074]

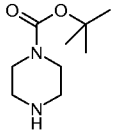


[A061] [A074]

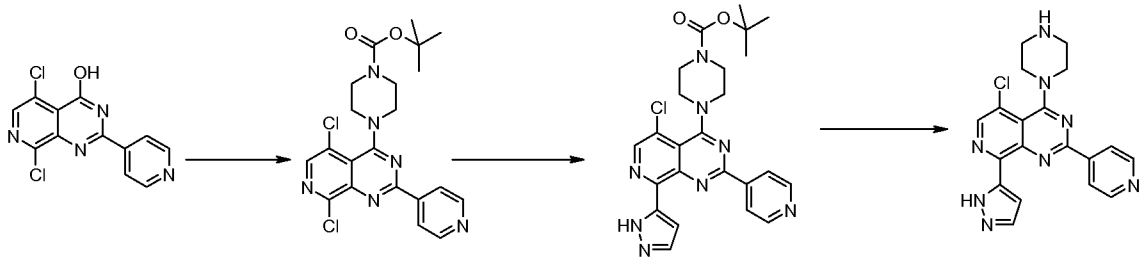
5-Benzyloxymethyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A074]
A mixture of5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061] (0.1g, 0.4 mmol), Potassium benzyloxymethyltrifluoroborate (0.1 g, 0.45 mmol), cesium carbonate (0.4 g, 1.2 mmol) and RuPhos (12 mg, 0.028 mmol) were placed in Biotage 5mL vessel and suspended in dioxane (1.8 mL) and water (0.2 mL). The mixture was subjected to spurging with vacuum/argon (x3) then the Pd(OAc)2 (3 mg, 0.014 mmol) was added and the vessel sealed and heated at 104°C overnight. DMA (1mL) was added and the mixture was heated in μwave at 150°C for 1hr. The RM was cooled and acetic acid (0.57mL)was added and the mixture and stirred for 10mins. Then flushed down SCX-2 cartridge (10 g) washing with MeOH (30-40mL). Then washed with ammonia (2N in MeOH, 40mL). Ammonia washes concentrated in vacuo to yield the title compound [A074] which was used without further purificatuion: method: 1, RT:3.31 min, MI 345 [M+H].

The following compounds were synthesised according to the general synthesis shown in scheme [A9]:

Ex	SM	Met - hod	Amine	Analysis	Name

140	[A074]	B		Method 1: RT: 4.78 min, MI: 413 [M+H]	(1H, 500MHz, d6-dmso) 9.18 (1H, s), 8.77 (2H, d), 8.69 (1H, s), 8.31 (2H, dd), 7.33-7.25 (5H, m), 4.99 (2H, s), 4.54 (2H, s), 3.51 (4H, br s), 2.79 (4H, t)	1-{5-[(benzyloxy)methyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl}piperazine

Synthesis of 5-Chloro-4-piperazin-1-yl-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [141]



[A063] [A075] [A076] [141]

4-(5,8-Dichloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A075]

A mixture of 5,8-Dichloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A063] (0.43 g, 1.47 mmol) Et_3N (0.51 mL, 3.6 mmol), DCM (10 mL), pyridine (2 mL) was sonicated for 2mins. Then DMAP (5 mg) was added followed by 2,4,6-triisopropylbenzene sulfonyl chloride (0.53 g, 1.77 mmol). The reaction mixture was left to stir at RT overnight. The dark brown solution was diluted with water and extracted with DCM (X3) and EtOAc (x1). Combined organics washed with brine (x1). Brine re-extracted with EtOAc (x1). Combined organics dried (MgSO4), filtered and concentrated in vacuo. The crude material was purified by normal phase chromatography (SiO_2 [SP1 (25g vwr cartridge, 0-10% MeOH/DCM]) to give the title compound [A075] (0.19g, 28% yield):. LCMS

method: 1, RT:4.17 min, MI 461 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.81 (2H, d), 8.45 (1H, s), 8.33 (2H, d), 3.76 (4H, br s), 3.33 (4H, br s), 1.40 (9H, br s).

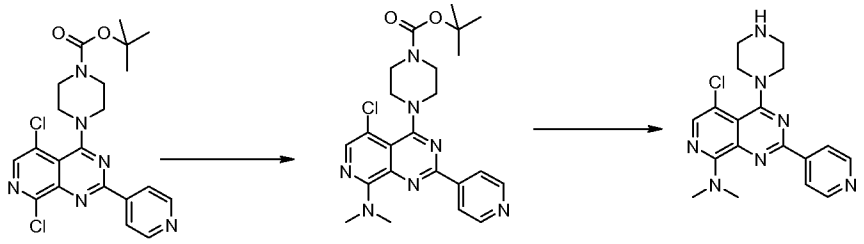
4-[5-Chloro-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [A076]

A mixture of 4-(5,8-Dichloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A075] (0.07 g, 0.15 mmol), potassium phosphate tribasic [K_3PO_4 212.27g/mol 21.2g in 100 mL deionised water] (0.3 mL, 0.3 mmol), tetrakis(triphenylphosphine)palladium (17 mg, 0.015 mmol), 1H-Pyrazole-5-boronic acid (24 mg, 0.21 mmol) and DMA (1 mL) were heated in μwave at 150°C for 30min. Acetic acid (0.52 mL) was added and the mixture was left to stir at rt for 20mins and then the crude product was loaded onto an SCX cartridge and the cartridge was washed with methanol then the product was eleuted with 2M ammonia / methanol. The eluent was concentrated under reduced pressure and the crude reaction mixture was purified by normal phase chromatography (SiO_2, ethyl acetate: cyclohexane elution) to give the title compound [A076]: LCMS method: 1, RT:5.62 min, MI 493 [M+H].

Chloro-4-piperazin-1-yl-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [141]

A mixurure of 4-[5-Chloro-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [A076] and HCl dioxane (4N, 1 mL) was stirred at rt for 48 hours. The crude reaction mixture was evapourated under reduced pressure and the crude product loaded onto a SCX-2 cartridge (1 g) and washed with methanol. The product was released from the cartridge using a solution of 2M ammonia / methanol. The ammonia / methanol eluent was concentrated under reduced pressure and the crude product was purified by preparative HPLC (method A) to yield to the title compound: LCMS: method: 1, RT:1.98 min, MI 393 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.76-8.75 (3H, m), 8.50 (1H, s), 8.17 (2H, dd), 7.90 (1H, d), 6.67pm (1H, dd), 3.76 (4H, br s), 2.93 (2H, br s), 2.80 (2H, br s)

Synthesis of 5-chloro-N,N-dimethyl-4-(piperazin-1-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-amine [142]



[A075] [A077] [142]

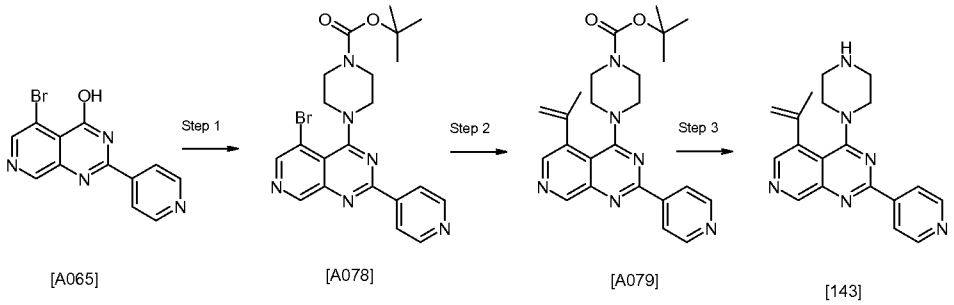
4-(5-Chloro-8-dimethylamino-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A077]

4-[5-Chloro-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [A075] (0.046 g, 0.1 mmol), DMF (2 mL) and dimethylamine in ethanol (0.5 mL) was warmed to 50°C in a sealed vessel and left to stir for 24 h. The crude reaction mixture was evapourated under reduced pressure to yield the title compound [A077] which was used in the next step without further purification: LCMS: method: 1, RT:4.41 min, MI 470 [M+H].

5-chloro-N,N-dimethyl-4-(piperazin-1-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-amine [142]

A mixture of 4-(5-Chloro-8-dimethylamino-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A077] (0.1 g, 0.22 mmol), DCM (3 mL) and HCl (1 mL of a 4N solution in dioxane) was stirred at RT for 2 h. The crude reaction mixture was evpourated under reduced pressure then the crude product was loaded onto an SCX cartridge and the cartridge was washed with methanol then the product was eleuted with 2M ammonia / methanol. The eluent was concentrated under reduced pressure and the crude reaction mixture was purified by normal phase chromatography (SiO_2, SP1 on 4g cartridge in 0-15% MeOH/DCM) to give the title compound: LCMS: method: 1, RT:5.40 min, MI 370 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.73 (2H, dd), 8.22 (2H, dd), 7.97 (1H, s), 3.76-3.68 (2H, m), 3.56-3.49 (2H, m), 3.16 (3H, s), 3.15 (3H, s), 2.95-2.87 (2H, m), 2.86.2-77 (2H, m)

Synthesis of 5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [143]



Step 1: Synthesis of 4-(5-Bromo-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A078]

A mixture of 5-Bromo-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A065] (0.74 g, 2.45 mmol) in DMF (15 mL), DIPEA (1.3 mL, 7.3 mmol) and DMAP (5 mg) was stirred at rt for 10 min. 2,4,6-triisopropylbenzene sulfonyl chloride (0.89 g, 2.94 mmol) was added and the mixture was left to stir at rt for 80 mins at RT, then boc-piperazine (0.5g, 2.94 mmol) was added in one portion and the rm was left to stir at rt over night. Water (30mL) was added and the mixture was stirred at RT for 20mins. The resultant solid was collected by filtration and the crude product was purified by column chromatography (SP1 (25 g cartridge) in 0-10% MeOH/DCM (~20vols, 4 vols at 10%MeOH/DCM)) to yield the title compound [A078] (0.69g, 60% yield): LCMS: method: 1, RT:5.83 min, MI 473 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.22 (1H, s), 8.78 (3H, m), 8.32 (2H, d), 3.79 (4H, br s), 3.61 (4H, br s), 1.41 (9H, br s).

Step 2: Synthesis of 4-(5-Isopropenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A079]

4-(5-Bromo-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A078] (0.2 mmol, 0.094g), potassium phosphate (tribasic) (0.60 mmol, 0.127g), and Isopropenylboronic acid pinacol ester (0.30mmol, 0.057mL) were suspended in anhydrous dioxane (2 mL), in a 5 mL Biotage vessel under nitrogen. The vessel was subjected to vacuum/argon (balloon) sparge (x3) and then dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.01mmol, 0.008 g) added and the reaction sealed and warmed to 96°C for 18 hours. The reaction mixture was cooled to room temperature under air, silica for chromatography added (1g) and the mixture concentrated in vacuo to a brown powder. This was dry loaded onto a silica cartridge and purified by chromatography (SP1 0-10% MeOH/DCM 15 col vols) to yield 4-(5-Isopropenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A079] (85mg) as a 85mg brown glass: NMR: (1H,

500MHz, $CDCl_3$); 9.31 (1H, s), 8.79 (2H, d), 8.50 (1H, s), 8.36 (2H, d), 5.40 (1H, s), 5.32 (1H, s), 3.58 (8H, br s), 2.21 (3H, s), 1.24 (9H, s); LCMS: method: 1, RT:5.66 min, MI 433 [M+H].

Step 3: Synthesis of 5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [143] To a solution of 4-(5-Isopropenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A079] (0.105mmol 0.045 g), in DCM (2 mL) at room temperature was added hydrogen chloride (4N in dioxane, 1mL), to obtain a thick yellowy-brown suspension, that was stirred overnight. The reaction mixture was then concentrated in vacuo, the residue re-dissolved in MeOH and washed onto SCX-2 cartridge. The cartridge was washed with DCM and MeOH (1:1, 20mL total). Then the SCX-2 was washed with ammonia (2N in MeOH, 15mL). The combined ammonia washes were concentrated to an orangey-brown solid, which was purified by column chromatography (SP1 4g cartridge, 0-20% MeOH/DCM, 15 col vols) to yield 5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [143] (0.011g) as a yellow glass: NMR: (1H, 500MHz, d4-MeOH) 9.15 (1H, s), 8.76 (2H, dd), 8.49 (1H, s), 8.31 (2H, dd), 5.40 (1H, s), 5.20 (1H, s), 3.56 (4H, br s), 2.79 (4H, t), 2.17 (3H, s); LCMS: method: 1, RT:1.88 min, MI 333 [M+H].LC-MS.

Example 151. 5-Methoxy-4-piperidin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine

151a) 3-tert-Butoxycarbonylamino-pyrrolidine-1,3-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester : 3-tert-Butoxycarbonylamino-pyrrolidine-3-carboxylic acid (1.50 g, 6.50 mmol) was added to a solution of Sodium carbonate (1.65 g, 15.6 mmol) in Water (16.7 mL, 926 mmol) and 1,4-Dioxane (9 mL, 100 mmol). The resulting solution was stirred and cooled in an ice bath. To the stirring reaction solution was added a solution of 9-Fluorenylmethyl chloroformate (1.76 g, 6.82 mmol) in 1,4-Dioxane (13 mL, 160 mmol). The mixture was stirred at room temperature for 2 h, poured into Water (300 mL) and extracted twice with ether. The aqueous phase was cooled in an ice bath and slowly treated with 3 M of Hydrogen Chloride in Water (7.80 mL, 23.4 mmol) to neutralize. The resulting mix was extracted with EtOAc (2x), the combined organics dried over Na2SO4, filtered, and concentrated. The residue was pumped under high vacuum for 4 h, leaving 3.12 g (106%) of foam, which was used for subsequent step without further manipulation.

151b) 3-tert-Butoxycarbonylamino-3-carbamoyl-pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester: At rt Di-tert-Butyldicarbonate (655 mg, 3.00 mmol) was added to a mixture of 3-tert-Butoxycarbonylamino-pyrrolidine-1,3-dicarboxylic acid 1-(9H-

fluoren-9-ylmethyl) ester (905 mg, 2.00 mmol) and Pyridine (0.324 mL, 4.00 mmol) in 1,4-Dioxane (5 mL, 60 mmol). After 15 minutes, Ammonium Bicarbonate (0.474 g, 6.00 mmol) was added, and the reaction mixture was stirred for 72 h. Added water (10 mL) to resulting solid mass and swirled. Filtered off solid and rinsed liberally with water. After air drying, dried resulting solid under high vacuum at rt. Obtained 1.12 g (124%) of tannish solid. Proceeded and used this tannish solid for subsequent step without further manipulation.

151c) (3-Carbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester 3-tert-Butoxycarbonylamino-3-carbamoyl-pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester (410 mg, 0.91 mmol) was suspended in Methanol (5 mL, 100 mmol), then at rt added Piperidine (1 mL, 10 mmol) neat. After 16 hours concentrated reaction under reduced pressure, then pumped on residue under high vacuum overnight (to remove as much piperidine as possible), and used crude directly for subsequent reaction.

151d): 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol (127 mg, 0.501 mmol), Triethylamine (216 uL, 1.55 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (167 mg, 0.552 mmol), and 4-Dimethylaminopyridine (6.9 mg, 0.057 mmol) in N,N-Dimethylformamide (2.0 mL, 26 mmol) were stirred at room temperature for 1 h. Gradual dissolution of starting material was observed, intermediate sulfonate observed by hplc . (3-Carbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester (126 mg, 0.550 mmol) was then added as a solution in N,N-Dimethylformamide and the reaction was stirred at room temperature. After 45 minutes concentrated reaction under reduced pressure, then partitioned residue between EtOAc and water. Took organic and washed with 3 mL of 1N HCl. Took aqueous solution, added small amount of DMSO and purified over two runs with preparative reverse phase HPLC. Combined purest fractions of each major product and lyophylized. Obtained 32 mg (14%) of yellow lyophilate of front running material [3-Carbamoyl-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-carbamic acid tert-butyl ester (LC/MS: M+H=466.2). Also obtained 35 mg (22%) of side product 5-Methoxy-4-piperidin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine (LC/MS: M+H=322.1), which was generated from piperidine left over from preparation of starting material (3-Carbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester. Proceeded on with [3-Carbamoyl-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-carbamic acid tert-butyl ester for subsequent reaction without further manipulation.

Example 152. 3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid amide

Added a solution of Trifluoroacetic Acid (1 mL, 10 mmol) in Methylene chloride (2 mL, 30 mmol) to [3-Carbamoyl-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-carbamic acid tert-butyl ester (30 mg, 0.06 mmol) at rt. After 30 minutes concentrated reaction mixture under reduced pressure, then to residue triturate with Et2O to get a solid. Filtered solid and washed liberally with Et2O. Obtainedwith 17 mg of title compound as a solid (LC/MS: +H=366.1).

Example 153. 3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid phenylamide

153a) 3-tert-Butoxycarbonylamino-3-phenylcarbamoyl-pyrrolidine-1-carboxylic acid-9H-fluoren-9-ylmethyl ester : N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (575 mg, 3.00 mmol) was added to a mixture of 3-tert-Butoxycarbonylamino-pyrrolidine-1,3-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester (905 mg, 2.00 mmol), 1-Hydroxybenzotriazole (2.70E2 mg, 2.00 mmol) and Aniline (228 uL, 2.50 mmol) in Tetrahydrofuran (25 mL, 310 mmol). After 10 minutes added N,N-Dimethylformamide (10 mL, 100 mmol) to facilitate dissolution. After 1.5 hour concentrated reaction mixture under reduced pressure. The residue was partitioned between EtOAc (2x) and saturated aqueous NaHCO3. The combined organic phases were dried over Na2SO4, filtered, and concentrated under reduced pressure to yield 0.97 g (92%) of foam (LC/MS: M+H=528.1), which was used for subsequent step without further manipulation.

153b) (3-Phenylcarbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester : 3-tert-Butoxycarbonylamino-3-phenylcarbamoyl-pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester (960 mg, 1.8 mmol) was combined with Methanol (10 mL, 200 mmol), then at toom temperature added Piperidine (2 mL, 20 mmol) neat and the reaction was stirred for 72 h. Concentrated reaction mixture under reduced pressure and Obtained a solid mass. Triturated entire sample with Et2O, filtered and rinsed solid liberally with Et2O. After air drying there remained 0.55 g (99%) of tannish solid. Proceeded and used this material in subsequent reaction without further manipulation.

153c) [1-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenylcarbamoyl-pyrrolidin-3-yl]-carbamic acid tert-butyl ester: 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-

d]pyrimidin-4-ol (254 mg, 1.00 mmol), Triethylamine (431 uL, 3.10 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (334 mg, 1.10 mmol), and 4-Dimethylaminopyridine (14 mg, 0.11 mmol) in N,N-Dimethylformamide (4.0 mL, 52 mmol) were stirred at room temperature for 1 hour. (3-Phenylcarbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester (335 mg, 1.10 mmol) was added neat and the reaction was stirred at room temperature overnight. The reaction was then concentrated under reduced pressure and partitioned residue between EtOAc and water. Had to filter before separating layers, as precipiated solid causing some problems between layers. The organic phase was dried over Na2SO4, filtered, and concentrated under reduced pressure to give 500 mg of crude product. Dissolved crude in DMSO (3.6 mL), filtered, and purified via preparative reverse phase HPLC. Took purest fractions and basified with saturated aqueous NaHCO3. Solid which crashed from the solution was filtered, and rinsed with water. After air drying there remained 50 mg (9%) off white solid. (LC/MS: M+H=542.1). Proceeded and used material for subsequent step without further manipulation.

153d) At rt dissolved [1-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenylcarbamoyl-pyrrolidin-3-yl]-carbamic acid tert-butyl ester (50.0 mg, 0.0923 mmol) in Methylene chloride (2.0 mL, 31 mmol) then added Trifluoroacetic Acid (1.0 mL, 13 mmol) neat. After 2.5 h concentrated reaction under reduced pressure, dissolved residue in 0.80 mL DMSO, filtered, and purified via preparative reverse phase HPLC. Combined and lyophilized purest fractions. Obtained 32 mg (78%) of title compound as a yellow lyophilate (LC/MS: M+H=442.1).

Example 154. 4-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid [(S)-1-(4-chloro-phenyl)-3-hydroxy-propyl]-amide

154a) 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid methyl ester : 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol (254 mg, 1.00 mmol), Triethylamine (0.432 mL, 3.10 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (334 mg, 1.10 mmol), and 4-Dimethylaminopyridine (14 mg, 0.11 mmol) were combined in N,N-Dimethylformamide (2.0 mL, 26 mmol), and stirred at room temperature. After 45 minutes 4-tert-Butoxycarbonylamino-piperidine-4-carboxylic acid methyl ester (284 mg, 1.10 mmol; Supplier = Oakwood) was added neat and stirred overnight. The reaction mixture was concentrated under reduced pressure and the residue partitioned between CH2Cl2 and water. The organic phase was dried over Na2SO4, filtered, and concentrated under

reduced pressure. Resulting 380 mg (77%) of residue was used for subsequent steps without further manipulation.

154b) 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid : Combined a solution of Lithium hydroxide (180 mg, 7.5 mmol) in water (3 mL, 200 mmol) to a solution of 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid methyl ester (370 mg, 0.75 mmol) in Methanol (10 mL, 200 mmol) at rt and let homogeneous solution stir at rt for 16 hours. After cooling, treated reaction mixture with 1 M of Hydrogen Chloride in Water (7.5 mL, 7.5 mmol), then concentrated off most of MeOH, leaving mostly aqueous as solvent. Filtered resulting solid, then took aqueous filtrate and concentrated. Obtained 292 mg . Added 2.5 mL of DMSO, filtered, then purified via preparative reverse phase HPLC, lyopylized purest fractions to yield 45 mg (12%) of desired product as a yellow lyophilate, which was used for subsequent steps without further manipulation.

154c) [4-[(S)-1-(4-Chloro-phenyl)-3-hydroxy-propylcarbamoyl]-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-carbamic acid tert-butyl ester : 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid (30.0 mg, 0.0624 mmol) was combined with N,N-Dimethylformamide (1 mL, 10 mmol), then 1-Hydroxybenzotriazole (8.44 mg, 0.0624 mmol) and (S)-3-Amino-3-(4-chloro-phenyl)-propan-1-ol; hydrochloride (27.7 mg, 0.125 mmol; Supplier = Oakwood) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (35.9 mg, 0.187 mmol). After 3 hours concentrated reaction under reduced pressure, then partitioned residue between EtOAc and water. The organic was then washed with saturated aqueous NaHCO3, dried over Na2SO4, filtered and concentrated. The crude residue was used for the subsequent step without further manipulation

154d) At rt dissolved [4-[(S)-1-(4-Chloro-phenyl)-3-hydroxy-propylcarbamoyl]-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-carbamic acid tert-butyl ester (70 mg, 0.1 mmol) in Methylene chloride (2.0 mL) then added Trifluoroacetic Acid (1.0 mL, 13 mmol) neat. After 2 hours concentrated reaction under reduced pressure, dissolved residue in 1 mL DMSO, filtered, and purified via preparative reverse

phase HPLC. Combined purest fractions and lyophylized overnight. Obtained 15 mg (20%) of title compound as a yellow lyophilate (LC/MS: M+H=548.1).

Example 155. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid methyl ester

155a) 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester : 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol (508 mg, 2.00 mmol), Triethylamine (863 uL, 6.19 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (668 mg, 2.20 mmol), and 4-Dimethylaminopyridine (28 mg, 0.23 mmol) in N,N-Dimethylformamide (10 mL) were stirred at room temperature for 2 hours. Gradual dissolution of starting material was observed and a considerable darkening of the solution. Piperazine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester (536 mg, 2.20 mmol) was added and the reaction was stirred at room temperature for two hours. Water was added, and the resulting solid product was collected by filtration, washed with water, and dried. Obtained 448 mg (47%) tan colored solid product, which was used for subsequent steps without further manipulation).

155b) At room temperature (rt) dissolved 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester (50 mg, 0.1 mmol) in Methylene chloride (2.0 mL) then added Trifluoroacetic Acid (1.0 mL, 13 mmol) neat. After 2.5 hours concentrated reaction solution under reduced pressure, then dissolved residue in 1 mL of DMSO and purified via preparative reverse phase HPLC. Combined desired fractions and lyophylized overnight. Obtained 23 mg (60%) of title compound as a yellow lyophilate (LC/MS: M+H=381.1).

Example 156. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenylamide

156a) 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester : At rt 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester (77.0 mg, 0.165 mmol) was combined with N,N-Dimethylformamide (3 mL), then 1-Hydroxybenzotriazole (22.3 mg, 0.165 mmol), 4-Methylmorpholine (36.3 uL, 0.330 mmol) and Aniline (22.6 uL, 0.247 mmol) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (94.9 mg, 0.495 mmol). After two hours the reaction mixture was concentrated under reduced pressure, and the resulting

residue partitioned between EtOAc and saturated aqueous NaHCO3. The organic phase was dried over Na2SO4, filtered and concentrated. The crude residue was dissolved in 0.95 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 42 mg (47%) of desired product as a yellow lyophilate (LC/MS: M+H=542.2).

156b) Trifluoroacetic Acid (1 mL, 10 mmol) and Methylene chloride (2 mL, 30 mmol) were combined with 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester (42.0 mg, 0.0775 mmol) at rt. After 1.5 h the reaction solution was concentrated under reduced pressure, after which the resulting residue was dissolved in 1.3 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophylized overnight to yield 29 mg (85%) of title compound as a yellow lypohilate (LC/MS: M+H=442.1).

Example 157. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid benzylamide

157a) 2-Benzylcarbamoyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester: At room temperature 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester (77.0 mg, 0.165 mmol) was combined with N,N-Dimethylformamide (3 mL), then 1-Hydroxybenzotriazole (22.3 mg, 0.165 mmol), 4-Methylmorpholine (36.3 uL, 0.330 mmol) and Benzylamine (27.0 uL, 0.247 mmol) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (94.9 mg, 0.495 mmol). After 1.5 h the reaction mixture was concentrated under reduced pressure and the resulting residue partitioned between EtOAc and saturated aqueous NaHCO3. The organic phase was dried over Na2SO4, filtered and concentrated. The crude residue was dissolved in 0.85 mL of DMSO, filtered, then purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 48 mg (52%) of desired product as a yellow lyophilate (LC/MS: M+H=556.2).

157b) A solution of Trifluoroacetic Acid (1 mL, 10 mmol) and Methylene chloride (2 mL, 30 mmol) was combined with 2-Benzylcarbamoyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (47.0 mg, 0.0846 mmol) at rt. After 1.5 h concentrated mixture under reduced pressure, then

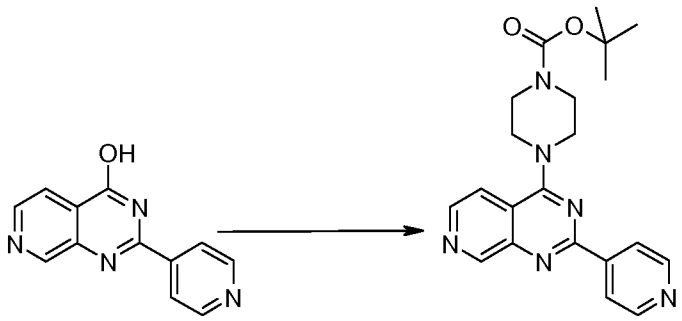
dissolved residue in 1.15 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 38 mg (99%) of title compound as a yellow lypohilate (LC/MS: M+H=456.1).

Example 158. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenethyl-amide

158a) 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenethylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester : At rt 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester (77.0 mg, 0.165 mmol) was combined with N,N-Dimethylformamide (3 mL, 30 mmol), then 1-Hydroxybenzotriazole (22.3 mg, 0.165 mmol), 4-Methylmorpholine (36.3 uL, 0.330 mmol) and Phenethylamine (31.1 uL, 0.248 mmol) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (94.9 mg, 0.495 mmol). After 16 h the reaction mixture was concentrated under reduced pressure and the resulting residue partitioned between EtOAc and saturated aqueous NaHCO3. The organic phase was dried over Na2SO4, filtered and concentrated. The crude residue was dissolved in 0.9 mL of DMSO, filtered, then purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 53 mg (56%) of desired product as a yellow lyophilate (LC/MS: M+H=570.2).

158b) A solution of Trifluoroacetic Acid (1 mL, 10 mmol) and Methylene chloride (2 mL) was combined with 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenethylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester (48.2 mg, 0.0846 mmol) at rt. After 1.5 h concentrated mixture under reduced pressure, then dissolved residue in 1.2 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 38 mg (96%) of title compound as a yellow lyophilate (LC/MS: M+H=470.2).

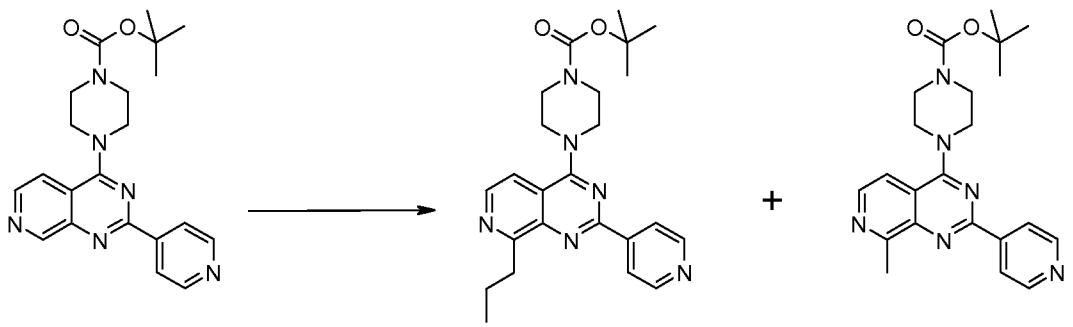
Synthesis of 4-(2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A080]



[A001] [A080]

A mixture of 2-Pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A001] (1.0g, 4.5 mmol), DMF (30 mL) and DIPEA (2.35 mL, 13.5 mmol) was stirred at room temperature under nitrogen. DMAP (5 mg) was added followed by 2,4,6-triisopropylbenzene sulfonyl chloride (1.64g, 5.4 mmol) and the mixture was left to stir for two hours. 1-Boc piperazine (0.83 g, 4.5 mmol) was added and the mixture left to stri at room temperature over night. Water (50 mL) was added and the mixture left to stir for 20 min, filtered and washed with water (x3). The solid was dissolved in DCM (50 mL) and dried (MgSO4), filtered and evaporated under reduced pressure to give the title compound (1.2g, 68% yield) which was used crude in the next step without further purification.

Synthesis of 4-(8-Propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A081] and 4-(8-Methyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A082]



[A080] [A081] [A082]

To a solution of 4-(2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A080] (0.196g, 0.5 mmol) , butyraldehyde (0.090 mL, 1.0 mmol), conc sulphuric acid (0.054 mL, 1.0 mmol) and iron sulphate heptahydrate (0.04g, 0.15 mmol) in DMSO (5 mL) was added hydrogen peroxide (35% solution in water, 0.146 mL,

1.5 mmol) dropwise over 2min. The reaction mixture was left to stir at room temperature overnight then water (5 mL) was added and the mixture was basified by addition of NaOH (1N) dropwise to pH ~7-8. The mixture was then extracted with DCM (x3) the organics were combined and washed with water (x1), brine (x1), dried (MgSO4), filtered and evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO2 column, ISCO eluting with 50-90% EtOAc/cHex on 120g column) to give: 4-(8-Propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (46 mg): LCMS: method: 5, RT:5.79 min, MI 435 [M+H]; ^{1}H NMR (1H, CDCl3, 500MHz), 8.77 (2H, dd), 8.50 (1H, d), 8.38 (2H, dd), 7.46 (1H, d), 3.91-3.89 (4H, m), 3.71-3.69 (4H, m), 3.49 (2H, dd), 2.00-1.92 (2H, dq), 1.51 (9H, s), 1.09 (3H, t) and 4-(8-Methyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (44 mg) as a colourless glass: LCMS: method: 5, RT:5.11 min, MI 407 [M+H]; ^{1}H NMR (CDCl3, 500MHz) 8.78 (2H, dd), 8.46 (1H, d), 8.39 (2H, dd), 7.47 (1H, d), 3.91-3.89 (4H, m), 3.71-3.69 (4H, m), 3.09 (3H, s), 1.51 (9H, s).

Example 159. 4-Piperazin-1-yl-8-propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine

A mixture of 4-(8-Propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid [A081] (0.046g, 0.105 mmol), DCM (3 mL) and HCl (4N in dioxane, 1 mL) was stirred at room temperature for 90 min. The mixture was evaporated under reduced pressure then the crude product was dissolved in methanol and added to SCX-2 cartridge (10g), washed with DCM/MeOH (1:1 10mL) and MeOH (20mL), then eluted with ammonia (7N in methanol, 30mL). The Ammonia washes were evaporated under reduced pressure to give the title compound (34 mg, 75% yield) as a yellow solid: LCMS: method: 5, RT:2.0 min, MI 335 [M+H]; ^{1}H NMR (d6-dmso, 500MHz), 8.76 (2H, dd), 8.45 (1H, d), 8.32 (2H, dd), 7.71 (1H, d), 3.89 (4H, t), 3.37 (2H, t), 2.95 (4H, t), 1.86 (2H, dq), 0.99 (3H, t).

Example 160. 8-Methyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine

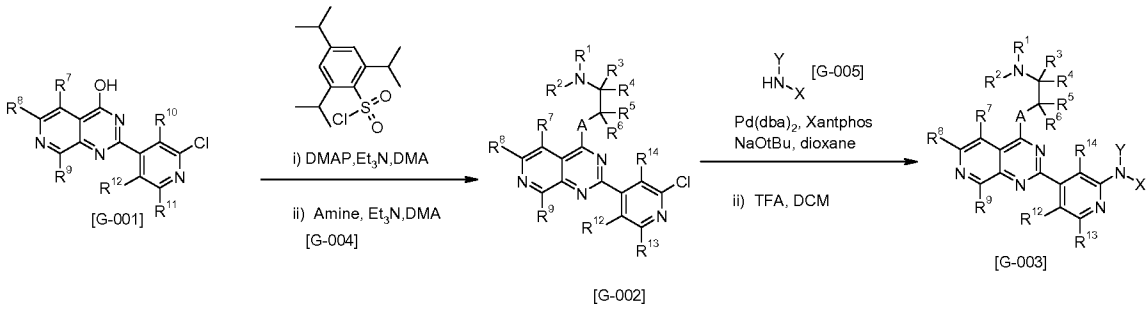
A mixture of 4-(8-Methyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid [A082] (0.045g, 0.11 mmol), DCM (3 mL) and HCl (4N in dioxane, 1 mL) was stirred at room temperature for 90 min. The mixture was evaporated under reduced pressure then the crude product was dissolved in methanol and added to SCX-2 cartridge (10g), washed with DCM/MeOH (1:1 10mL) and MeOH (20mL), then eluted with ammonia (7N in methanol, 30mL). The Ammonia washes were evaporated under reduced pressure to give the title compound (29 mg, 75% yield) as a brown gum: LCMS:

method: 5, RT:2.17 min, MI 307 [M+H]; ^{1}H NMR (d6-dmso, 500MHz), 8.76 (2H, dd), 8.40 (1H, d), 8.33 (2H, dd), 7.70 (1H, d), 3.88 (4H, t), 2.94-2.92 (4H, m), 2.93 (3H, s)

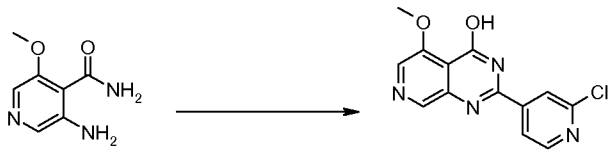
General synthesis of substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-003] Scheme B1

2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-002] were prepared by the reaction of a 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [G-001] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [G-004], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. The 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-002] was involved in a Buchwald type reaction utilising a suitable amine, of general formula [G-005], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor, to yield substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-003]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme B1



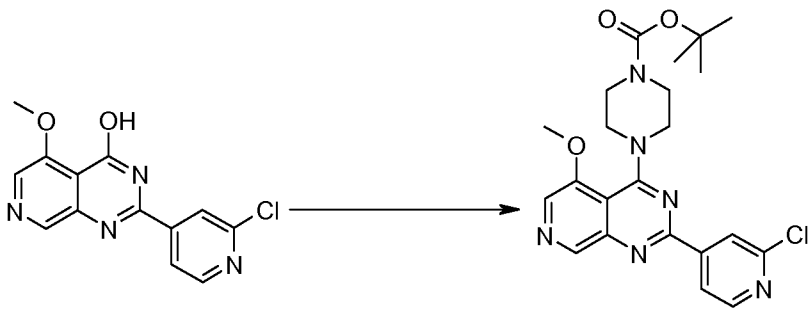
Synthesis of [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine [200]



[B001]

2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [B001]

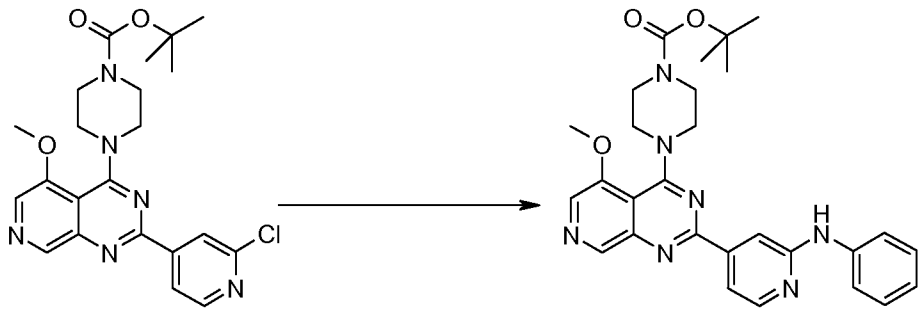
To a solution of 2-chloro-4-pyridinecarbonitrile (0.97g, 7.03 mmol) in MeOH (35 mL) at RT, under nitrogen, was added NaOMe (0.08 g, 1.46 mmol) and left to stir for 60mins. Then a solution of 3-Amino-5-methoxy-isonicotinic acid (1 g, 5.86 mmol) in MeOH (15 mL) was added to the the dark brown mixture dropwise over 5-10mins (via syringe). The solution was stired at rt for 2 h and then overnight at 85° C. After cooling down, the solid was filtered and, washed with methanol and used without further purification to yield the title compound [B001] (0.97 g 57 %yield: LCMS: method: 5, RT:6.32 min, MI 287.34 [M+H].



[B001] [B002]

4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B002].

A mixture of 2-(2-chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [B001] (0.58 g, 2 mmol), anhydrous DMA (5 mL), triethylamine (0.58 mL, 4 mmol) and DMAP (20 mg, 0.16 mmol) was sonicated for 10 min then stirred at room temperature for 10 min. 2,4,6-Triisopropyl -benzenesulfonyl chloride (0.67 g, 2.2 mmol) was added and the mixture was sonicated for 5 min then left to stir at room temperature for 2 hours. During this time the material went into solution to form a viscous solution. A solution of Boc piperazine (0.56 g, 3 mmol) in anhydrous DMA (1 mL) was added and the reaction mixture was left to stir at room temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with DCM (2 x 30 mL), the extracts were combined and washed with water (20 mL), saturated bicarbonate solution (2 x 20 mL) and water (20 mL), dried ($MgSO_4$) filtered and evaporated under reduced pressure to give a pale yellow oil, which was purified by flash column chromatography (SP1, 50 g SiO_2 cartridge 100% EtOAc up to 95% EtOAc : 5 % MeOH gradient) to give the *title compound* [B002] as a colourless solid (0.22g 24% yield). LCMS: method: 5, RT:10.86 min, MI 457 [M+H]; NMR: (1H, 500MHz, $CDCl_3$); 9.0 (1H, s), 8.53 (1H, d), 8.35 (1H, s), 8.28 (1H, 1H, d), 8.23 (1H, s), 3.70 (4H, br s), 3.64 (4H, br s), 1.50 (9H, s)

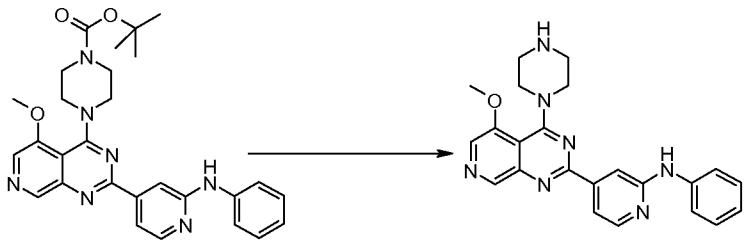


[B002] [B003]

4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B003]

A mixture of 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B002] (0.100 g, 0.22 mmol), $Pd(dba)_2$ (10 mg, 0.013 mmol), Xantphos (17.5 mg, 0.025 mmol), NaOtBu (43 mg, 0.440 mmol) and anhydrous dioxane (4 ml) was added to a microwave vial. Aniline was then added the vial was sealed and heated at 150°C for 20 min. Water (10 mL) was added and the reaction mixture was extracted with DCM (2 x 10 mL), the extracts were combined and washed

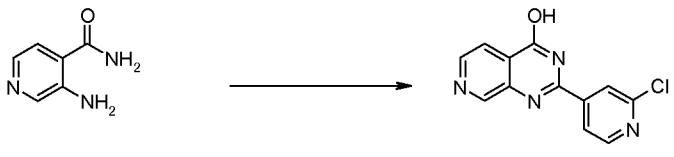
with water (10 mL), saturated bicarbonate (2 x 10 mL) and water (10 mL), dried with MgSO4 filtered and evaporated to give a pale yellow oil, which was purified by flash column chromatography (SP1, 25 g SiO2 cartridge 100% EtOAc up to 95% EtOAc : 5 % MeOH gradient) to give the title compound [B003] as a colourless solid (0.04g 36% yield). LCMS: method: 5, RT:7.80 min, MI 514 [M+H]; NMR: (1H, 500MHz, $CDCl_3$); 8.93 (1H, s), 8.65 (1H, d), 8.41 (1H, s), 7.39 (1H, d), 7.58 (5H, m), 6.55 (1H, br s), 3.63 (4H, m), 3.57 (4H, m), 1.49 (9H, s).



[B003] [200]

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine [200]

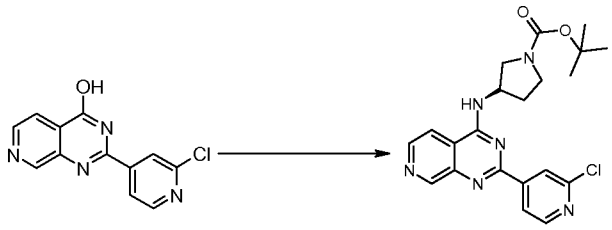
To a mixture of 4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B003] (0.040 g, 0.080 mmol) in DCM (1 ml) was added TFA (1 ml) and the mixture was left to stir at room temperature for 2 hours. After completion the crude reaction mixture was diluted with DCM (5 mL) and poured onto a 1g SCX-2 cartridge and washed with DCM and MeOH before eluting with 2N NH3/MeOH which was evaporated to give a pale yellow oil, which was evaporated in a genevac to give a pale yellow solid (25 mg). LCMS: method: 5, RT:3.12 min, MI: 414.22 [M+H]; NMR: (1H, 500MHz, d6-dmso); 9.32 (1H, br s), 8.8 (1H, s), 8.29 (2H, m), 7.88 (1H, s), 7.76 (2H, d), 7.64 (1H, d), 7.29 (2H, m), 6.88 (2H, m), 4.04 (3H, s), 3.64 (4H, m), 2.88 (4H, m).



[B004]

2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [B004]

To a solution of 2-chloro-4-pyridinecarbonitrile (2.18g, 15.77 mmol) in dry THF (20 mL) was added 3-Amino-isonicotinic acid methyl ester (2g, 13.1 mmol) followed by Potassium tert-pentoxide (15.5 mL, 26.3 mmol1.7M in toluene). The reaction was stirred overnight at RT. The precipitate was collected by filtration to yield the title compound which was used without further purification: LCMS: method: 5, RT:4.05 min, MI 259 [M+H].



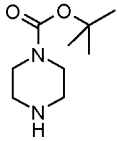
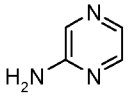
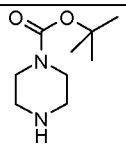
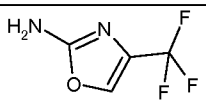
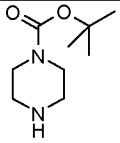
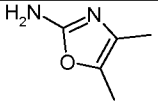
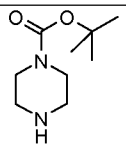
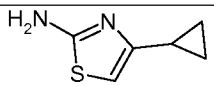
[B004] [B005]

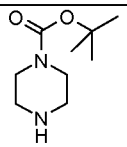
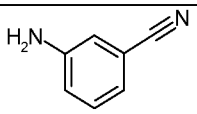
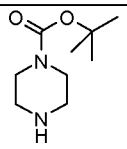
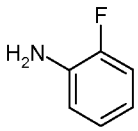
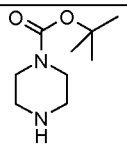
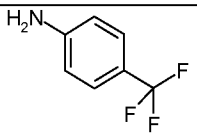
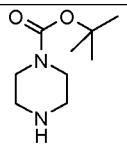
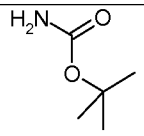
(R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester [B005]

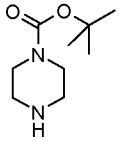
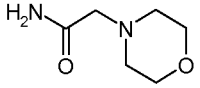
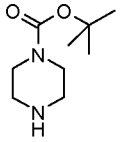
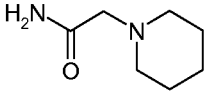
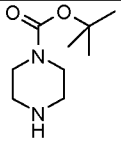
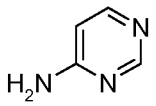
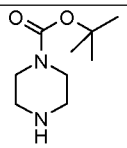
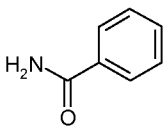
A mixture of 2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [B003] (1 g, 3.86 mmol), anhydrous DMA (10 mL), triethylamine (1.1 mL, 7.73 mmol), 2,4,6-Triisopropylbenzenesulfonyl chloride (1.29 g, 3.25 mmol), and DMAP (47 mg, 0.386 mmol) was stirred at room temperature for 1h and (R)-3-Amino-pyrrolidine-1-carboxylic acid tert-butyl ester (940 mg, 5.02 mmol) was added. The reaction mixture was stirred overnight and the solvent was evaporated under reduced pressure. DCM and Et_2O were added and the resulting solid was collected and used without further purification in the next step. LCMS: method: 5, RT 6.19 min, MI 427 [M+H].

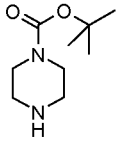
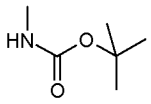
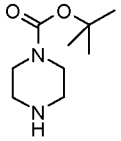
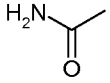
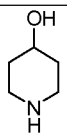
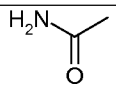
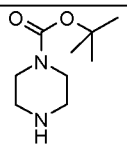
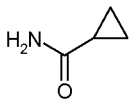
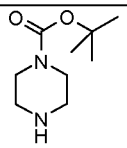
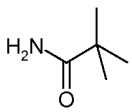
The following compounds were synthesised according to the general synthesis shown in scheme [B1] (Example1):

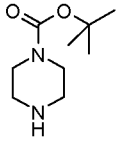
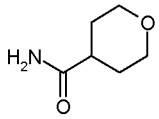
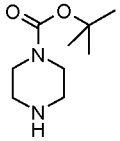
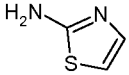
Ex	SM [G-002]	Amine	Aniline	Analysis		Name
				LCMS	NMR	

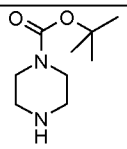
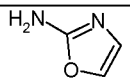
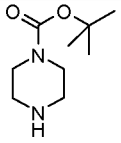
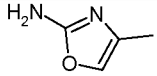
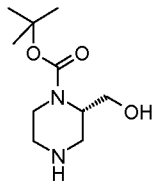
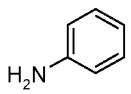
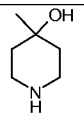
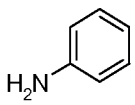
201	[B003]			Method 1: RT: 1.91 min, MI: 416.17 [M+H]	(1H, 300MH, $CDCl_3$) 10.22 (1H, m), 9.16 (1H, m), 8.82 (1H, m), 7.72 (1H, m), 8.43 (1H, m), 8.33 (1H, m), 8.30 (1H, m), 8.26 (1H, m), 7.85 (1H, m), 4.10 (3H, s), 3.71 (4H, m), 2.96 (4H, m)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine
202	[B003]			Method 1: RT: 3.27 min, MI: 473.2 [M+H]	(1H, 500MHz, d6-dmso) 9.35 (1H, s), 9.10 (1H, s), 8.91 (1H, s), 8.53 (1H, m), 8.46 (1H, d), 8.42 (1H, s), 7.99 (1H, dd), 4.09 (3H, s), 3.93 (4H, m, br), 3.27 (4H, m, br)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-oxazol-2-yl)-amine
203	[B003]			Method 1: RT: 2.40 min, MI: 433.1 [M+H]	(1H, 500MHz, d6-dmso) 10.55 (1H, s), 9.14 (1H, s), 8.81 (1H, s), 8.34 (1H, d), 8.31 (1H, s), 7.84 (1H, d), 4.06 (3H, s), 3.68 (4H, m), 2.90 (4H, m), 2.19 (3H, s), 2.01 (3H, s)	(4,5-Dimethyl-oxazol-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
204	[B003]			Method 1: RT: 3.73 min, MI: 461.20 [M+H]	(1H, 500MHz, d6-dmso) 9.68 (1H, s, br), 9.56 (2H, s, br), 8.96 (1H, s), 8.46 (1H, d), 8.42 (1H, s), 8.23 (1H, s), 7.88 (1H, dd), 4.10 (3H, s), 3.96 (4H, m), 3.32 (1H, m), 3.27 (4H, m), 0.86 (2H, m), 0.80 (2H, m)	(4-Cyclopropyl-thiazol-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

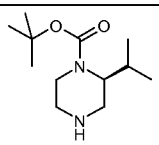
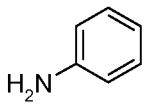
205	[B003]			Method 1: RT: 3.47 min, MI: 439.2 [M+H]	(1H, 300MHz, d6-dmso) 9.82 (1H, s), 9.10 (1H, s, br), 8.89 (1H, s), 8.41 (2H, s, br), 8.40 (1H, s), 7.97 (1H, s), 7.89 (1H, d), 7.78 (1H, d), 7.48 (1H, t), 7.32 (1H, d), 4.09 (3H, s), 3.90 (4H, m), 3.31 (4H, m)	3-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile
206	[B003]			Method 1: RT: 2.69 min, MI: 482.03 [M+H]	(1H, 300MHz, d6-dmso) 8.95 (1H, s), 8.79 (1H, s), 8.31 (1H, s), 8.23 (1H, d), 8.20 (1H, dt), 8.01 (1H, s), 7.68 (1H, dd), 7.21 (1H, ddd), 7.14 (1H, td), 7.01-6.99 (1H, m), 4.06 (3H, s), 3.65 (4H, m, br), 2.87 (4H, m, br)	(2-Fluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
207	[B003]				(1H, 300MHz, d6-dmso) 9.83 (1H, s), 8.85 (1H, s), 8.38 (1H, d), 8.36 (1H, s), 7.98 (2H, s), 7.96 (1H, s), 7.76 (1H, d), 7.61 (2H, d), 4.07 (3H, s), 3.79 (4H, m, br), 3.11 (4H, m, br)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine
208	[B003]			Method 1: RT: 3.51 min, MI: 338.2 [M+H]	(1H, 300MHz, d6-dmso) 8.78 (1H, s), 8.30 (1H, s), 8.27 (1H, s), 8.04 (1H, d), 7.47 (1H, s), 7.41 (1H, d), 6.10 (2H, s, br), 4.06 (3H, s), 3.66 (4H, m, br), 2.95 (4H, m, br)	4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamine

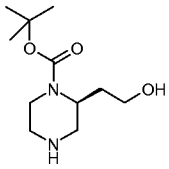
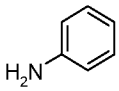
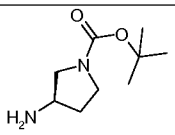
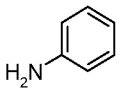
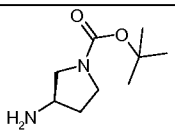
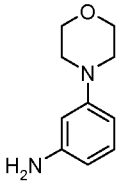
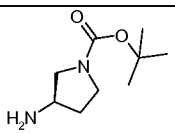
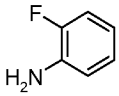
209	[B003]			Method 1: RT: 1.80 min, MI: 465.2 [M+H]	(1H, 300MHz, d6-dmso) 10.11 (1H, s), 9.10 (1H, s), 8.88 (1H, s), 8.47 (1H, d), 8.37 (1H, s), 8.05 (1H, d), 4.08 (3H, s), 3.80 (4H, m, br), 3.64 (4H, t, br), 3.23 (2H, s), 3.15 (4H, m, br), 2.55 (4H, m, br)	N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-morpholin-4-yl-acetamide
210	[B003]			Method 1: RT: 1.51 min, MI: 463.2 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.79 (1H, s), 8.41 (1H, d), 8.21 (1H, s), 8.10 (1H, d), 4.11 (3H, s), 3.77 (4H, m), 3.19 (2H, s), 3.01 (4H, m), 2.59 (4H, m), 1.73-1.69 (4H, m), 1.52 (2H, m)	N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-piperidin-1-yl-acetamide
211	[B003]			Method 1: RT: 2.05 min, MI: 416.14 [M+H]	(1H, 300MHz, d6-dmso) 10.42 (1H, s), 8.85 (1H, s), 8.75 (2H, s), 8.45 (2H, d), 8.35 (1H, s), 8.22 (1H, s), 7.90 (1H, dd), 4.08 (3H, s), 3.73 (4H, m), 2.98 (4H, m)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-4-yl-amine
212	[B003]			Method 1: RT: 2.69 min, MI: 442.13	(1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.85 (1H, s), 8.54 (1H, d), 8.33 (1H, s), 8.22 (1H, s), 8.09-8.05 (3H, m), 7.62-7.59 (1H, m), 7.54-7.51 (2H, m)	N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-benzamide

213	[B003]			Method 1: RT: 3.98 min, MI: 352.3 [M+H]	(1H, 300MHz, d6-dmso) 8.80 (1H, s), 8.31 (1H, s), 8.11 (1H, d), 7.47 (1H, s), 7.39 (1H, d), 6.72 (1H, d), 4.05 (3H, s), 3.71 (4H, m), 3.03 (4H, m), 2.81 (3H, d)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-methyl-amine
214	[B003]			Method 1: RT: 2.33 min MI: 380.18 [M+H]	(1H, 300MHz, d6-dmso) 10.58 (1H, s), 9.05 (1H, s), 8.81 (1H, s), 8.43 (1H, d), 8.29 (1H, s), 7.97 (1H, d), 4.05 (3H, s), 3.63 (4H, m), 3.15 (1H, d, br), 2.87 (4H, m), 2.12 (3H, s)	N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide
215	[B003]			Method 1: RT: 3.87 min, MI: 395.11 [M+H]	(1H, 300MHz, d6-dmso) 10.58 (1H, s), 9.05 (1H, s), 8.81 (1H, s), 8.43 (1H, d), 8.32 (1H, s), 7.98 (1H, dd), 4.79 (1H, d), 4.06 (3H, s), 4.00 (1H, m, br), 3.81 (1H, m, br), 3.39 (3H, m, br), 2.12 (3H, s), 1.89 (2H, d, br), 1.56 (2H, m, br).	N-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide
216	[B003]			Method 1: RT: 2.66 min, MI: 406.13 [M+H]	(1H, 300MHz, d6-dmso) 8.28 (1H, s), 8.01 (1H, s), 7.61 (1H, d), 7.42 (1H, s), 7.26 (1H, dd), 3.32 (3H, s), 2.99 (4H, m), 2.27 (4H, m), 1.13 (1H, m), 0.22 (2H, m), 0.12 (2H, m)	Cyclopropane-carboxylic acid [4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide
217	[B003]			Method 1: RT: 3.13	(1H, 300MHz, d6-dmso) 9.89 (1H, s), 9.03 (1H, s), 8.84 (1H, s), 8.46 (1H, d),	N-[4-(5-Methoxy-4-piperazin-

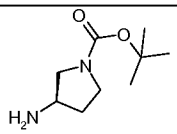
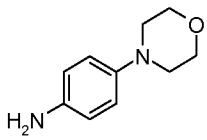
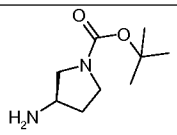
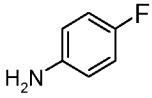
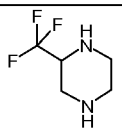
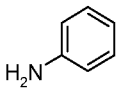
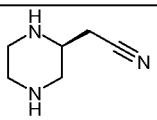
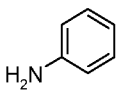
				min, MI: 422.2 [M+H]	8.33 (1H, s), 8.01 (1H, dd), 4.06 (3H, s), 3.68 (4H, m, br), 2.95 (4H, m ,br), 1.27 (9H, s)	1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2,2-dimethyl-propionamide
218	[B003]			Method 1: RT: 2.82 min, MI: 450.20 [M+H]	(1H, 300MHz, d6-dmso) 10.59 (1H, s), 9.10 (1H, s), 8.87 (1H, s), 8.46 (1H, d), 8.36 (1H, s), 8.01 (1H, dd), 4.07 (3H, s), 3.90 (2H, dd, br), 3.78 (4H, m, br), 3.35 (2H, m), 3.13 (4H, m, br), 2.79 (1H, m), 1.74-1.66 (4H, m)	Tetrahydro-pyran-4-carboxylic acid[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide
219	[B003]			Method 1: RT: 3.12 min, MI: 241.09 [M+H]	(1H, 300MHz, d6-dmso) 8.84 (1H, s), 8.43 (1H, d), 8.35 (1H, s), 8.15 (1H, s), 7.82 (1H, dd), 7.40 (1H, d), 7.01 (1H, s), 4.07 (3H, s), 3.75 (4H, m), 3.04 (4H, m)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-thiazol-2-yl-amine

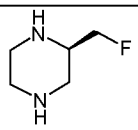
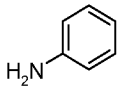
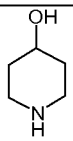
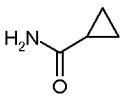
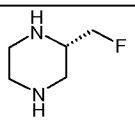
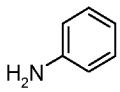
220	[B003]			Method 1: RT: 2.28 min, MI: 405.10 [M+H]	(1H, 500MHz, d6-dmso) 10.82 (1H, s), 9.04 (1H, s), 8.84 (1H, s), 8.38 (1H, d), 8.34 (1H, s), 7.87 (1H, d), 7.74 (1H, s), 7.09 (1H, s), 4.07 (3H, s), 3.74 (4H, m), 3.01 (4H, m)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-oxazol-2-yl-amine
221	[B003]			Method 1: RT: 2.44 min, MI: 419.18 [M+H]	(1H, 500MHz, d6-dmso) 10.77 (1H, s), 9.19 (1H, s), 8.91 (1H, s), 8.40 (1H, s), 8.39 (1H, d), 7.88 (1H, d), 7.44 (1H, s), 4.09 (3H, s), 3.92 (4H, m), 3.29 (4H, m), 2.10 (3H, s)	[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-oxazol-2-yl)-amine
222	[B003]			Method 1: RT: 2.38 min, MI: 444.2 [M+H]	(1H, 500MHz, d6-dmso) 9.39 (1H, s), 8.88 (1H, s), 8.39 (1H, s), 8.31 (1H, d), 7.94 (1H, s), 7.75 (2H, d), 7.68 (1H, d), 7.27 (2H, t), 6.89 (1H, t), 4.30 (2H, m), 4.09 (3H, s), 3.70 (2H, m), 3.48-3.36 (5H, m)	{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol
223	[B003]			Method 5: RT: 4.34 min, MI: 443.19 [M+H]	(1H, 500MHz, d6-dmso) 9.29 (1H, s), 8.78 (1H, s), 8.30 (1H, s), 8.28 (1H, d), 7.89 (1H, d), 7.73 (2H, d), 7.65 (1H, dd), 7.27 (2H, t), 6.88 (1H, t), 4.47 (1H, s), 4.06 (3H, s), 3.94 (2H, m, br), 3.53 (2H, m), 1.64 (4H, m), 1.19 (3H, s)	1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-4-methyl-piperidin-4-ol

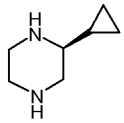
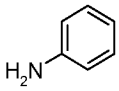
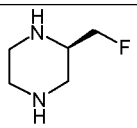
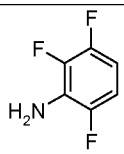
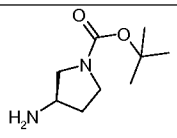
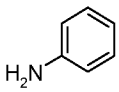
224	[B003]			Method 5: RT: 2.87 min, MI: 456.23 [M+H]	(1H, 500MHz, d6-dmso) 9.30 (1H, s), 8.81 (1H, s), 8.32 (1H, s), 8.29 (1H, d), 7.88 (1H, s), 7.74 (2H, d), 7.64 (1H, dd), 7.27 (2H, t), 6.89 (1H, t), 4.24-4.12 (2H, m), 4.06 (3H, s), 3.15-3.06 (2H, m), 2.82 (2H, m), 2.59 (1H, m), 1.66 (1H, m), 0.96 (6H, dd)	{4-[4-((S)-3-Isopropyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine

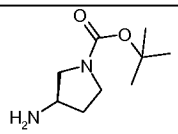
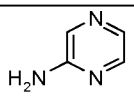
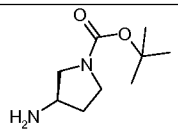
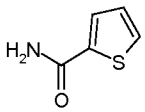
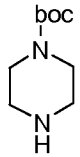
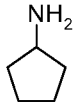
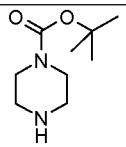
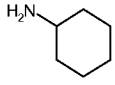
225	[B003]			Method 5: RT: 2.49 min, MI: 458.18 [M+H]]	(1H, 500MHz, d6-dmso) 9.30 (1H, s), 8.82 (1H, s), 8.34 (1H, s), 8.29 (1H, d), 7.90 (1H, s), 7.73 (2H, d), 7.67 (1H, dd), 7.27 (2H, t), 6.89 (1H, t), 4.21 (2H, m, br), 4.06 (3H, s), 3.58 (2H, t), 3.22 (1H, t, br), 3.16-3.14 (2H, m), 2.95 (2H, m), 1.63 (2H, m)	2-{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-ethanol
226	[B003]			Method 5: RT: 2.11 min, MI: 457.20 [M+H]	(1H, 500MHz, d6-dmso) 8.90 (1H, s, br), 8.75 (1H, s), 8.32 (1H, s), 8.19 (1H, d), 8.07 (1H, d), 7.78 (1H, s), 7.55 (1H, d), 7.47 (2H, d), 6.72 (2H, d), 4.76-4.70 (1H, m), 4.12 (3H, s), 3.29 (1H, dd), 3.10-3.02 (1H, m), 2.93-2.87 (1H, m), 2.83 (6H, s), 2.32-2.23 (1H, m), 1.90-1.76 (1H, m)	N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-N',N'-dimethyl-benzene-1,4-diamine
227	[B003]			Method 5: RT: 2.53 min, MI: 499.26 [M+H]	(1H, 500MHz, d6-dmso) 9.23 (1H, s, br), 8.75 (1H, s), 8.32 (1H, s), 8.28 (1H, d), 8.09 (1H, d), 7.90 (1H, s), 7.65 (1H, d), 7.36 (1H, s), 7.22 (1H, s), 7.12 (1H, t), 6.53 (1H, dd), 4.81-4.75 (1H, m), 4.12 (3H, s), 3.75 (4H, m), 3.37-3.31 (1H, dd), 3.08 (4H, m), 2.95-2.90 (1H, m), 2.35-2.26 (1H, m), 1.88-1.82 (1H, m)	{5-Methoxy-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine
228	[B003]			Method 5: RT: 2.63	(1H, 500MHz, d6-dmso) 9.00 (1H, s), 8.76 (1H, s), 8.33 (1H, s), 8.26 (1H, d),	{2-[2-(2-Fluoro-phenylamino)-pyridin-

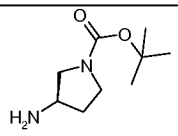
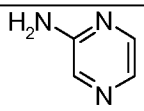
				min, MI: 432.14 [M+H]	8.16 (1H, t), 8.10 (1H, d), 8.01 (1H, s), 7.71 (1H, d), 7.23 (1H, t), 7.14 (1H, t), 7.01 (1H, t), 4.82-4.74 (1H, m), 4.13 (3H, s), 3.37-3.31 (1H, m), 3.12-3.04 (1H, m), 2.97-2.89 (1H, m), 2.35-2.25 (1H, m), 1.89-1.82 (1H, m)	4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

229	[B003]			Method 5: RT: 2.34 min, MI: 499.25 [M+H]	(1H, 500MHz, d6-dmso) 9.06 (1H, s), 8.76 (1H, s), 8.33 (1H, s), 8.22 (1H, d), 8.09 (1H, d), 7.83 (1H, s), 7.60 (1H, s), 7.58 (2H, d), 6.90 (2H, d), 4.81-4.74 (1H, m), 4.13 (3H, s), 3.73 (4H, t), 3.02 (4H, t), 2.96-2.93 (2H, m), 2.33-2.25 (1H, m), 1.89-1.82 (1H, m)	{5-Methoxy-2-[2-(4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine
230	[B003]			Method 5: RT: 2.48 min, MI: 432.14 [M+H]	(1H, 300MHz, d6-dmso) 9.46 (1H, s), 8.78 (1H, s), 8.35 (1H, s), 8.32 (1H, s), 8.27 (1H, d), 8.15 (1H, d), 7.89 (1H, s), 7.75 (2H, dd), 7.67 (1H, d), 7.11 (2H, t), 4.88-4.84 (1H, m), 4.14 (3H, s), 3.49-3.44 (1H, m), 3.21-3.16 (1H, m), 3.07-3.02 (1H, m), 2.35-2.32 (1H, m), 1.99-1.94 (1H, m)	{2-[2-(4-Fluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine
231	[B003]			Method 5: RT: 5.08 min, MI 482.2 [M+H]	(1H, 300MHz, d6-dmso) 9.34 (1H, s), 8.85 (1H, s), 8.36 (1H, s), 8.31 (1H, d), 7.89 (1H, s), 7.74 (2H, d), 7.64 (1H, dd), 7.28 (1H, d), 7.24 (1H, s), 6.89 (1H, t), 4.23 (1H, d), 4.07 (3H, s), 3.71-3.62 (1H, m), 3.22 (2H, dd), 3.08 (2H, d), 2.89-2.81 (1H, m)	{4-[5-Methoxy-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
232	[B003]			Method 5: RT: 2.68 min, MI: 453.17	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.82 (1H, s), 8.33 (1H, s), 8.29 (1H, d), 7.89 (1H, s), 7.75 (2H, d), 7.67 (1H, d), 7.27 (2H, t), 6.89	{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-

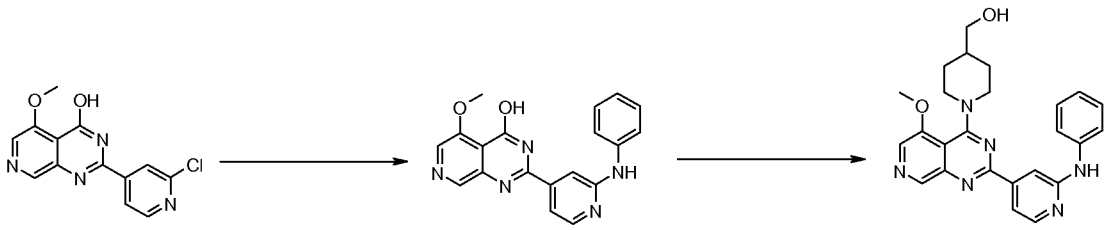
				[M+H]	(1H, t), 4.18 (1H, dd), 4.07 (3H, s), 3.29 (1H, m), 3.12-3.02 (3H, m), 2.93 (1H, t), 2.82 (1H, t), 2.71 (2H, d)	d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile
233	[B003]			Method 5: RT: 2.43 min, MI: 446.18 [M+H]	(1H, 300MHz, d6-dmso) 9.30 (1H, s), 8.81 (1H, s), 8.33 (1H, s), 8.29 (1H, d), 7.88 (1H, s), 7.73 (2H, d), 7.65 (1H, d), 7.27 (1H, t), 6.89 (1H, t), 4.49 (1H, dd), 4.39 (1H, dd), 4.15 (2H, t, br), 4.06 (3H, s), 3.15-3.11 (2H, m), 3.04 (1H, dd), 2.97 (1H, dd), 2.83 (1H, t, br), 2.60 (1H, m, br)	{4-[4-((R)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
234	[B003]			Method 5: RT: 4.39 min, MI: 421.20 [M+H]	(1H, 500MHz, d6-dmso)10.89 (1H, s), 9.06 (1H, s), 8.80 (1H, s), 8.44 (1H, d), 8.31 (1H, s), 7.98 (1H, d), 4.79 (1H, d), 4.06 (1H, s), 3.99 (2H, d, br), 3.80 (1H, m), 3.38 (1H, m), 2.04 (1H, m), 1.89 (2H, d, br), 1.56 (2H, d, br), 0.86-0.81 (4H, m)	Cyclopropane-carboxylic acid {4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide
235	[B003]			Method 5: RT: 2.43 min, MI: 446.18 [M+H]	(1H, 500MHz, d6-dmso) 9.30 (1H, s), 8.81 (1H, s), 8.33 (1H, s), 8.29 (1H, d), 7.89 (1H, s), 7.73 (2H, d), 7.65 (1H, d), 7.27 (2H, t), 6.89 (1H, t), 4.49 (1H, d, br), 4.39 (1H, d, br), 4.15 (2H, t, br), 4.06 (3H,s), 3.13 (2H, m, br), 3.03 (1H, d, br), 2.97 (1H, t, br), 2.83 (1H, t, br)	{4-[4-((S)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine

236	[B003]			Method 5: RT: 5.50 min, MI: 454.40 [M+H]	(1H, 500MHz, d6-dmso) 9.31 (1H, s), 8.80 (1H, s), 8.32 (1H, s), 8.30 (1H, d), 7.88 (1H, s), 7.73 (2H, d), 7.63 (1H, dd), 7.27 (2H, t), 6.89 (1H, t), 4.20 (1H, d, br), 4.09 (1H, d, br), 4.04 (3H, s), 3.12 (1H, t), 3.00 (1H, d), 2.93 (1H, t), 2.73 (1H, t), 2.05 (1H, t), 0.76 (1H, m), 0.42 (2H, d, br), 0.28 (2H, m)	{4-[4-((S)-3-Cyclopropyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
237	[B003]			Method 5: RT: 3.15 min, MI: 500.18 [M+H]	(1H, 500MHz, d6-dmso) 9.02 (1H, s), 8.82 (1H, s), 8.33 (1H, s), 8.18 (1H, d), 7.84 (1H, s), 7.68 (1H, dd), 7.30 (1H, m), 7.19 (1H, m), 4.48 (1H, d), 4.39 (1H, d), 4.18 (1H, d, br), 4.12 (1H, m), 4.06 (3H, s), 3.13 (2H, m), 2.98 (2H, m), 2.84 (1H, t, br)	{4-[4-((R)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,3,6-trifluoro-phenyl)-amine
238	[B003]			Method 5: RT: 2.41 min, MI: 414 [M+H]	(1H, 300MHz, d6-dmso) 2.03 (m, 1H), water peak very broad!!, 4.13 (s, 3H), 4.87 (brs, 1H), 6.89 (t, 1H), 7.27 (t, 2H), 7.68 (d, 1H), 7.76(d, 2H), 7.93 (s, 1H), 8.30 (d, 1H), 8.35 (s, 1H), 8.79 (s, 1H), 9.44 (s, 1H)	[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine

239	[B003]			Method 5: RT: 2.10 min, MI: 416 [M+H]	(1H, 300MHz, d6-dmso) large water peak 4.84 (brs, 1H), 6.60 (brs, 1H), 7.90 (d, 1H), 8.12 (d, 2H), 8.26 (d, 1H), 8.36 (s, 1H), 8.44 (d, 1H), 8.78 (d, 1H), 8.81 (s, 1H), 9.11 (s, 1H), 10.30 (s, 1H)	{5-Methoxy-2-[2-(pyrazin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine
240	[B003]			Method 5: RT: 3.23 min, MI: 448 [M+H]	(1H, 300MHz, d6-dmso) 1.92-2.05 (m, 2H), huge water peak, 3.81 (s, 3H), 4.87 (brs, 1H), 7.22 (dd, 1H), 7.91 (d, 1H), 8.11 (d, 1H), 8.19 (d, 1H), 8.26-8.29 (m, 2H), 8.37 (s, 1H), 8.55 (d, 1H), 8.83 (s, 1H), 9.16 (s, 1H), 11.07 (br s, 1H)	Thiophene-2-carboxylic acid {4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide
241	[B003]			Method 5: RT: 2.05 min, MI: 406.20 [M+H]	(1H, 300MHz, d6-dmso) 8.84 (1H, s), 8.36 (1H, s), 8.09 (1H, d), 7.52 (1H, s), 7.37 (1H, dd), 6.79 (1H, s), 4.18 (1H, m), 4.07 (3H, s), 3.87 (4H, m, br), 3.27 (4H, m, br), 1.92 (2H, m, br), 1.69 (2H, m, br), 1.55-1.45 (4H, m).	Cyclopentyl-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
242	[B003]			Method 5: RT: 2.18 min, MI: 420.23 [M+H]	(1H, 500MHz, d6-dmso) 8.79 (1H, s), 8.31 (1H, s), 8.06 (1H, d), 7.49 (1H, s), 7.34 (1H, dd), 6.62 (1H, d), 4.06 (3H, s), 3.74 (1H, m), 3.70 (4H, m), 3.01 (4H, m), 1.93 (2H, d, br), 1.71 (2H, m), 1.58 (1H, m), 1.33-1.28	Cyclohexyl-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

					(2H, m), 1.20-1.16 (3H, m)	
243	[B005]			Method 5: RT: 1.84 min, MI: 386.0 [M+H]	(1H, 500MHz, d6-dmso): 10.32 (1H, s), 9.20 (1H, s), 9.15 (1H, d), 8.79 (1H, d), 8.66 (1H,d), 8.35-8.44 (2H, m), 8.29 (1H, s), 8.10 (1H, s), 7.92 (1H, d), 4.95 (1H, br s), 3.58 (1H, dd), 3.26 (3H, m), 2.35 (1H, m), 2.17 (1H, m).	{2-[2-(Pyrazin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

Synthesis of {1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol [244]



[B003] [B006] [244]

5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [B006]

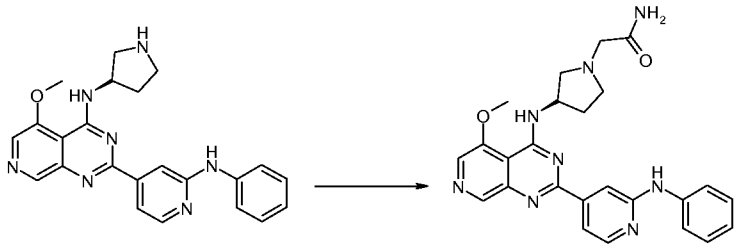
A mixture of 4 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [B003] (0.100 g, 0.346 mmol), $Pd(OAc)_2$ (4 mg, 0.018 mmol), Xantphos (21 mg, 0.035 mmol), cesium carbonate (225 mg, 0.695 mmol) and anhydrous dioxane (1 ml) was heated at 90° overnight. Water (5 mL) was added and the reaction mixture triturated for 30 min after which a yellow solid was collected by filtration and washed with water (20 ml) and DCM (20 ml) to give the *title* compound as a yellow solid (0.07g, 59% yield) which was used without further purification in the next step. LCMS method: 1, RT:2.23 min, MI 346.24 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.30 (1H, s), 8.60 (1H, s), 8.25 (1H, d), 7.71 (2H, d), 7.65 (1H, s), 7.45 (1H, dd), 7.26 (2H, t), 6.89 (1H, t), 3.96 (3H, s).

{1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol [244]

5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [B003] (70 mg, 0.203 mmol), TEA (84 µl, 0.609 mmol) and DMAP (25 mg, 0.203 mmol) were sonicated in DMF (1.5 ml) for 30 min. 2,4,6-Triisopropylbenzenesulfonyl chloride (74 mg, 0.243 mmol) was then added and the reaction mixture stirred at room temperature for 3 hr. 4-Piperidinemethanol (28 mg, 0.243 mmol) was then added and the reaction mixture stirred at room temperature overnight. The solvent was evaporated under reduced pressure to give a pale yellow solid, which was purified by flash column chromatography (SP1, 12 g SiO_2 cartridge 100% DCM up to 95% DCM: 5 % MeOH gradient) to give the *title compound* as a yellow solid (38 mg, 42% yield). LCMS method: 1, RT:5.26 min, MI 443.35 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.30 (1H, s), 8.79 (1H, s), 8.31 (1H, s), 8.28 (1H, d), 7.89 (1H, s), 7.74 (2H, d), 7.65 (1H, d), 7.27 (2H, t), 6.88 (1H, t), 4.52 (1H, t), 4.30 (2H, d, br),

4.07 (3H, s), 3.16 (1H, d), 3.11 (2H, t, br), 1.83 (2H, d, br), 1.72 (1H, s, br), 1.33 (2H, q, br), 1.13 (2H, dd)

Synthesis of 2-{3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-R-pyrrolidin-1-yl}-acetamide [245]



[238] [245]

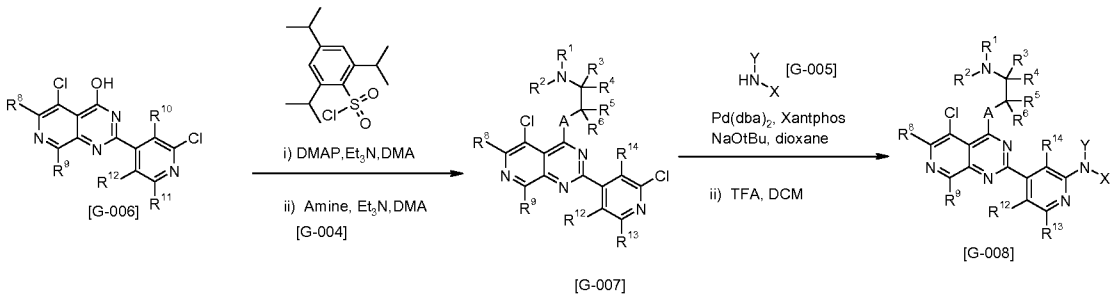
To a mixture of [5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine [238] (50 mg, 0.121 mmol) and K_2CO_3 (50 mg, 0.363 mmol) in DMF (1 mL) was added 2-bromoacetamide (17 mg, 0.121 mmol). The reaction mixture was heated at 80°C for 4 hr. Water (10 mL) was added and the reaction mixture was extracted with EtOAc (2 x 10 mL), the extracts were combined and washed with brine (20 mL), dried ($MgSO_4$) filtered and evaporated under reduced pressure to give a pale yellow oil, which was diluted with MeOH (5 mL) and poured onto a 1g SCX-2 cartridge and washed with MeOH before eluting with 2N NH3/MeOH which was evaporated. The resulting oil was triturated in Et_2O to give the *title compound* as a white solid (12 mg, 17% yield). LCMS method: 1, RT:2.17 min, MI 471 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.32 (1H, s), 8.78 (1H, s), 8.35 (1H, s), 8.31 (1H, d), 8.23 (1H,d), 7.76 (2H, d), 7.70 (1H, d), 7.28 (2H, t), 7.13 (1H, s), 6.90 (1H, t), 4.82 (1H, s), 4.15 (3H, s), 3.10 (2H, d), 3.00 (1H, m), 2.89 (1H, m), 2.81 (1H, m), 2.57 (1H, m), 2.40 (1H, m), 1.88 (1H, m).

General synthesis of 5-chloro substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-008] Scheme B2

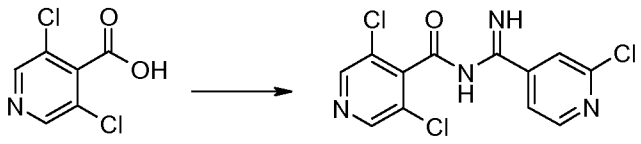
5-chloro 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-007] were prepared by the reaction of a 5-chloro 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [G-006] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl ester was then reacted with a primary or

secondary amino derivative, of general formula [G-004], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. 5-chloro 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-007] was involved in a Buchwald type reaction utilising a suitable amine, of general formula [G-005], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme B2



Synthesis of [4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine [246]

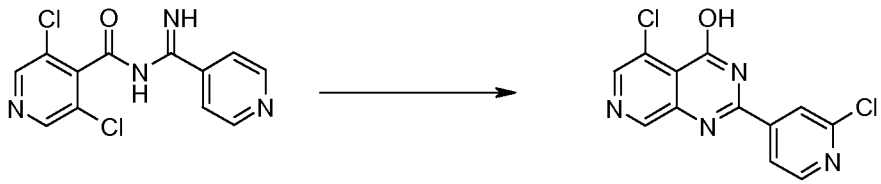


[B007]

3,5-Dichloro-N-[(2-chloro-pyridin-4-yl)-imino-methyl]-isonicotinamide [B007]

A mixture of 3,5-dichloropyridine-4-carboxylic acid (15 g, 78.12 mmol), DIPEA (37.5 mL, 214 mmol) in DMF (400 mL) was stirred at room temperature then HATU (29.7g,

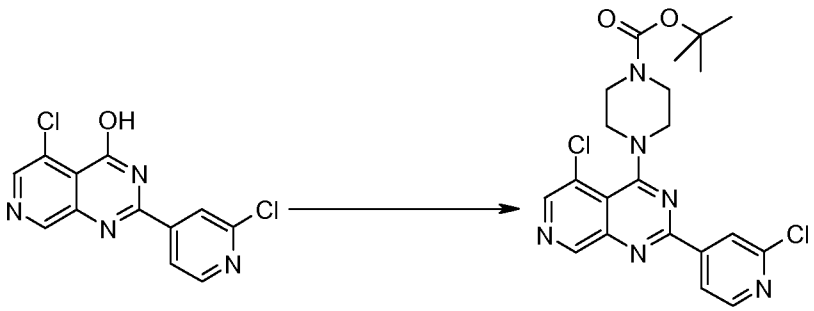
78.12 mmol) was added in one portion and the mixture was left to stir for 45 min. 2-Chloro-isonicotinamide (14.25g, 74.2 mmol) was added and the mixture left to stir for a further 2 hours. The crude reaction mixture was then poured onto water (800 mL) and left to stir overnight. The crude reaction mixture was filtered and the solid washed with water, then dried in in a vacuum oven over night to give the title compound (22g, 85% yield) as an off white solid: LCMS method: 1, RT:4.89 min, MI 330 [M+H]; NMR: (1H, 300MHz, d6-dmso); 10.25 (1H, br s), 10.10 (1H, br s), 8.70 (2H, s), 8.57 (1H, s), 7.99 (1H, s), 7.88 (1H, s).



[B007] [B008]

5-Chloro-2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [B008]

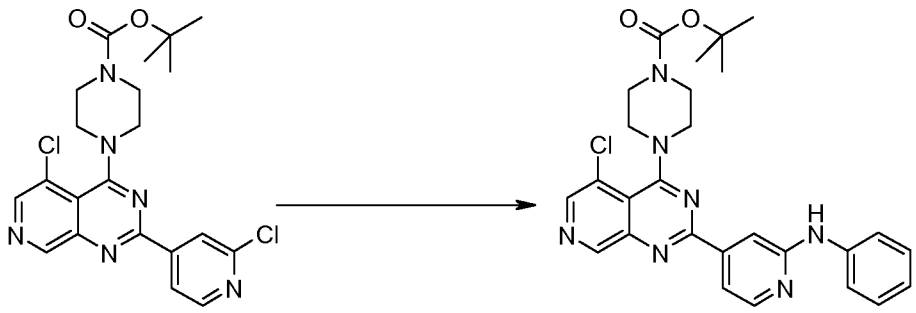
3,5-Dichloro-N-[(2-chloro-pyridin-4-yl)-imino-methyl]-isonicotinamide [B007] (10g, 30.34 mmol) cesium carbonate (19.8 g, 60.69 mmol) and DMA (180 mL) were stirred at room temperature. The mixture was flushed with nitrogen then iron(III) chloride (0.98 g, 6.07 mmol) was added and the mixture heated at 140 C overnight under an atmosphere of nitrogen. The crude reaction mixture was cooled then poured onto a mixture of ice water, the mixture was then acidified by the additionof glacial acetic acid, and the mixture was then left to stir at room temperature for 2 hours. The solid precipitate was collected by filtration, washed with water then dried in a vacuum oven over night to give the title compound (5.26g, 59% yield) as a pale brown solid: LCMS method: 1, RT:4.83 min, MI 293 [M+H];



[B008] [B009]

4-[5-Chloro-2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B009]

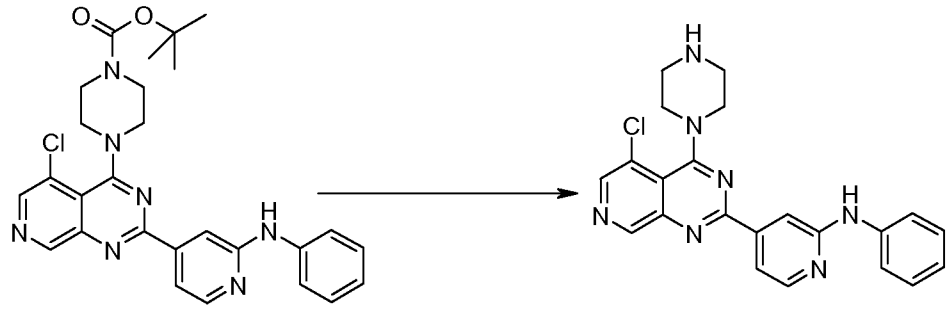
A mixture of 5-Chloro-2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [B008] (1.05 g, 3.58 mmol), anhydrous DMF (40 mL), triethylamine (1.5 mL, 10.7 mmol) and DMAP (440 mg, 3.58 mmol) was sonicated for 45 min. 2,4,6-Triisopropyl - benzenesulfonyl chloride (1.3 g, 4.3 mmol) was added and the reaction mixture left to stir at room temperature for 2 hr. During this time the material went into solution to form a viscous solution. 1-Boc-piperazine (0.800 g, 4.3 mmol) was added and the reaction mixture was left to stir at room temperature overnight. The solvent was evaporated under reduced pressure and residue triturated in DCM to give brown solid, which was purified by flash column chromatography (SP1, 20 g SiO_2 cartridge 100% DCM up to 95% DCM: 5 % MeOH gradient) to give the *title compound* [B009] as a beige solid (1.1g, 67% yield). LCMS method: 1, RT:5.50 min, MI: 461 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.20 (1H, s), 8.67 (1H, s), 8.62 (1H, d), 8.33 (1H, d), 8.32 (1H, s), 7.94 (1H, s), 3.72 (4H, m, br), 3.53 (4H, m, br), 1.41 (9H, s).



[B009] [B010]

4-[5-Chloro-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B010]

A mixture of 4-[5-Chloro-2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B009] (0.150 g, 0.325 mmol), Aniline (61 µL , 0.650 mml), $Pd(OAc)_2$ (4mg, 0.017 mmol), Xantphos (19 mg, 0.033 mmol), cesium carbonate (212 mg, 0.650 mmol) and anhydrous dioxane (1 ml) was heated at 90° overnight. Solvent evaporated under reduced pressure and residue purified by flash column chromatography (SP1, 20 g SiO_2 cartridge 100% DCM up to 97% DCM: 3 % MeOH gradient) to give the *title compound* [B010]as a beige solid (65 mg, 39% yield). LCMS method: 1, RT:4.34 min, MI: 518.31 [M+H].

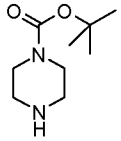


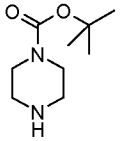
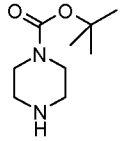
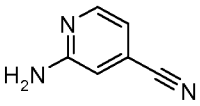
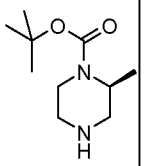
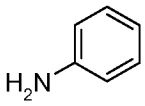
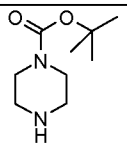
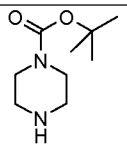
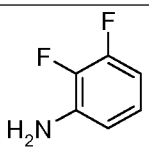
[B010] [246]

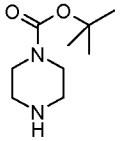
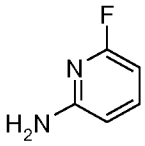
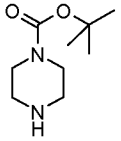
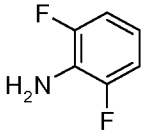
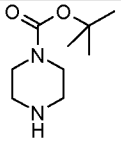
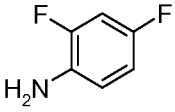
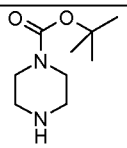
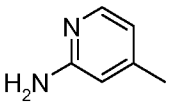
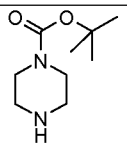
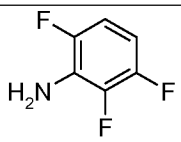
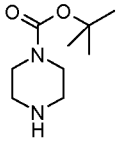
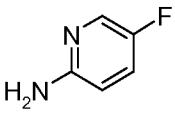
[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine [246]

A mixture of 4-[5-Chloro-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B010] (60 mg, 0.125 mmol) in 4N HCl in dioxane (1mL) was stirred at room temperature for 2 hours. After completion solvent was evaporated in vacuo and residue diluted with MeOH (5 mL) and poured onto a 1g SCX-2 cartridge and washed with DCM and MeOH before eluting with 2N NH3/MeOH which was evaporated evaporated under reduced pressure. The residue purified by flash column chromatography (SP1, 20 g SiO_2 cartridge 100% DCM up to 90% DCM: 10 % MeOH gradient) to give the *title compound* [246] as a yellow solid (23 mg, 44% yield). LCMS method: 1, RT:5.48 min, MI: 418.29 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.33 (1H, s), 9.12 (1H, s), 8.60 (1H, s), 8.32 (1H, d), 7.89 (1H, s), 7.74 (2H, d), 7.65 (1H, dd), 7.27 (2H, t), 6.89 (1H, t), 3.68 (4H, m), 3.15 (1H, d), 2.86 (4H, m).

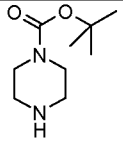
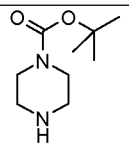
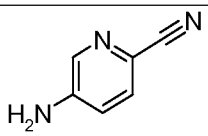
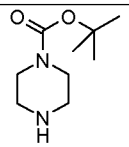
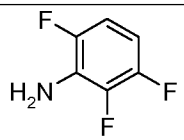
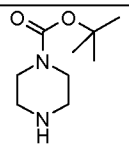
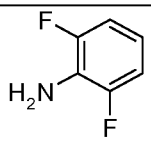
The following compounds were synthesised according to the general synthesis shown in scheme [B2]

Ex	Amine	Aniline	Analysis		Name
			LCMS	NMR	
247			Method 5: RT: 3.18 min, MI: 436 [M+H]	(1H, 500MHz, d6-dmso) 8.99 (1H, s), 8.60 (1H, s), 8.29 (1H, d), 8. 19 (1H, m), 8.02 (1H, d) , 7.69 (1H, d), 7.22 (1H, m), 7.14 (1H, m), 7.00 (1H, m), 3.68 (4H, br s), 2.86 (4H, br s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine

248			Method 5: RT: 3.37 min, MI: 511 [M+H]	(1H, 500MHz, d6-dmso) 8.97 (1H, s), 8.74 (1H, s), 8.41 (1H, s), 8.29 (1H,d), 8.22 (1H, t), 8.04 (1H, s), 7.72 (1H, d), 7.31 (1H, m), 7.22 (1H, m), 7.14 (1H, m), 7.09 (2H, m), 7 (1H, m), 3.54 (4H, s), 2.83 (4H, s)	(2-Fluoro-phenyl)-{2-[2-(2-fluoro-phenylamino) -pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-5-yl}-amine
249			Method 5: RT: 2.58 min, MI: 444 [M+H]	(1H, 500MHz, d6-dmso) 10.51 (1H, s), 9.25 (1H, s), 8.70 (1H, s), 8.65 (1H, s), 8.50 (2H, dd), 7.91 (1H, d), 7.31 (1H, d), 3.91 (4H, br s), 3.33 (4H, br s)	4-{5-(4-Cyano-pyridin-2-ylamino)-2-[2-(4-cyano-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine
250			Method 5: RT: 2.80 min, MI: 432.15 [M+H]	(1H, 500MHz, d6-dmso) 9.33 (1H, s), 9.12 (1H, s), 8.59 (1H, s), 8.31 (1H, d), 7.89 (1H, s), 7.73 (2H, d), 7.64 (1H, d), 7.27 (2H, t), 6.90 (1H, t), 4.09 (2H, m, br), 3.31 (2H, m, br), 3.16 (1H, d), 2.88 (2H, m, br), 1.01 (3H, s)	{4-[5-Chloro-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
251			Method 5: RT: 2.64 min, MI: 384.08 [M+H]	(1H, 500MHz, d6-dmso) 10.64 (1H, s), 9.20 (1H, s), 9.09 (1H, s), 8.64 (1H, s), 8.47 (1H, d), 8.00 (1H, d), 3.77 (4H, m), 3.05 (4H, m), 2.13 (3H, s)	N-[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide
252			Method 5: RT: 3.60 min, MI: 454 [M+H]	(1H, 300MHz, d6-dmso) 9.26 (1H, bs), 9.19 (1H, s), 8.66 (1H, s), 8.35 (1H, d), 8.09 (2H, m), 7.75 (1H, dd), 7.14 (1H, m), 7.04 (1H, m), 3.79 (4H, s), 3.08 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-difluoro-phenyl)-amine

253			Method 5: RT: 2.69 min, MI: 437 [M+H]	(1H, 500MHz, d6-dmso) 10.15 (1H, s), 9.16 (1H, s), 8.69 (1H, s), 8.63 (1H, s), 8.38 (1H, s), 7.82 (2H, s), 7.72 (1H, s), 6.58 (1H, s), 3.88 (4H, s), 3.25 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine
254			Method 5: RT: 2.17 min, MI: 454 [M+H]	(1H, 300MHz, d6-dmso) 9.24 (1H, s), 8.85 (1H, s), 8.71 (1H, s), 8.20 (1H, d), 7.82 (1H, s), 7.69 (1H, dd), 7.17 (2H, m), 3.87 (4H, s), 3.31 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine
255			Method 5: RT: 3.29 min, MI: 454 [M+H]	(1H, 300MHz, d6-dmso) 9.15 (1H, s), 8.98 (1H, s), 8.62 (1H, s), 8.27 (1H, d), 8.20 (1H, s), 8.13 (1H, m), 7.97 (1H, s), 7.70 (1H, dd), 7.30 (1H, m), 7.06 (1H, m), 3.72 (4H, s), 2.93 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-phenyl)-amine
256			Method 5: RT: 2.24 min, MI: 433 [M+H]	(1H, 300MHz, d6-dmso) 9.83 (1H, s), 9.16 (1H, s), 8.79 (1H, s), 8.61 (1H, s), 8.38 (1H, d), 8.13 (1H, d), 7.78 (1H, dd), 7.64 (1H, s), 6.76 (1H, d), 3.71 (4H, s), 2.88 (4H, s), 2.29 (3H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine
257			Method 5: RT: 3.42 min, MI: 472 [M+H]	(1H, 500MHz, d6-dmso) 9.19 (1H, s), 9.08 (1H, s), 8.65 (1H, s), 8.22 (1H, d), 7.88 (1H, s), 7.71 (1H, d), 7.35-7.29 (1H, m), 7.23-7.14 (1H, m), 3.79(4H, s), 3.12 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine
258			Method 5: RT: 5.38 min, MI: 437 [M+H]	(1H, 500MHz, d6-dmso) 10.02 (1H, s), 9.25 (1H, s), 8.72 (1H, s), 8.69 (1H, s), 8.41 (1H, d), 8.28 (1H, d), 7.93 (1H, dd), 7.82 (1H, dd), 7.69 (1H, m), 3.89 (4H, s), 3.27 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-pyridin-2-yl)-

					amine

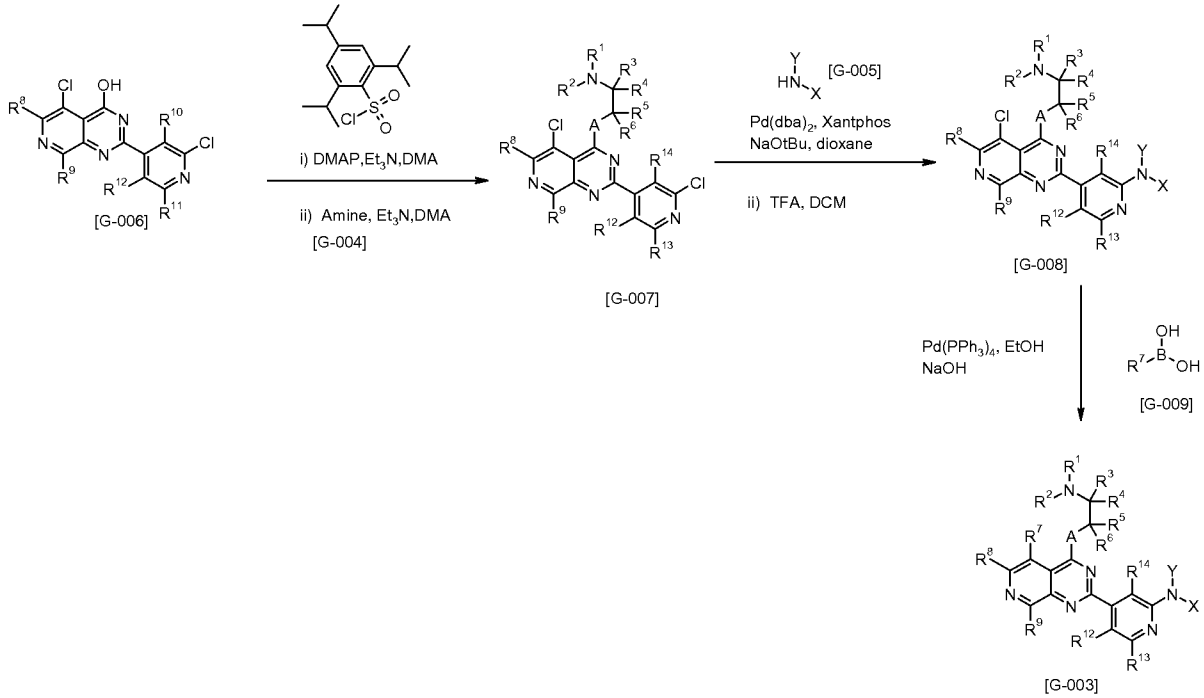
259			Method 5: RT: 5.92 min, MI: 487 [M+H]	(1H, 500MHz, d6-dmso) 10.40 (1H, s), 9.21 (1H, s), 8.72 (1H, s), 8.66 (1H, s), 8.52 (1H, d), 8.47 (1H, d), 8.32 (1H, s), 7.88 (1H, d), 7.23 (1H, d), 3.81 (4H, s), 3.07 (4H, s)	[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine
260			Method 5: RT: 5.32 min, MI: 444 [M+H]	(1H, 500MHz, d6-dmso) 10.25 (1H, s), 9.19 (1H, s), 8.94 (1H, s), 8.66 (1H, s), 8.58 (1H, dd), 8.48 (1H, d), 8.03 (1H, s), 7.93 (1H, d), 7.89 (1H, d), 3.80 (4H, s), 3.08 (4H, s)	5-[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile
261			Method 5: RT: 5.27 min, MI: 583 [M+H]	(1H, 500MHz, d6-dmso) 9.05 (1H, s), 8.74 (1H, s), 8.37 (1H, s), 8.23 (1H, s), 8.21 (1H, s), 7.88 (1H, s), 7.72 (1H, dd), 7.37-7.17 (4H, m), 3.62 (4H, s), 2.88 (4H, s)	{4-Piperazin-1-yl-2-[2-(2,3,6-trifluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-5-yl}-(2,3,6-trifluoro-phenyl)-amine
262			Method 5: RT: 3.37 min, MI: 511 [M+H]	(1H, 500MHz, d6-dmso) 8.97 (1H, s), 8.74 (1H, s), 8.41 (1H, s), 8.29 (1H, d), 8.22 (1H, t), 8.04 (1H, s), 7.72 (1H, d), 7.31 (1H, m), 7.22 (1H, m), 7.14 (1H, m), 7.09 (2H, m), 7 (1H, m), 3.54 (4H, m), 2.83 (4H, s)	(2,6-Difluoro-phenyl)-{2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-5-yl}-amine

General synthesis of substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-003] Scheme B3

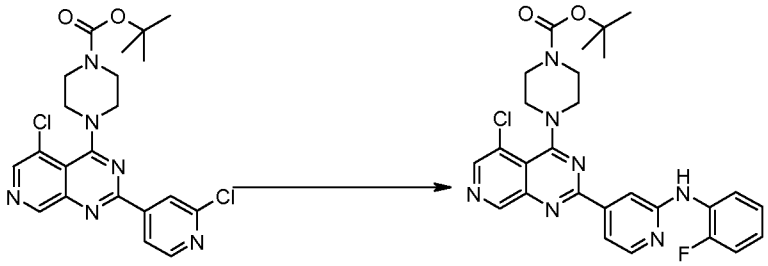
5-chloro 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-007] were prepared by the reaction of a 5-chloro 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [G-006] with 2,4,6-

triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [G-004], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. 5-chloro 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-007] was involved in a Buchwald type reaction utilising a suitable amine, of general formula [G-005], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. The 5-chlotro 2-amino-pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-008]. were reacted in a Suzuki type reaction utilising a suitable boronic acid or boronic ester, of general formula [G-009], a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ a base such as Et_3N, KOH, Na_2CO_3 or NaOH in a polar solvent such as EtOH, THF, DMA or dioxane at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme B3


[G-006]
i) DMAP,Et3N,DMA
ii) Amine, Et3N,DMA
[G-004]
[G-007]
[G-005]
Pd(dba)2, Xantphos
NaOtBu, dioxane
ii) TFA, DCM
[G-008]
Pd(PPh3)4, EtOH
NaOH
[G-009]
[G-003]

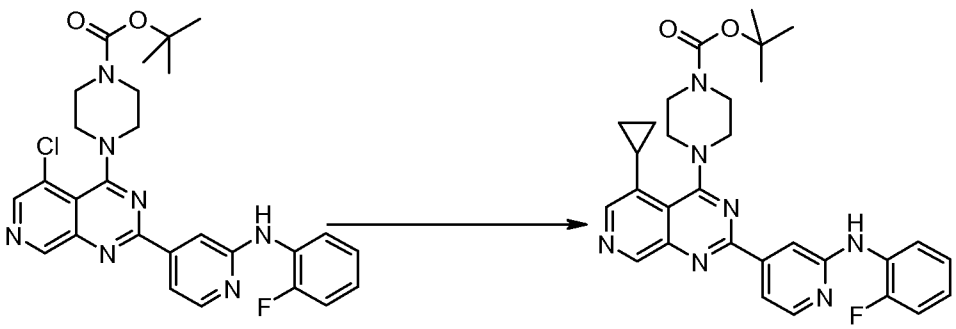
Synthesis of [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine [263]



[B009] [B010]

4-{5-Chloro-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [B010]

A mixture of 4-[5-Chloro-2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B009] (3 g, 6.48 mmol), 2-fluoroaniline (654 µL , 6.48 mml), $Pd(OAc)_2$ (79 mg, 0.324 mmol), Xantphos (375 mg, 0.648 mmol), ceasium carbonate (4.11 g, 12.6 mmol) and anhydrous dioxane (20 ml) was heated at 90° overnight. Solvent was evaporated under reduced pressure and residue purified by flash column chromatography (ISCO, 120 g SiO_2 cartridge 100% cyclohexane up to 70% cyclohexane: 30 % Ethylacetate gradient) to give the *title compound* [B010]as a yellow solid (1.2 g, 52% yield). LCMS method: 5, RT:4.19 min, MI 516.57 [M+H].

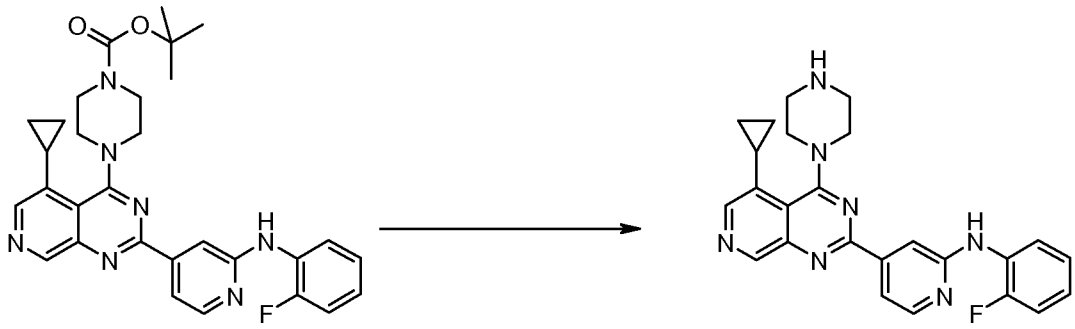


[B010] [B011]

4-{5-Cyclopropyl-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [B011]

A mixture of 4-{5-Chloro-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [B010] (1.8 g, 3.36 mmol), $Pd(dppf)Cl_2.CH_2Cl_2$ (137 mg, 0.168 mmol), K_3PO_4 (2.14 g, 10.075 mmol), cyclopropyl boronic acid (578 mg, 6.72 mmol) and anhydrous dioxane (30 ml) plus few drops of DMA was added to a microwave vial. Solvent was evaporated under reduced pressure and

residue purified by flash column chromatography (ISCO, 40 g SiO_2 cartridge 100% cyclohexane up to 70% cyclohexane: 30 % Ethylacetate gradient) to give the *title compound* [B011] as a yellow solid (950 mg, 52% yield). LCMS method: 5, RT:4.72 min, MI 542 [M+H].

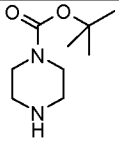
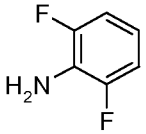
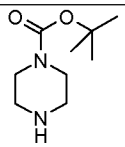
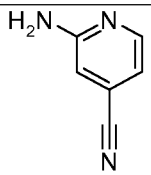
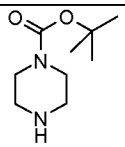
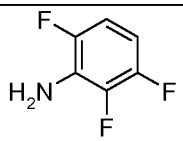
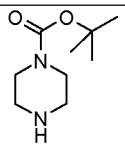
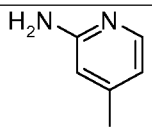
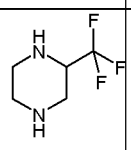
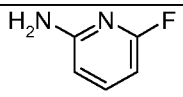


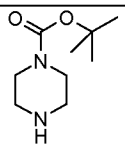
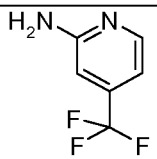
[B011] [263]

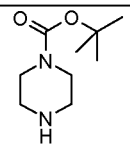
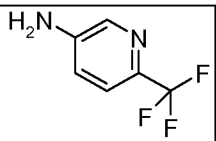
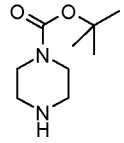
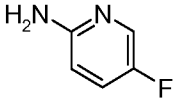
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine [263]

A mixture of 4-{5-Cyclopropyl-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [B011] (300 mg, 0.554 mmol) in 4N HCl in dioxane (1.5 mL) was stirred at room temperature for 2 hours. Solvent was evaporated under reduced pressure and residue purified by reverse phase flash column chromatography (ISCO, 24g SiO_2 cartridge, 100% H_2O:0.1% formic acid up to 20% H_2O:0.1% formic acid: 80 % MeOH: 0.1% formic acid gradient) The residue was diluted with MeOH (5 mL) and poured onto a 1g SCX-2 cartridge and washed with DCM and MeOH before eluting with 2N NH3/MeOH which was evaporated under reduced pressure to give the *title compound* [263] as a yellow solid (110 mg, 45% yield). LCMS method: 1, RT:4.03 min, MI 442 [M+H]; NMR: (1H, 500MHz, d6-dmso); 8.95 (1H,s), 8.27 (1H,d), 8.21 (1H,m), 8.08 (1H,s), 8.03 (1H.s), 7.70-7.69 (1H,dd), 7.23 (1H,m), 7.14 (1H,m), 6.99 (1H,m), 3.78 -3.62 (4H,m), 2.84 (4H,s), 2.61 (1H,m), 1.25-1.24 (2H,m), 1.02-1.01 (2H,m).

The following compounds were synthesised according to the general synthesis shown in scheme [B3]

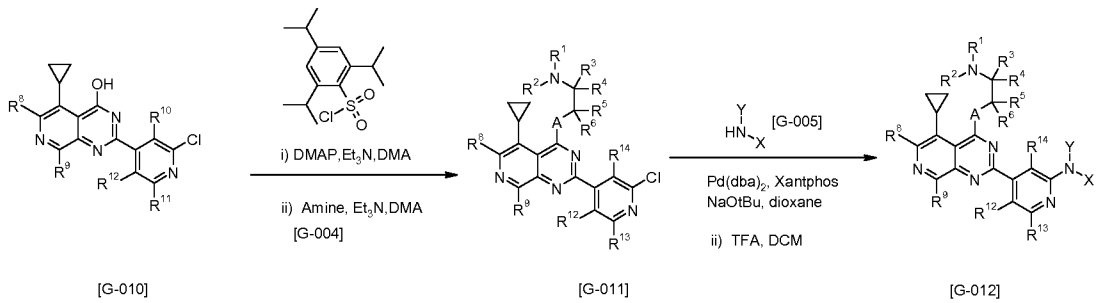
Ex	Amine	Aniline	Analysis		Name
			LCMS	NMR	
264			Method 5: RT: 3.01 min, MI: 460 [M+H]	(1H, 500MHz, d6-dmso) 8.95 (1H, s), 8.14 (1H, d), 8.08 (1H, s), 7.79 (1H, s), 7.64 (1H, d), 7.26 (1H, m), 7.15 (2H, m), 3.68 (4H, br s), 2.83 (4H, s), 2.61 (1H, m), 1.23 (2H, m), 1.02 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine
265			Method 5: RT: 2.62 min, MI: 450 [M+H]	(1H, 500MHz, d6-dmso) 10.39 (1H, s), 9.05 (1H, s), 8.36 (1H, s), 8.48 (2H, dd), 8.35 (1H, s), 7.91 (1H, d), 7.31 (1H, d), 3.91 (4H, s), 3.33 (4H, s), 2.67 (1H, s), 1.24-1.26 (2H, m), 1.07-1.09 (2H, m).	2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile
266			Method 5: RT: 2.60 min, MI: 478 [M+H]	(1H, 500MHz, d6-dmso) 9.04 (1H, s), 9.00 (1H, s), 8.21 (1H, d), 8.13 (1H, s), 7.88 (1H, s), 7.72 (1H, dd), 7.32 (1H, m), 7.20 (1H, m), 3.76 (4H, s), 3.02 (4H, s), 2.63 (1H, m), 1.25 (2H, m), 1.05 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine
267			Method 5: RT: 9.34 min, MI: 439 [M+H]	(1H, 300MHz, d6-dmso) 9.80 (1H, s), 8.99 (1H, s), 8.78 (1H, s), 8.38 (1H, d), 8.10 (2H, m), 7.79 (1H, d), 7.66 (1H, s), 6.74 (1H, d), 3.73 (4H, bs), 2.92 (4H, s), 2.63 (1H, m), 2.29 (3H, s), 1.27 (2H, m), 1.04 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine
268			Method 5: RT: 4.80 min, MI:	(1H, 500MHz, d6-dmso) 10.19 (1H, s), 9.02 (1H, s), 8.72 (1H, s), 8.43 (1H, d), 7.86 (2H, m),	{4-[5-Cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-

			511 [M+H]	7.74 (1H, d), 7.62-7.53 (1H, m), 6.60 (1H, dd), 4.05 (1H, m), 3.61 (2H, m), 3.05 (4H, s), 2.63 (1H, t), 1.29 (2H, m), 1.08 (2H, m)	d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine
269			Method 5: RT: 3.21 min, MI: 493 [M+H]	(1H, 500MHz, d6-dmso) 10.39 (s, 1H), 9.08 (s, 1H), 8.73 (s, 1H), 8.53 (d, 1H), 8.47 (d, 1H), 8.33 (s, 1H), 8.19 (s, 1H), 7.90 (d, 1H), 7.23 (d, 1H), 3.93 (s, 4H), 3.32 (s, 4H), 2.69 (m, 1H), 1.27 (m, 2H), 1.078 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine

270			Method 5: RT: 5.71 min, MI: 493 [M+H]	(1H, 500MHz, d6-dmso) 10.11 (s, 1H), 9.06 (s, 1H), 8.96 (d, 1H), 8.62 (dd, 1H), 8.46 (d, 1H), 8.18 (s, 1H), 8.05 (s, 1H), 7.87 (dd, 1H), 7.82 (d, 1H), 3.85 (s, 4H), 3.28 (s, 4H), 2.68 (m, 1H), 1.27 (m, 2H), 1.08 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine
271			Method 5: RT: 5.25 min, MI: 443 [M+H]	(1H, 500MHz, d6-dmso) 9.99 (1H, s), 9.07 (1H, s), 8.71 (1H, s), 8.40 (1H, d), 8.27 (1H, d), 8.18 (1H, s), 7.94 (1H, dd), 7.83 (1H, dd), 7.68 (1H, m), 3.93 (4H, s), 3.27 (4H, s), 2.70 (1H, m), 1.26 (2H, m), 1.07 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-pyridin-2-yl)-amine

General synthesis of 5-cyclopropyl substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-012]

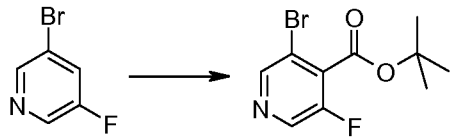
Scheme B4



5-cyclopropyl 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-011] were prepared by the reaction of a 5-cyclopropylo 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [G-010] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF,

NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [G-004], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. 5-cyclopropyl 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-011] was involved in a Buchwald type reaction utilising a suitable amine, of general formula [G-005], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Synthesis of [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,5-dimethyl-oxazol-2-yl)-amine [272],

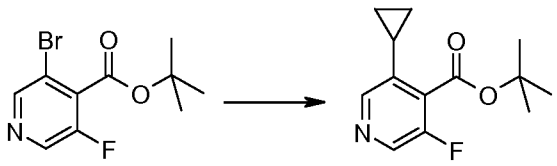


[B012]

Synthesis of 3-Bromo-5-fluoro-isonicotinic acid *tert*-butyl ester [B012]

To a solution of LDA (2M, 72mL, 144mmol) in THF (100mL) cooled to approximately -70°C was added dropwise via cannula a solution of 3-bromo-5-fluoropyridine (21.12g, 120mmol) in anhydrous THF (50 mL) pre-cooled to -70°C. The rate of addition was controlled such that the internal temperature did not rise above -65°C. The dark red-brown solution was stirred for 1 hour. Di-*tert*-butyldicarbonate (52.4g, 240mmol) in THF (50 mL) was cooled to -10°C in a methanol/ice bath then added dropwise via cannula to the

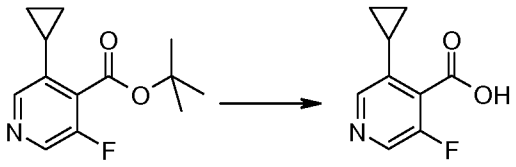
dark red-brown solution. The mixture was stirred for 2 hours then allowed to warm to room temperature and stirred for another 1 hour. Saturated aqueous ammonium chloride (100 mL) was added slowly and then water (200mL) and EtOAc (200mL) and the mixture was vigorously stirred for 45 minutes. The mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with EtOAc (200 mL). The THF and EtOAc layers were combined, dried over magnesium sulfate, filtered and evaporated. The recovered dark red-brown oil was purified by column chromatography (Cyclohexane/AcOEt: 1/0 to 97/3). Fractions containing desired material were concentrated in vacuo to yield the title compound [B012] as a pale yellow oil (14g, 85%). LCMS method: 1, RT:5.44 min, MI: 277 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.56 (s, 1H), 8.43 (s, 1H), 1.62 (s, 9H).



[B012] [B013]

Synthesis of 3-Cyclopropyl-5-fluoro-isonicotinic acid *tert*-butyl ester [B013]

A solution containing 3-Bromo-5-fluoro-isonicotinic acid *tert*-butyl ester [B012] (5.52g, 20mmol), potassium phosphate tribasic (12.74g, 60mmol) and cyclopropyl boronic acid (2.58g, 30mmol), in anhydrous dioxane (100mL) was subjected to vacuum / argon balloon (three times). Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.408g, 0.5mmol) was added and the reaction heated at 96°C overnight under positive pressure of nitrogen. The mixture was cooled to room temperature and was filtered through a pad of 200g silica and washed with EtOAc (1L). The filtrate was concentrated in vacuo and the crude was purified by column chromatography (Cyclohexane/AcOEt: 98:2 to 96:4). The combined fractions were concentrated under reduced pressure to yield the title compound [B013] as a colourless oil (3.42g, 72%). LCMS method: 1, RT: 5.36 min, MI: 238 [M+H].



[B013] [B014]

Synthesis of 3-Cyclopropyl-5-fluoro-isonicotinic acid [B014]

In a microwave vial, 3-cyclopropyl-5-fluoro-isonicotinic acid *tert*-butyl ester [B013] (1.186g, 5mmol) was dissolved in anhydrous methanol and then heated in microwave at 140°C for 1hr. The reaction was concentrated in vacuo to give the title compound [B014] 0.84 g (92%) as a white crystalline solid. LCMS method: 1, RT:1.51 min, MI: 182 [M+H].

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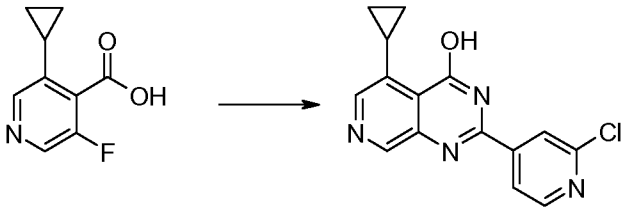
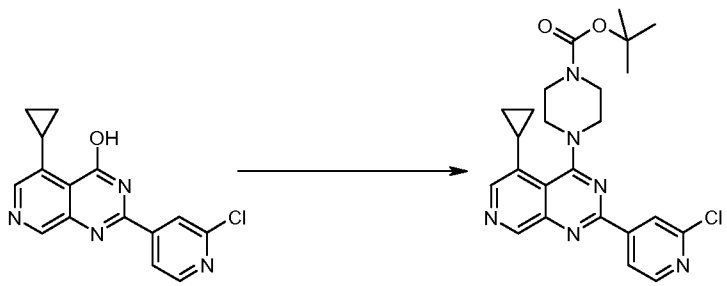


[B014] [B015]

Synthesis of 2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-ol [B015]

A mixture of 3-Cyclopropyl-5-fluoro-isonicotinic acid [B014] (5g, 27.6 mmol) and HATU (10.5g, 82.86 mmol) was stirred in DMF (35 mL) and DIPEA (14.5 mL, 82.86 mmol) was added. The mixture was left to stir at rt for 1 hour then 2-Chloro-isonicotinamidine hydrochloride (5.3g, 27.52 mmol) was added in one portion and the mixture was left to stir at rt for 18 hours. The crude reaction mixture was poured onto water (180mL) and left to stir for stirred for 2 hours and then the beige solid was collected by filtration, washed with water and dried in a vacuum oven to give N-[(2-Chloro-pyridin-4-yl)-imino-methyl]-3-cyclopropyl-5-fluoro-isonicotinamide (6.60 g, 75% yield) which was used in the next step without further purification: LCMS method: 1, RT:3.45 min, MI: 319 [M+H]; NMR: (1H, 300MHz, d6-dmso); 10.25 (s, br, 1H), 9.92(s, br, 1H), 8.59 (d, 1H), 8.42 (s, 1H), 8.11 (s, 1H), 8.00 (s, 1H), 7.92 (dd, 1H), 2.01 (m, 1H), 0.98 (m, 2H), 0.85 (m, 2H).

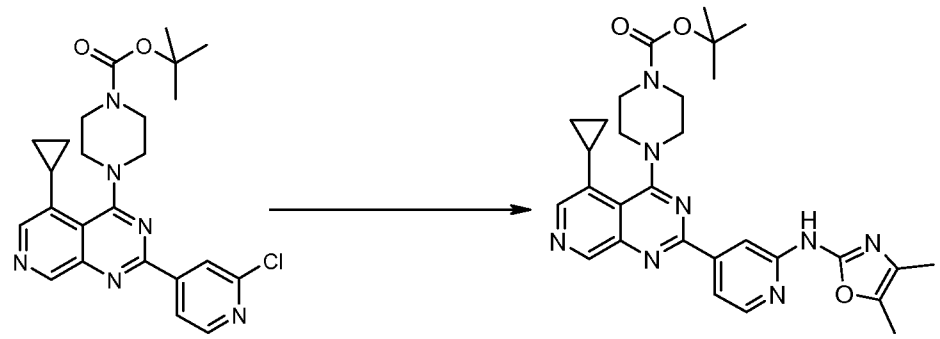
A mixture of N-[(2-Chloro-pyridin-4-yl)-imino-methyl]-3-cyclopropyl-5-fluoro-isonicotinamide (6.60 g, 20.70 mmol) and Cs2CO3 (6.7g, 20.7 mmol) and DMA (90 mL) was heated at 90 °C overnight. The reaction mixture was poured into ice/water (100ml), then acidified by the dropwise adition of glacial acetic acid and the mixture was left to stir at 0 °C for 1 hour. The beige precipitate was collected by filtration and washed with water then dried in a vacuum oven to give the title compound [B015] (4.8g, 78 % yield). LCMS method: 1, RT: 3.90 min, MI: 299 [M+H]; NMR: (1H, 300MHz, d6-dmso);. 12.92 (s, 1H), 8.88 (s, 1H), 8.66 (d, 1H), 8.25 (dd, 2H), 8.16 (dd, 1H), 3.39 (m, 1H), 1.11 (m, 2H), 0.94(m, 2H).



[B015] [B016]

4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B016]

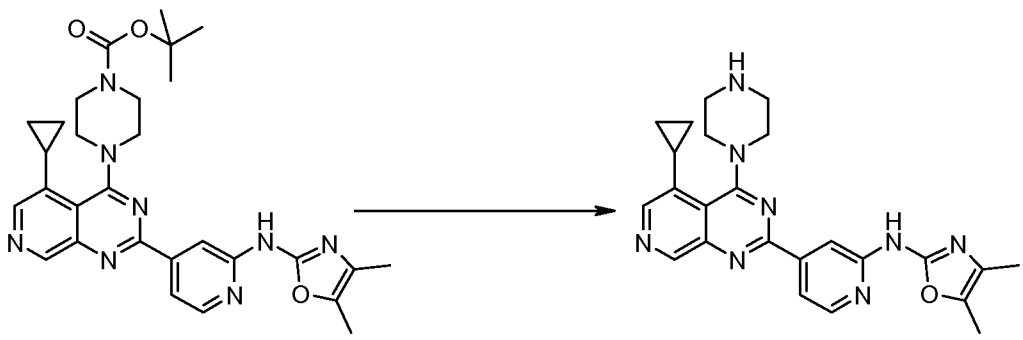
A mixture of of 2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-ol [B015] (280 mg, 0.937 mmol), anhydrous DMF (9 mL), triethylamine (0.390 mL, 2.81 mmol) and DMAP (115 mg, 0.937 mmol) was sonicated for 10 min then stirred at room temperature for 10 min. 2,4,6-Triisopropyl -benzenesulfonyl chloride (340 mg, 1.12 mmol) was added and the mixture was sonicated for 5 min then left to stir at room temperature for 2 hours. During this time the material went into solution to form a viscous solution. 1-Boc-piperazine (190 mg, 1.03 mmol) was added and the reaction mixture was left to stir at room temperature overnight. Solvent was evaporated under reduced pressure and residue purified by flash column chromatography (SP1, 20 g SiO_2 cartridge 100% DCM up to 95% DCM: 5 % MeOH gradient) to give the *title compound* [B016] as a yellow solid (276 mg, 63% yield). LCMS method: 5, RT:5.16 min, MI: 467 [M+H]; NMR: (1H, 500MHz, d6-dmso);. 9.02 (1H, s), 8.61 (1H, dd), 8.34 (2H, m), 8.15 (1H,s), 3.68-3.83(4H, very broad s), 3.51 (4H,br s), 2.59 (1H,m), 1.24 (2H,m), 1.16 (2H,m).



[B016] [B017]

4-{5-Cyclopropyl-2-[2-(4,5-dimethyl-oxazol-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [B017]

A mixture of 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B016] (280 mg, 0.591 mmol), 4,5-dimethyl-oxazol-2-ylamine (132 mg , 1.18 mml), $Pd(OAc)_2$ (7mg, 0.030 mmol), Xantphos (35 mg, 0.060 mmol), ceasium carbonate (384 mg, 1.18 mmol) and anhydrous dioxane (1.5 ml) was heated at 90° overnight. Solvent was evaporated under reduced pressure and residue purified by flash column chromatography (SP1, 20 g SiO_2 cartridge 100% DCM up to 96% DCM: 4 % MeOH gradient) to give the *title compound* [B017] as a beige solid (61 mg, 19% yield). LCMS method: 5, RT: 4.07 min, MI: 543 [M+H].



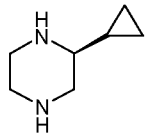
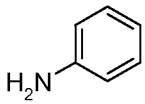
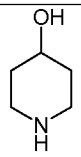
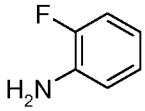
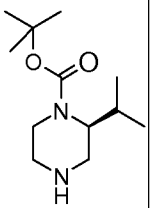
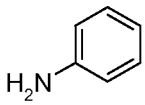
[B017] [272]

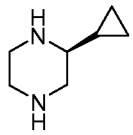
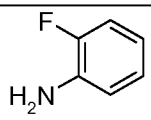
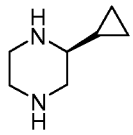
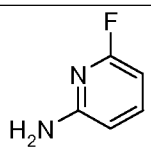
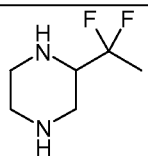
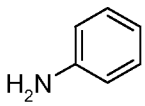
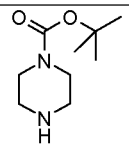
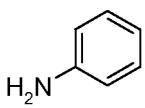
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,5-dimethyl-oxazol-2-yl)-amine [272]

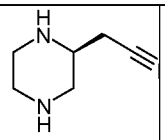
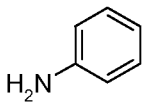
A mixture of 4-{5-Cyclopropyl-2-[2-(4,5-dimethyl-oxazol-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [B017] (60 mg, 0.112 mmol) in 4N HCl in dioxane (1 mL) was stirred at room temperature for 2 hours. After completion solvent was evaporated under reduced pressure and residue diluted with

MeOH (5 mL) and poured onto a 1g SCX-2 cartridge and washed with DCM and MeOH before eluting with 2N NH3/MeOH which was evaporated under reduced pressure. The residue was then purified by flash column chromatography (SP1, 10 g SiO_2 cartridge 100% DCM up to 90% DCM: 10 % MeOH gradient) to give the *title compound* [272] as a yellow solid (22 mg, 44% yield). LCMS method: 5, RT:2.70 min, MI: 443 [M+H]; NMR: (1H, 500MHz, d6-dmso); 10.61 (1H, s), 9.17 (1H, s), 9.05 (1H, s), 8.38 (1H, d), 8.16 (1H, s), 7.87 (1H, d), 3.94 (1H, s, br), 3.26 (4H, m, br), 2.69 (2H, m), 2.19 (3H, s), 2.04 (3H, s), 1.25-1.22 (3H, m), 1.06-1.05 (2H, m).

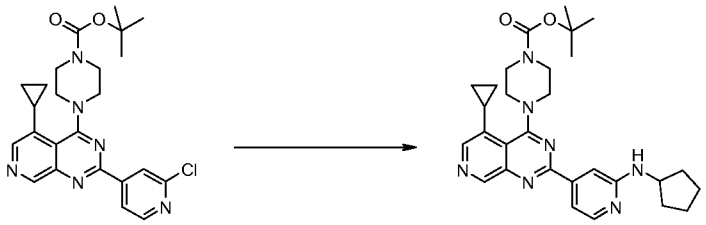
The following compounds were synthesised according to the general synthesis shown in scheme [B4]

Ex	Amine	Aniline	Analysis		Name
			LCMS	NMR	
273			Method 5: RT: 1.91 min, MI: 416.17 [M+H]	(1H, 500MHz, d6-dmso) 8.98 (1H, s), 8.93 (1H, s), 8.32 (1H, d), 8.13 (1H, s), 7.92 (1H, s), 7.71-7.67 (3H, m), 7.29 (2H, t), 6.93 (1H, t), 4.28 (1H, d), 4.16 (1H, d), 3.28 (1H, t), 3.05 (1H, dd), 2.78 (1H, t), 2.63 (1H, m), 2.17 (1H, m), 1.25 (2H, m), 1.02-0.95 (2H, m), 0.77 (1H, m), 0.43 (2H, dd), 0.29-0.25 (2H, m)	{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
274			Method 5: RT: 4.93 min, MI: 457 [M+H]	(1H, 500MHz, d6-dmso) 8.97 (1H, s), 8.95 (1H, s), 8.26 (1H, d), 8.20 (1H, t), 8.08 (1H, s), 8.04 (1H, s), 7.70 (1H, dd), 7.22 (1H, dd), 7.14 (1H, t), 7.00 (1H, m), 4.07 (2H, m, br), 3.78 (1H, m, br), 3.54-3.40 (2H, m, br), 3.15 (1H, d), 2.59 (1H, m, br), 1.86 (2H, d, br), 1.25 (2H, d, br), 1.02 (2H, m, br).	1-{5-Cyclopropyl-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
275			Method 5: RT: 3.24 min, MI: 466 [M+H]	(1H, 400MHz, d6-dmso 90 °C) 8.98 (1H, s), 8.91 (1H, s), 8.31 (1H, d), 8.12 (1H, s), 7.92 (1H, s), 7.71-7.68 (3H, m), 7.29 (2H, t), 6.93 (1H, t), 4.31 (1H, d), 4.20 (1H, d), 3.70 (1H, s, br), 3.29 (1H, t), 3.22 (2H, s), 3.05 (1H, dd), 2.81 (1H, t), 2.68-1.63 (1H, m), 1.65 (1H,	{4-[5-Cyclopropyl-4-((S)-3-isopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-

				m), 1.27-1.25 (2H, m), 1.03 (1H, m), 0.96 (6H, dd)	amine
276			Method 5: RT: 2.48 min, MI: 482.25 [M+H]	(1H, 400MHz, d6-dmso, 90 °C) 8.97 (1H, s), 8.53 (1H, s), 8.29 (1H, dd), 8.13 (1H, s), 8.07 (1H, td), 7.95 (1H, s), 7.71 (1H, dd), 7.23 (1H, dd), 7.21-7.14 (1H, m), 7.07-7.04 (1H, m), 4.28 (1H, d), 4.14 (1H, d), 3.27 (1H, t), 3.22 (1H, s), 3.04 (1H, m), 2.77 (1H, t), 2.62 (1H, m), 2.16 (1H, t), 1.24 (1H, m), 1.02-0.95 (2H, m), 0.78 (1H, m), 0.42 (2H, dd), 0.29-0.24 (2H, m)	{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-phenyl)-amine
277			Method 5: RT: 3.20 min, MI: 483 [M+H]	(1H, 400MHz, d6-dmso, 90 °C) 9.75 (1H, s), 8.99 (1H, s), 8.69 (1H, s), 8.41 (1H, d), 8.14 (1H, s), 7.86 (1H, dd), 7.82 (1H, qd), 7.70 (1H, dd), 6.55 (1H, dd), 4.29 (1H, d), 4.20 (1H, d), 3.30 (1H, t), 3.09-3.05 (1H, m), 2.80 (1H, t), 2.68-2.63 (1H, m), 2.16 (1H, t), 1.26-1.24 (2H, m), 1.03-0.95 (2H, m), 0.81-0.75 (1H, m), 0.42-0.40 (2H, m), 0.28-0.24 (2H, m)	{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine
278			Method 5: RT: 5.65 min, MI: 488 [M+H]	(1H, 500MHz, d6-dmso) 9.52 (1H, s, br), 9.18 (1H, s, br), 8.51 (1H, s), 8.30 (1H, s), 8.09 (1H, s), 7.94 (2H, d, br), 7.86 (1H, s), 7.46 (2H, m, br), 7.09 (1H, t, br), 4.27 (2H, m, br), 3.34 (2H, m, br), 3.09 (2H, m, br), 2.82 (1H, m, br), 1.88-1.81 (3H, m, br), 1.48 (1H, s, br), 1.38 (3H, m, br), 1.24-1.19 (2H, m, br)	(4-{5-Cyclopropyl-4-[3-(1,1-difluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine
279			Method 5: RT: 5.48 min, MI: 424 [M+H]	(1H, 500MHz, d6-dmso) 9.10 (1H, s), 8.35 (1H, d), 8.04 (1h, s), 8.00 (1H, s), 7.79 (1H, d), 7.44 (2H, d), 7.36 (2H, t), 7.06 (1H, t), 6.77 (1H, s), 3.76 (4H, m, br), 3.01 (4H, m), 2.68 (1H, m), 1.26 (2H, m), 0.99 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine

280			Method 5: RT: 3.26 min, MI: 463 [M+H]	(1H, 500MHz, d6-dmso) 9.28 (1H, s), 8.98 (1H, s), 8.31 (1H, d), 8.11 (1H, s), 7.91 (1H, s), 7.75 (2H, d), 7.69 (1H, d), 7.27 (1H, t), 6.89 (1H, t), 4.12 (2H, m, br), 3.20 (1H, m, br), 2.94 (3H, m, br), 2.71 (4H, m, br), 1.25 (2H, m, br), 1.03 (2H, m, br)	{(S)-4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile

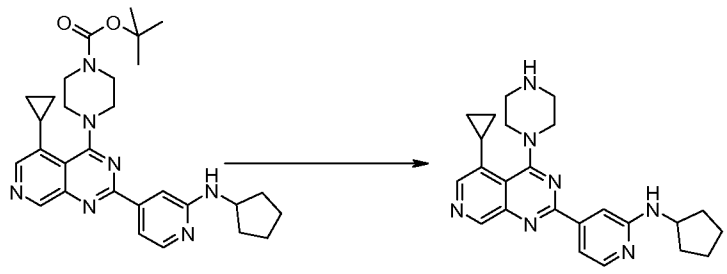
Synthesis of Cyclopentyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine [281]



[B016] [B018]

4-[2-(2-Cyclopentylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B018]

A mixture of 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B016] [prepared according to the general synthesis shown in Scheme B4] (170 mg, 0.364 mmol), cyclopentylamine (73 µL, 0.728 mmol), $Pd(t\text{-}Bu_3P)_2$ (38 mg, 0.073 mmol), sodium tert-butoxide (54 mg, 0.546 mmol) and anhydrous dioxane (2 ml) was heated at 110°C overnight. Solvent was evaporated under reduced pressure and residue purified by flash column chromatography (SP1, 20 g SiO_2 cartridge 100% DCM up to 96% DCM: 4 % MeOH gradient) to give the *title compound* [B018] as a yellow solid (92 mg, 48% yield). LCMS: method: 5, RT: 4.19 min, MI 516.57 [M+H].



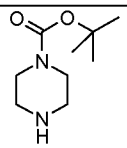
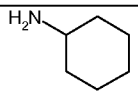
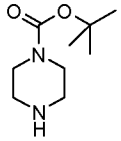
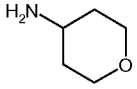
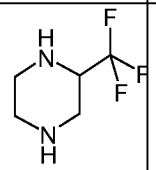
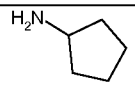
[B018] [281]

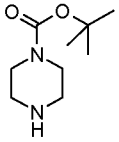
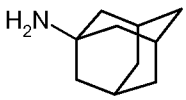
Cyclopentyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine [281]

A mixture of 4-[2-(2-Cyclopentylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B018] (90 mg, 0.178 mmol) in 4N HCl in dioxane (2 mL) was stirred at room temperature for 2 hours. Solvent was evaporated under reduced pressure and residue diluted with MeOH (5 mL) and poured onto a 1g SCX-2 cartridge and washed with DCM and MeOH before eluting with 2N

NH3/MeOH which was evaporated under reduced pressure. The residue was then purified by flash column chromatography (SP1, 10 g SiO_2 cartridge 100% DCM up to 95% DCM: 5 % MeOH gradient) to give the *title compound* [281] as a yellow solid to give the *title compound* as a yellow solid (26 mg, 37% yield). LCMS: method: 5, RT:2.22 min, MI 416.25 [M+H]; NMR: (1H, 500MHz, d6-dmso); 8.95 (1H, s), 8.10 (2H, d), 8.08 (1H, s), 7.51 (1H, s), 7.38 (1H, dd), 6.75 (1H, d), 4.17 (1H, m), 3.84-3.65 (4H, m), 3.11 (4H, m), 2.91 (1H, m), 2.62 (2H, m), 1.98-1.92 (2H, m), 1.69 (2H, m), 1.55 (2H, m), 1.46 (2H, m), 1.24-1.22 (2H, m), 1.03 (2H, m).

The following compounds were synthesised according to the general synthesis shown in scheme [B4]

Ex	Amine 1	Amine 2	Analysis		Name
			LCMS	NMR	
282			Method 5: RT: 2.43 min, MI: 430.28 [M+H]	(1H, 500MHz, d6-dmso) 8.93 (1H, s), 8.07 (1H, d), 8.06 (1H, s), 7.50 (1H, s), 7.35 (1H, dd), 6.63 (1H, d), 3.76-3.58 (4H, m, br), 2.87 (4H, m, br), 2.67 (2H, m), 1.94 (2H, d, br), 1.72 (2H, dt, br), 1.59 (1H, d, br), 1.37-1.17 (7H, m), 1.02 (2H, m)	Cyclohexyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
283			Method 5: RT: 1.93 min, MI: 432.23 [M+H]	(1H, 500MHz, d6-dmso) 8.94 (1H, s), 8.10 (1H, d), 8.07 (1H, s), 7.53 (1H, s), 7.40 (1H, d), 6.77 (1H, d), 4.09-3.97 (2H, m), 3.88-3.86 (2H, m), 3.75-3.57 (4H, m), 3.41 (2H, t), 3.15 (1H, d), 2.93 (4H, m), 2.62 (1H, m), 1.90 (2H, d, br), 1.48-1.40 (2H, m), 1.28-1.23 (2H, m), 1.03 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(tetrahydro-pyran-4-yl)-amine
284			Method 5: RT: 3.75 min, MI: 484.21 [M+H]	(1H, 400MHz, d4-MeOH 50 °C) 9.01 (1H, s), 8.09 (1H, s), 8.07 (1H, d), 7.59 (1H, s), 7.54 (1H, dd), 4.16-4.07 (1H, m), 3.71-3.66 (1H, m), 3.13-3.07 (1H, m), 2.75-2.68 (1H, m), 2.13-2.05 (2H, m), 1.82-1.76 (2H, m), 1.69-1.65 (2H, m), 1.60-1.52 (2H, m), 1.28-1.23	Cyclopentyl-{4-[5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-

				(3H, m), 1.06-0.96 (2H, m)	2-yl]-pyridin-2-yl}-amine
285			Method 5: RT: 3.05 min, MI: 482.25 [M+H]	(1H, 500MHz, d6-dmso) 8.92 (1H, s), 8.05 (2H, m), 7.55 (1H, s), 7.33 (1H, d), 6.36 (1H, s), 3.80-3.52 (4H, m), 2.85 (4H, m, br), 2.62-2.60 (1H, m), 2.10 (6H, m, br), 2.05 (3H, m, br), 1.66 (6H, m, br), 1.24-1.23 (2H, m, br), 1.18-1.16 (1H, m), 1.10-1.08 (1H, m), 1.03-1.00 (2H, m)	Adamantan-1-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

Example 303. 2-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide

303a) 2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol was prepared from 2-Chloro-isonicotinonitrile (0.60 g, 4.3 mmol) and 3-Amino-isonicotinic acid (0.50 g, 3.6 mmol) in an analogous manner to Example 1a. Product isolated as a tan solid (0.479 g, 51%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 13.13 (br s, 1H), 9.19 (s, 1H), 8.74 (d, J=4.2 Hz, 1H), 8.66 (d, J=5.1 Hz, 1H), 8.24 (s, 1H), 8.15 (d, J=5.1 Hz, 1H), 8.02 (d, J=4.8 Hz, 1H). MS = 259, 261 (MH)+.

303b) (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol (1.50 g, 5.80 mmol) and (R)-3-Amino-pyrrolidine-1-carboxylic acid tert-butyl ester (1.1 mL, 6.6 mmol) in an analogous manner to [B016]. Product was isolated as a yellow foam (2.15 g, 87%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.22 (s, 1H), 8.76 (d, J=5.7 Hz, 1H), 8.69 (d, J=5.4 Hz, 1H), 8.61 (d, J=4.6 Hz, 1H), 8.37-8.29 (m, 3H), 4.94 (br s, 1H), 3.88-3.71 (m, 1H), 3.55-3.29 (m, 3H), 2.37-2.25 (m, 1H), 2.19-2.04 (m, 1H), 1.46-1.39 (m, 9H). MS = 427, 429(MH)+.

303c) A tube was charged with (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol), 2-Amino-benzamide (35.0 mg, 0.257 mmol), Palladium Acetate (5.0 mg, 0.022 mmol), 4,5-Bis-(di-tert-butyl-phosphanyl)-9,9-dimethyl-9H-xanthene (12.0 mg, 0.0241 mmol), Cesium Carbonate (115.0 mg, 0.3530 mmol) and 1,4-Dioxane (1 mL, 10 mmol) under an atmosphere of Nitrogen. The tube was carefully evacuated and backflushed with nitrogen once. The tube was sealed and heated at 100°C and stirred overnight. The mixture was cooled to room temperature, diluted with dichloromethane (10 mL), filtered through a plug

of diatomaceous earth and evaporated to a dark resin. To the residue was added Trifluoroacetic acid (0.5 mL) and dichloromethane (0.5 mL). The mixture was stirred for 1 hour and the volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus (10%→30% Acetonitrile:Water w/ TFA modifier). 2-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide as the trifluoroacetic acid salt was isolated as a yellow lyophilate (0.009 g, 9%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.28 (s, 1H), 9.15 (s, 1H), 8.88 (br s, 2H), 8.75-8.70 (m, 2H), 8.55 (d, J=5.1 Hz, 1H), 8.27 (d, J=5.4 Hz, 1H), 8.13 (d, J=4.3 Hz, 1H), 7.77 (d, J=8.4 Hz, 1H), 7.24 (t, J=8.4 Hz, 1H), 6.80 (d, J=8.6 Hz, 1H), 6.60 (t, J=7.2 Hz, 1H), 4.93 (br s, 1H), 3.80-3.70 (m, 1H), 3.52-3.35 (m, 3H), 2.53-2.40 (m, 2H), 2.32-2.24 (m, 1H). MS = 427(MH)+.

Example 304. 4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide

4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 4-Amino-benzamide (35.0 mg, 0.257 mmol) in an analogous manner to Example 303c. Product was isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.008 g, 8%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.67 (s, 1H), 9.24 (s, 1H), 8.87 (br s, 2H), 8.74-8.69 (m, 1H), 8.40 (d, J=5.2 Hz, 1H), 8.26 (d, J=5.7 Hz, 1H), 8.02 (s, 1H), 7.84-7.74 (m, 6H), 7.13 (br s, 1H), 4.95 (br s, 1H), 3.80-3.30 (m, 3H), 2.52-2.38 (m, 2H), 2.31-2.22 (m, 1H). MS = 427 (MH)+.

Example 305. 4-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide

4-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide was a byproduct from Example 304 isolated as the trifluoroacetic acid salt as an orange-brown lyophilate (0.012 g, 12%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.41 (s, 1H), 9.28 (s, 1H), 9.23 (s, 1H), 8.87 (br s, 2H), 8.75-8.70 (m, 2H), 8.54-8.50 (m, 1H), 8.27 (d, J=5.2 Hz, 1H), 8.10 (d, J=4.8 Hz, 1H), 7.85 (d, J=8.1 Hz, 2H), 6.61 (d, J=7.7 Hz, 2H), 4.95-4.88 (m, 1H), 3.82-3.30 (m, 3H), 2.55-2.40 (m, 2H), 2.33-2.25 (m, 1H).MS = 427(MH)+.

Example 306. {4-[(1S,4S)-4-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine

306a) (1S,4S)-5-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-2,5-diaza-bicyclo[2.2.1]heptane-2-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol (250.0 mg, 0.9665 mmol) and (1S,4S)-2,5-Diaza-bicyclo[2.2.1]heptane-2-carboxylic acid tert-butyl ester (215.0 mg, 1.084 mmol) in an analogous manner to Example 301b. Product isolated as a yellow resin (0.110 g, 26%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.22 (s, 1H), 8.62-8.55 (m, 2H), 8.37-8.32 (m, 2H), 8.07-8.03 (m, 1H), 5.53 (d, J=18.5 Hz, 1H), 4.62 (d, J=18.5 Hz, 1H), 4.33 (br s, 1H), 3.92 (br s, 1H), 3.62-3.44 (m, 2H), 2.08-2.00 (m, 2H), 1.45-1.30 (m, 9H). MS = 439, 441(MH)+.

306b) {4-[(1S,4S)-4-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine was prepared from (1S,4S)-5-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-2,5-diaza-bicyclo[2.2.1]heptane-2-carboxylic acid tert-butyl ester (115.0 mg, 0.2620 mmol) and Aniline (27.0 µL, 0.296 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.133 g, 128%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.49 (br s, 1H), 9.28 (s, 1H), 9.23 (br s, 1H), 8.65 (d, J=5.4 Hz, 1H), 8.45 (br s, 1H), 8.33-8.29 (m, 1H), 8.03 (d, J=5.6 Hz, 1H), 7.99 (s, 1H), 7.76-7.70 (m, 3H), 7.32 (t, J=7.4 Hz, 2H), 7.00-6.93 (m, 1H), 5.49 (s, 1H), 4.62 (s, 1H), 4.44 (d, J=10.8 Hz, 1H), 4.12 (d, J=11.1 Hz, 1H), 3.61-3.41 (m, 2H), 2.34 (d, J=10.4 Hz, 1H), 2.07 (d, J=10.9 Hz, 1H). MS = 396(MH)+.

Example 307. Pyrazine-2-carboxylic acid {4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide

Pyrazine-2-carboxylic acid {4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and Pyrazine-2-carboxylic acid amide (32.0 mg, 0.260 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.099 g, 100%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.50 (s, 1H), 9.40 (s, 1H), 9.34 (s, 1H), 9.30 (s, 1H), 9.02-8.86 (m, 4H), 8.77 (d, J=4.4 Hz, 1H), 8.74 (d, J=5.4 Hz, 1H), 8.60 (d, J=5.0 Hz, 1H), 8.28 (d, J=5.5 Hz, 1H), 8.21 (d, J=5.1 Hz, 1H), 4.98-4.90 (m, 1H), 3.84-3.74 (m, 2H), 3.54-3.38 (m, 3H), 2.53-2.42 (m, 1H), 2.35-2.25 (m, 1H). MS = 414(MH)+.

Example 308. 3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide

3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 3-Amino-benzamide (35.0 mg, 0.257 mmol) in an analogous manner to Example 303c. Product isolated as the bis-trifluoroacetic acid salt as yellow lyophilate (0.005 g, 5%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.49 (s, 1H), 9.24 (s, 1H), 8.85 (br s, 1H), 8.72 (d, J=5.1 Hz, 1H), 8.70-8.67 (m, 1H), 8.36 (d, J=5.4 Hz, 1H), 8.24 (d, J=5.0 Hz, 1H), 8.18 (s, 1H), 7.99 (s, 1H), 7.95-7.88 (m, 2H), 7.77 (d, J=4.5 Hz, 1H), 7.41 (d, J=7.2 Hz, 1H), 7.37 (d, J=8.1 Hz, 1H), 7.34-7.29 (m, 1H), 4.99-4.91 (m, 1H), 3.76-3.69 (m, 1H), 3.51-3.45 (m, 1H), 3.43-3.34 (m, 3H), 2.50-2.38 (m, 2H), 2.31-2.22 (m, 1H). MS = 427(MH)+.

Example 309. 3-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide

3-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide was a byproduct from Example 309 isolated as a free base as an off-white solid (0.007g, 7%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.53 (s, 1H), 9.21 (s, 2H), 8.66 (d, J=5.3 Hz, 1H), 8.54 (br s, 1H), 8.53 (d, J=4.5 Hz, 1H), 8.35-8.30 (m, 1H), 8.12 (d, J=4.8 Hz, 1H), 7.24-7.19 (m, 2H), 7.15 (t, J=7.5 Hz, 1H), 6.77 (d, J=7.7 Hz, 1H), 5.31 (s, 2H), 4.77 (br s, 1H), 3.24 (br s, 1H), 3.05-2.80 (m, 3H), 2.23 (br s, 1H), 1.90 (br s, 1H).MS = 427(MH)+.

Example 310. 2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide

310a) To a stirred suspension of 4-Nitrophenol (2.00 g, 14.4 mmol) and Potassium carbonate (3.0 g, 22 mmol) in Acetone (20 mL, 300 mmol) was added Ethyl bromoacetate (1.60 mL, 14.4 mmol). The mixture was heated at 30°C overnight. The mixture was cooled to room temperature, diluted with ether (50 mL) and filtered through a plug of diatomaceous earth and evaporated. (4-Nitro-phenoxy)-acetic acid ethyl ester was isolated as an off-white solid (3.20 g, 99%). ^{1}HNMR (400 MHz, CDCl3,δ, ppm): 8.22 (d, J=7.8 Hz, 2H), 6.98 (d, J=7.8 Hz, 2H), 4.72 (s, 2H), 4.29 (q, J=7.1 Hz, 2H), 1.31 (t, J=7.1 Hz, 3H). MS = 226 (MH)+.

310b) A Paar bottle (500 mL) was charged with 10% Palladium on Carbon (50% Wet)(5:45:50, Palladium:carbon black:Water, 3.0 g, 1.4 mmol) followed by a solution of (4-Nitro-phenoxy)-acetic acid ethyl ester (3.20 g, 14.2 mmol) in 2:1 Ethyl acetate:Methanol(2:1, Ethyl acetate:Methanol, 75 mL, 510 mmol). The mixture was degassed and charged with Hydrogen (50 psi). The mixture was shaken on a Paar

apparatus until adsorption of Hydrogen ceased. The mixture was degassed and backflushed with nitrogen. The mixture was filtered through a plug of diatomaceous earth and evaporated. (4-Amino-phenoxy)-acetic acid ethyl ester was isolated as a tan solid (2.65 g, 96%). ^{1}HNMR (400 MHz, CDCl3,δ, ppm): 6.77 (d, J=7.9 Hz, 1H), 6.63 (d, J=7.8 Hz, 1H), 4.54 (s, 2H), 4.26 (q, J=7.1 Hz, 2H), 3.40 (br s, 2H), 1.29 (t, J=7.1 Hz, 3H). MS = 196 (MH)+.

310c) (R)-3-{2-[2-(4-Ethoxycarbonylmethoxy-phenylamino)-pyridin-4-yl]-pyrido[3, 4-d]pyrimidin-4-ylamino}-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (200.0 mg, 0.4685 mmol) and (4-Amino-phenoxy)-acetic acid ethyl ester (100.0 mg, 0.5122 mmol) in an analogous manner to Example 303c. The orange residue was suspended in Methanol (1 mL, 20 mmol) and Water (1 mL, 60 mmol) and Lithium hydroxide monohydrate (25.0 mg, 0.596 mmol) was added. The mixture was stirred at room temperature overnight. The volatiles were evaporated to yield an orange solid. The orange solid was suspended in 1,4-Dioxane (5 mL, 60 mmol). Pyridine (0.1 mL, 1 mmol) was added followed by Di-tert-Butyldicarbonate (105.0 mg, 0.4811 mmol) and Ammonium Carbonate (70.0 mg, 0.728 mmol). The mixture was stirred at room temperature for overnight. The mixture was diluted with dichloromethane (25 mL) and filtered through a plug of diatomaceous earth and the filtrate was evaporated. The solid was dissolved in dichloromethane (1 mL) and trifluoroacetic acid (0.5 mL) was added. The mixture was stirred for 1 hour at room temperature then the volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus (5%→30% Acetonitrile:Water w/ 0.1% TFA modifier). 2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide was isolated as the trifluoroacetic acid salt as an orange-yellow lyophilate (0.118 g, 55%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.62 (br s, 1H), 9.24 (s, 1H), 8.98 (br s, 2H), 8.76 (d, J=4.5 Hz, 1H), 8.73 (d, J=5.3 Hz, 1H), 8.27 (d, J=5.6 Hz, 1H), 8.21 (d, J=5.3 Hz, 1H), 7.96 (s, 1H), 7.74 (d, J=5.5 Hz, 1H), 7.57 (d, J=8.1 Hz, 2H), 7.54 (s, 1H), 7.42 (s, 1H), 6.99 (d, J=8.4 Hz, 2H), 4.96-4.86 (m, 1H), 4.43 (s, 2H), 3.74-3.64 (m, 1H), 3.54-3.34 (m, 3H), 2.45-2.35 (m, 1H), 2.31-2.21 (m, 1H). MS = 457 (MH)+.

Example 311. 2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide

311a) (3-Nitro-phenoxy)-acetic acid ethyl ester was prepared from m-Nitrophenol (2.00 g, 14.4 mmol) and Ethyl bromoacetate (1.60 mL, 14.4 mmol) in an analogous manner to

Example 310a. Product isolated as a yellow oil (3.20 g, 99%). ^{1}HNMR (400 MHz, CDCl3,δ, ppm): 7.88 (d, J=8.1 Hz, 1H), 7.73 (s, 1H), 7.46 (t, J=8.3 Hz, 1H), 7.27 (d, J=8.5 Hz, 1H), 4.71 (s, 2H), 4.30 (q, J=7.1 Hz, 2H), 1.32 (t, J=7.1 Hz, 3H). LC/MS = 248 (M+Na)+.

311b) (3-Amino-phenoxy)-acetic acid ethyl ester was prepared from (3-Nitro-phenoxy)-acetic acid ethyl ester (3.20 g, 14.2 mmol) in an analogous manner to Example 310b. Product isolated as an orange oil (2.60 g, 94%). ^{1}HNMR (400 MHz, CDCl3,δ, ppm): 7.05 (t, J=7.8 Hz, 1H), 6.35-6.26 (m, 3H), 4.57 (s, 2H), 4.27 (q, J=7.2 Hz, 2H), 3.67 (br s, 2H), 1.30 (t, J=7.1 Hz, 3H). MS = 196 (MH)+.

311c) 2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (200.0 mg, 0.4685 mmol) and (3-Amino-phenoxy)-acetic acid ethyl ester (100.0 mg, 0.5122 mmol) in an analogous manner to Example 310c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.011 g, 5%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.40 (br s, 1H), 9.23 (s, 1H), 8.85 (br s, 2H), 8.72 (d, J=5.3 Hz, 1H), 8.69 D, J=5.1 Hz, 1H), 8.35 (d, J=4.8 Hz, 1H), 8.26 (d, J=5.3 Hz, 1H), 7.98 (s, 1H), 7.75 (d, J=5.2 Hz, 1H), 7.55 (s, 1H), 7.52 (s, 1H), 7.39 (s, 1H), 7.28 (d, J=7.9 Hz, 1H), 7.20 (t, J=7.9 Hz, 1H), 6.51 (d, J=8.3 Hz, 1H), 4.98-4.90 (m, 1H), 4.41 (s, 2H), 3.76-3.70 (m, 1H), 3.52-3.33 (m, 3H), 2.45-2.38 (m, 1H), 2.30-2.23 (m, 1H). MS = 457(MH)+.

Example 313. 2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide

313a) To a stirred suspension of [A] 4-Nitrophenylacetic Acid (1.0 g, 5.5 mmol) and Pyridine (0.27 mL, 3.3 mmol) in 1,4-Dioxane (10 mL, 100 mmol) was added Di-tert-Butyldicarbonate (1.3 g, 6.1 mmol). The mixture was stirred for 10 minutes at room temperature then Ammonium Carbonate (0.80 g, 8.3 mmol) was added. The mixture was stirred at room temperature overnight. The volatiles were evaporated to a leave an off-white solid. The solid was triturated with methanol, filtered and rinsed with methanol. The methanolic filtrate was evaporated. 2-(4-Nitro-phenyl)-acetamide was isolated as an off-white solid (0.65 g, 65%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm):8.18 (d, J=7.9 Hz, 2H), 7.59 (br s, 1H), 7.54 (d, J=7.9 Hz, 2H), 7.01 (br s, 1H), 3.55 (s, 2H). LC/MS = 181 (MH)+.

313b) 2-(4-Amino-phenyl)-acetamide was prepared from 2-(4-Nitro-phenyl)-acetamide (0.65 g, 3.6 mmol) in an analogous manner to Example 310b. Product isolated as a pale yellow solid (0.57 g, 99%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 7.25 (br s, 1H), 6.89

(d, J=8.1 Hz, 2H), 6.74 (br s, 1H), 6.47 (d, J=8.2 Hz, 2H), 4.89 (br s, 2H), 3.14 (s, 2H). MS = 151 (MH)+.

313c) . 2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide was prepared from [A] (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (200.0 mg, 0.4685 mmol) and 2-(4-Amino-phenyl)-acetamide (85.0 mg, 0.566 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.029 g, 14%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.36 (br s, 1H), 9.23 (s, 1H), 8.85 (br s, 2H), 8.72 (d, J=5.6 Hz, 1H), 8.70-8.67 (m, 1H), 8.30 (d, J=5.1 Hz, 1H), 8.25 (d, J=5.5 Hz, 1H), 7.96 (s, 1H), 7.72 (d, J=5.2 Hz, 1H), 7.63 (d, J=7.4 Hz, 2H), 7.42 (br s, 1H), 7.20 (d, J=8.3 Hz, 2H), 6.86 (br s, 1H), 4.96-4.87 (m, 1H), 3.75-3.65 (m, 1H), 3.51-3.30 (m, 5H), 2.46-2.36 (m, 1H), 2.31-2.21 (m, 1H). MS = 441 (MH)+.

Example 314. 2-(4-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(4-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was a byproduct from Example 313. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.018 g, 8%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.84 (s, 1H), 9.24 (s, 1H), 9.12 (s, 1H), 8.94 (br s, 2H), 8.71 (d, J=5.5 Hz, 2H), 8.50 (d, J=5.2 Hz, 1H), 8.26 (d, J=5.7 Hz, 1H), 8.09 (d, J=4.6 Hz, 1H), 7.34 (d, J=8.0 Hz, 2H), 7.08 (d, J=7.5 Hz, 2H), 4.95-4.87 (m, 1H), 3.77-3.65 (m, 3H), 3.51-3.33 (m, 3H), 2.47-2.36 (m, 1H), 2.31-2.21 (m, 1H). MS = 441 (MH)+.

Example 316. 2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide

316a) 2-(3-Nitro-phenyl)-acetamide was prepared from (3-Nitro-phenyl)-acetic acid (1.0 g, 5.5 mmol) in an analogous manner to Example 13a. Product isolated as a crude off-white solid (1.2 g, 50%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.15 (s, 1H), 8.10 (d, J=8.2 Hz, 1H), 7.71 (d, J=7.7 Hz, 1H), 7.63-7.54 (m, 2H), 7.01 (br s, 1H), 3.56 (s, 2H). MS = 181 (MH)+.

316b) 2-(3-Amino-phenyl)-acetamide was prepared from 2-(3-Nitro-phenyl)-acetamide (1.2 g, 6.7 mmol) in an analogous manner to Example 10b. Product isolated as an off-white solid (1.0 g, 70%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 7.32 (br s, 1H), 6.90 (t, J=7.7 Hz, 1H), 6.79 (br s, 1H), 6.46 (s, 1H), 6.42-6.37 (m, 2H), 4.97 (br s, 2H), 3.18 (s, 2H). MS = 151 (MH)+.

316c) 2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (200.0 mg, 0.4685 mmol) and 2-(3-Amino-phenyl)-acetamide (85.0 mg, 0.566 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.055 g, 26%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.50 (br s, 1H), 9.24 (s, 1H), 8.91 (br s, 2H), 8.72 (d, J=5.5 Hz, 1H), 8.31 (d, J=5.4 Hz, 1H), 8.26 (d, J=5.7 Hz, 1H), 7.99 (s, 1H), 7.75 (d, J=5.4 HZ, 1H), 7.66 (d, J=8.6 Hz, 1H), 7.54 (s, 1H), 7.48 (br s, 1H), 7.25 (t, J=7.7 Hz, 1H), 6.93-6.86 (m, 2H), 4.97-4.87 (m, 1H), 3.76-3.66 (m, 1H), 3.54-3.34 (m, 5H), 2.46-2.36 (m, 1H), 2.31-2.21 (m, 1H). MS = 441 (MH)+.

Example 317. 2-(3-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(3-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was a byproduct from Example 16. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.047 g, 23%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.90 (s, 1H), 9.24 (s, 1H), 9.14 (s, 1H), 8.94 (br s, 2H), 8.75-8.70 (m, 2H), 8.51 (d, J=5.1 Hz, 1H), 8.26 (d, J=5.5 Hz, 1H), 8.10 (dd, J=5.1, 1.1 Hz, 1H), 7.28 (t, J=7.8 Hz, 1H), 7.10-7.02 (m, 3H), 6.94 (d, J=6.6 Hz, 1H), 6.40-4.00 (m, 3H), 3.76 (s, 2H), 3.75-3.65 (m, 1H), 3.52-3.32 (m, 3H), 2.47-2.36 (m, 1H), 2.31-2.21 (m, 1H). MS = 441(MH)+.

Example 318. {2-[2-(5-Phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

2-[2-(5-Phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 5-Phenyl-pyridin-2-ylamine (36.0 mg, 0.212 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.098 g, 97%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.28 (s, 1H), 8.92 (br s, 2H), 8.78-8.74 (m, 2H), 8.66-8.63 (m, 2H), 8.49 (d, J=5.8 Hz, 1H), 8.29 (d, J=5.2 Hz, 1H), 8.24-8.18 (m, 1H), 8.04-8.01 (m, 1H), 7.80-7.71 (m, 3H), 7.55-7.49 (m, 2H), 7.44-7.39 (m, 1H), 5.00-4.92 (m, 1H), 3.80-3.71 (m, 1H), 3.55-3.35 (m, 3H), 2.48-2.40 (m, 1H), 2.34-2.25 (m, 1H). MS = 461 (MH)+.

Example 319. {2-[2-(6-Morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(6-Morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 6-Morpholin-4-yl-pyridin-3-ylamine (39.0 mg, 0.218 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as an orange-brown lyophilate (0.082 g, 80%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.71 (br s, 1H), 9.24 (s, 1H), 9.01 (br s, 2H), 8.77 (d, J=5.5 Hz, 1H), 8.73 (d, J=5.5 Hz, 1H), 8.62 (br s, 1H), 8.29-8.24 (m, 2H), 8.01-7.95 (m, 2H), 7.78 (dd, J=5.5, 1.3 Hz, 1H), 7.15 (d, J=9.2 Hz, 1H), 4.98-4.90 (m, 1H), 3.78-3.67 (m, 5H), 3.55-3.34 (m, 8H), 2.46-2.36 (m, 1H), 2.31-2.21 (m, 1H). MS = 470 (MH)+.

Example 320. (2-{2-[6-(4-Methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine

(2-{2-[6-(4-Methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 6-(4-Methyl-piperazin-1-yl)-pyridin-3-ylamine (41.0 mg, 0.213 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a brown lyophilate (0.094 g, 90%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.86 (br s, 1H), 9.45 (br s, 1H), 9.22 (s, 1H), 9.04 (br s, 2H), 8.76 (d, J=5.4 Hz, 1H), 8.72 (d, J=5.6 Hz, 1H), 8.51 (d, J=2.7 Hz, 1H), 8.27 (d, J=5.8 Hz, 1H), 8.24 (d, J=5.6 Hz, 1H), 8.02 (dd, J=9.0, 2.6 Hz, 1H), 7.93 (s, 1H), 7.73 (dd, J=5.4, 1.2 Hz, 1H), 7.02 (d, J=9.2 Hz, 1H), 4.99-4.90 (m, 1H), 4.38-4.25 (m, 2H), 3.78-3.68 (m, 1H), 3.59-3.34 (m, 5H), 3.18-3.02 (m, 4H), 2.87 (s, 3H), 2.47-2.36 (m, 1H), 2.31-2.22 (m, 1H). MS = 483 (MH)+.

Example 321. 2-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

2-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 2-Amino-isonicotinonitrile (25.0 mg, 0.210 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.012 g, 13%).

Example 322. {2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 4-Imidazol-1-ylmethyl-phenylamine (37.0 mg, 0.214 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.097 g, 95%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.56 (s, 1H), 9.24 (t, J=1.4 Hz, 1H), 9.22 (s, 1H), 9.06 (br s, 2H), 8.77 (d, J=5.4 Hz, 1H), 8.71 (d, J=5.5 Hz, 1H), 8.33 (d, J=5.5 Hz, 1H), 8.27 (d, J=5.8 Hz, 1H), 7.97 (s, 1H), 7.83-7.76 (m, 4H), 7.70 (t, J=1.7 Hz, 1H), 7.38 (d, J=8.7 Hz, 2H), 5.36 (s, 2H), 5.01-4.92 (m, 1H), 3.78-3.69 (m, 1H), 3.55-3.34 (m, 3H), 2.47-2.36 (m, 1H), 2.31-2.22 (m, 1H). MS = 464 (MH)+.

Example 323. 2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide

2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide was prepared from R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (150.0 mg, 0.3283 mmol) and (3-Amino-phenoxy)-acetic acid ethyl ester (75.0 mg, 0.384 mmol) in an analogous manner to Example 303c and Example 10c and Example 1c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.082 g, 41%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.42 (s, 1H), 8.94 (br s, 1H), 8.89-8.80 (m, 2H), 8.41 (s, 1H), 8.34 (d, J=5.2 Hz, 1H), 8.16 (d, J=6.2 Hz, 1H), 7.95 (s, 1H), 7.72 (dd, J=5.4, 1.3 Hz, 1H), 7.54 (t, J=2.1 Hz, 1H), 7.52 (s, 1H), 7.38 (s, 1H), 7.30-7.25 (m, 1H), 7.20 (t, J=8.2 Hz, 1H), 6.51 (dd, J=7.8, 1.7 Hz, 1H), 5.05-4.95 (m, 1H), 4.41 (s, 2H), 4.16 (m, 3H), 3.73-3.64 (m, 1H), 3.52-3.30 (m, 3H), 2.53-2.45 (m, 1H), 2.27-2.16 (m, 1H). MS = 487 (MH)+.

Example 324. 2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide

2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin- 2-yl]-pyridin-2-ylamino}-phenyl)-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (150.0 mg, 0.3283 mmol) and 2-(3-Amino-phenyl)-acetamide (60.0 mg, 0.400 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.043 g, 22%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.36 (s, 1H),

9.00-8.77 (m, 3H), 8.40 (s, 1H), 8.31 (d, J=5.4 Hz, 1H), 8.15 (d, J=6.2 Hz, 1H), 7.94 (s, 1H), 7.72-7.65 (m, 2H), 7.56 (s, 1H), 7.46 (s, 1H), 7.22 (t, J=7.7 Hz, 1H), 6.90-6.83 (m, 2H), 5.05-4.95 (m, 1H), 4.16 (s, 3H), 3.73-3.63 (m, 1H), 3.50-3.23 (m, 5H), 2.55-2.45 (m, 1H), 2.26-2.16 (m, 1H). MS = 471(MH)+.

Example 325. 2-(3-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(3-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was a byproduct from Example 24. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.033 g, 17%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.84 (s, 1H), 9.11 (s, 1H), 9.00-8.78 (m, 3H), 8.50 (d, J=5.5 Hz, 1H), 8.40 (s, 1H), 8.15 (d, J=5.9 Hz, 1H), 8.06 (dd, J=5.2, 1.4 Hz, 1H), 7.25-7.10 (m, 1H), 7.00-6.65 (m, 3H), 5.00-4.01 (m, 1H), 4.15 (s, 3H), 3.80-3.28 (m, 8H), 2.55-2.45 (m, 1H), 2.26-2.16 (m, 1H). MS = 471 (MH)+

Example 326. 2-(4-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide

2-(4-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (150.0 mg, 0.3283 mmol) and 2-(4-Amino-phenyl)-acetamide (60.0 mg, 0.400 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.072 g, 37%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.29 (s, 1H), 9.10-8.80 (m, 3H), 8.40 (s, 1H), 8.31 (d, J=5.3 Hz, 1H), 8.15 (d, J=6.1 Hz, 1H), 7.92 (s, 1H), 7.68 (dd, J=5.3, 1.3 Hz, 1H), 7.63 (d, J=8.5 Hz, 2H), 7.43-7.39 (m, 1H), 7.18 (d, J=8.5 Hz, 2H), 6.84 (s, 1H), 5.05-4.95 (m, 1H), 4.16 (s, 3H), 3.72-3.63 (m, 1H), 3.50-3.20 (m, 5H), 2.54-2.45 (m, 1H), 2.26-2.16 (m, 1H). MS = 471 (MH)+.

Example 327. 2-(4-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(4-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was a byproduct from Example 26. Product isolated as the trifluoroacetic acid salt was isolated as a yellow lyophilate (0.025g, 13%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.81 (s, 1H), 9.09 (s, 1H), 9.02-8.83 (m, 3H), 8.49 (dd, J=5.2, 0.70 Hz, 1H), 8.40 (s, 1H), 8.16 (d, J=6.0 Hz, 1H), 8.05 (dd, J=5.2, 1.5 Hz, 1H), 7.28 (d, J=7.8 Hz, 2H), 7.00-6.93 (m, 2H), 5.01-4.91 (m, 1H), 4.15 (s, 3H), 3.72-3.61 (m, 3H), 3.47-3.28 (m, 3H), 2.54-2.44 (m, 1H), 2.26-2.16 (m, 1H). MS = 471 (MH)+.

Example 328. 1-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile

1-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 1H-Pyrrolo[2,3-b]pyridine-4-carbonitrile (30.0 mg, 0.210 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as an off-white lyophilate (0.068 g, 71%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.83 (s, 1H), 9.31 (s, 1H), 8.89 (br s, 2H), 8.79-8.75 (m, 4H), 8.72 (d, J=4.9 Hz, 1H), 8.37 (d, J=5.2 Hz, 1H), 8.30 (d, J=5.6 Hz, 1H), 7.87 (d, J=4.9 Hz, 1H), 7.04 (d, J=3.9 Hz, 1H), 5.00-4.91 (m, 1H), 3.83-3.74 (m, 1H), 3.57-3.39 (m, 3H), 2.54-2.44 (m, 1H), 2.37-2.30 (m, 1H). MS = 434 (MH)+.

Example 329. {5-Methoxy-2-[2-(5-phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{5-Methoxy-2-[2-(5-phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.164 mmol) and 5-Phenyl-pyridin-2-ylamine (31.0 mg, 0.182 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.043 g, 43%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.04-8.85 (m, 3H), 8.66-8.61 (m, 2H), 8.48 (d, J=5.5 Hz, 1H), 8.44 (s, 1H), 8.23-8.15 (m, 2H), 8.00-7.95 (m, 1H), 7.82-7.75 (m, 1H), 7.74-7.71 (m, 2H), 7.51 (t, J=7.6 Hz, 2H), 7.41 (t, J=7.1 Hz, 1H), 5.07-5.00 (m, 1H), 4.18 (s, 3H), 3.76-3.66 (m, 1H), 3.54-3.30 (m, 3H), 2.55-2.45 (m, 1H), 2.30-2.20 (m, 1H). MS = 491 (MH)+.

Example 330. {5-Methoxy-2-[2-(6-morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{5-Methoxy-2-[2-(6-morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.164 mmol) and 6-Morpholin-4-yl-pyridin-3-ylamine (33.0 mg, 0.184 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a tan lyophilate (0.033 g, 33%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.02-8.82 (m, 3H), 8.60-8.52 (m, 1H), 8.41 (s, 1H), 8.26 (d, J=4.8 Hz, 1H), 8.17 (d, J=4.4 Hz, 1H), 8.00-7.95 (m, 1H), 7.89 (s, 1H), 7.72-7.68 (m, 1H), 7.10-6.98

(m, 1H), 5.05-4.95 (m, 1H), 4.16 (s, 3H), 3.76-3.63 (m, 5H), 3.50-3.29 (m, 7H), 2.54-2.45 (m, 1H), 2.26-2.16 (m, 1H). MS = 500 (MH)+.

Example 331. (5-Methoxy-2-{2-[6-(4-methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine

(5-Methoxy-2-{2-[6-(4-methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.164 mmol) and 6-(4-Methyl-piperazin-1-yl)-pyridin-3-ylamine (35.0 mg, 0.182 mmol) in an analogous manner to Example 303c. Product isolated as the bis-trifluoroacetic acid salt as a brown lyophilate (0.036 g, 29%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.69 (br s, 1H), 9.26 (br s, 1H), 9.06-8.81 (m, 3H), 8.51 (d, J=2.6 Hz, 1H), 8.40 (s, 1H), 8.25 (d, J=5.5 Hz, 1H), 8.16 (d, J=6.0 Hz, 1H), 8.04 (dd, J=9.1, 2.6 Hz, 1H), 7.86 (s, 1H), 7.67 (d, J=5.3 Hz, 1H), 6.98 (d, J=9.0 Hz, 1H), 5.04-4.98 (m, 1H), 4.32-4.26 (m, 2H), 4.16 (s, 3H), 3.71-3.65 (m, 1H), 3.55-3.50 (m, 2H), 3.50-3.30 (m, 3H), 3.16-3.01 (m, 4H), 2.86 (d, J=4.3 Hz, 3H), 2.53-2.43 (m, 1H), 2.26-2.16 (m, 1H). MS = 513 (MH)+.

Example 332. 2-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

2-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.164 mmol) and 2-Amino-isonicotinonitrile (22.0 mg, 0.185 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.014 g, 15%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.42 (s, 1H), 8.98-8.80 (m, 3H), 8.60 (s, 1H), 8.51 (d, J=5.1 Hz, 1H), 8.48 (d, J=5.3 Hz, 1H), 8.42 (s, 1H), 8.34 (s, 1H), 8.16 (d, J=5.8 Hz, 1H), 7.92 (dd, J=5.2, 1.3 Hz, 1H), 7.32 (dd, J=5.0, 1.3 Hz, 1H), 5.03-4.95 (m, 1H), 4.17 (s, 3H), 3.75-3.66 (m, 1H), 3.50-3.30 (m, 3H), 2.55-2.45 (m, 1H), 2.28-2.18 (m, 1H). MS = 440 (MH)+.

Example 333. {2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.164 mmol) and 4-Imidazol-1-ylmethyl-phenylamine (32.0 mg,

0.185 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow-orange lyophilate (0.037 g, 37%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.53 (s, 1H), 9.24-9.22 (m, 1H), 9.18-8.92 (m, 2H), 8.82 (s, 1H), 8.40 (s, 1H), 8.33 (d, J=5.3 Hz, 1H), 8.18 (d, J=6.3 Hz, 1H), 7.94 (s, 1H), 7.81 (d, J=8.6 Hz, 2H), 7.78 (t, J=1.7 Hz, 1H), 7.74 (dd, J=5.2, 1.3 Hz, 1H), 7.70 (t, J=1.7 Hz, 1H), 7.37 (d, J=8.7 Hz, 2H), 5.36 (s, 2H), 5.08-4.99 (m, 1H), 4.16 (s, 3H), 3.74-3.64 (m, 1H), 3.52-3.29 (m, 3H), 2.53-2.43 (m, 1H), 2.26-2.16 (m, 1H). MS = 494 (MH)+.

Example 334. 2-Phenyl-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-Phenyl-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and Benzeneacetamide (27.0 mg, 0.200 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a tan lyophilate (0.036 g, 38%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.89 (s, 1H), 9.25 (s, 1H), 9.14 (s, 1H), 8.90 (br s, 2H), 8.73-8.69 (m, 2H), 8.50 (dd, J=5.2, 0.6 Hz, 1H), 8.25 (d, J=5.2 Hz, 1H), 8.09 (dd, J=5.2, 1.4 Hz, 1H), 7.41-7.24 (m, 5H), 4.93-4.85 (m, 1H), 3.79 (s, 2H), 3.75-3.65 (m, 1H), 3.51-3.33 (m, 3H), 2.47-2.37 (m, 1H), 2.31-2.21 (m, 1H). MS = 426 (MH)+.

Example 335. 2-(4-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(4-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 4-Methoxyphenylacetamide (33.0 mg, 0.200 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.021 g, 21%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.81 (s, 1H), 9.24 (s, 1H), 9.13 (s, 1H), 8.88 (br s, 2H), 8.71 (d, J=5.6 Hz, 1H), 8.69 (d, J=4.8 Hz, 1H), 8.49 (d, J=5.2 Hz, 1H), 8.25 (d, J=5.3 Hz, 1H), 8.08 (dd, J=5.1, 1.5 Hz, 1H), 7.30 (d, J=8.7 Hz, 2H), 6.91 (d, J=8.7 Hz, 2H), 4.93-4.85 (m, 1H), 3.75-3.65 (m, 6H), 3.49-3.34 (m, 3H), 2.47-2.37 (m, 1H), 2.31-2.21 (m, 1H). MS = 456 (MH)+.

Example 336. 2-(2-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

336a) 2-(2-Methoxy-phenyl)-acetamide was prepared from 2-Methoxybenzeneacetic acid (1.0 g, 6.0 mmol) in an analogous manner to Example 13a. Product isolated as a white

solid (0.64 g, 64%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 7.24-7.18 (m, 2H), 7.15 (dd, J=7.5, 1.6 Hz, 1H), 6.95 (d, J=7.7 Hz, 1H), 6.90-6.84 (m, 1H), 6.81 (br s, 1H), 3.75 (s, 3H), 3.35 (s, 2H). MS = 166 (MH)+.

336b) 2-(2-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol;) and 2-(2-Methoxy-phenyl)-acetamide (32.0 mg, 0.194 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a tan lyophilate (0.048 g, 48%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.66 (s, 1H), 9.24 (s, 1H), 9.12 (s, 1H), 8.84 (br s, 2H), 8.71 (d, J=5.7 Hz, 1H), 8.69-8.65 (m, 1H), 8.50 (d, J=5.2 Hz, 1H), 8.25 (d, J=5.3 Hz, 1H), 8.08 (dd, J=5.3, 1.3 Hz, 1H), 7.30-7.23 (m, 2H), 7.01 (d, J=7.8 Hz, 1H), 6.95-6.90 (m, 1H), 4.93-4.85 (m, 1H), 3.80-3.74 (m, 5H), 3.72-3.63 (m, 1H), 3.49-3.30 (m, 3H), 2.45-2.37 (m, 1H), 2.30-2.20 (m, 1H). MS = 456 (MH)+.

Example 337. 2-(3-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(3-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (75.0 mg, 0.176 mmol) and 2-(3-Methoxy-phenyl)-acetamide (32.0 mg, 0.194 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a tan lyophilate (0.099 g). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.86 (s, 1H), 9.25 (s, 1H), 9.13 (s, 1H), 8.89 (br s, 2H), 8.73-8.68 (m, 2H), 8.50 (d, J=5.2 Hz, 1H), 8.25 (d, J=5.2 Hz, 1H), 8.09 (dd, J=5.2, 1.5 Hz, 1H), 7.26 (t, J=7.8 Hz, 1H), 6.98-6.94 (m, 2H), 6.86-6.82 (m, 1H), 4.94-4.85 (m, 1H), 3.77-3.65 (m, 6H), 3.51-3.34 (m, 3H), 2.47-2.37 (m, 1H), 2.31-2.21 (m, 1H). MS = 456 (MH)+.

Example 338. {2-[2-(4-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(4-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 4-Methyl-pyridin-2-ylamine (31.0 mg, 0.287 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.107 g). ^{1}HNMR= 31550651 (400 MHz, d6-DMSO,δ, ppm): 9.28-9.27 (m, 1H), 8.99 (br s, 2H), 8.84-8.79 (m, 1H), 8.77-8.74 (m, 1H), 8.55 (d, J=5.4 Hz, 1H), 8.42-8.36 (m,

1H), 8.31-8.26 (m, 2H), 8.18-8.14 (m, 1H), 7.27 (s, 1H), 7.16-7.12 (m, 1H), 5.04-4.94 (m, 1H), 3.78-3.68 (m, 1H), 3.54-3.34 (m, 3H), 2.48 (s, 3H), 2.46-2.36 (m, 1H), 2.32-2.22 (m, 1H). MS = 399 (MH)+.

Example 339. {2-[2-(4-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(4-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (105.0 mg, 0.2460 mmol) and 4-Chloro-pyridin-2-ylamine (37.0 mg, 0.288 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.124 g, 96%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.43 (br s, 1H), 9.26 (s, 1H), 8.90 (br s, 2H), 8.75-8.70 (m, 2H), 8.64 (s, 1H), 8.46 (d, J=5.6 Hz, 1H), 8.30-8.25 (m, 2H), 8.01 (s, 1H), 7.95 (d, J=5.4 Hz, 1H), 7.07 (d, J=5.3 Hz, 1H), 4.97-4.89 (m, 1H), 3.80-3.70 (m, 1H), 3.53-3.35 (m, 3H), 2.49-2.39 (m, 1H), 2.34-2.24 (m, 1H). MS = 419 (MH)+.

Example 340. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (352.0 mg, 0.7704 mmol) and 2-Aminopyrazine (81 mg, 0.85 mmol) in an analogous manner to Example 303c. Product was isolated as the free base as an off-white solid (0.050 g, 16%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.22 (s, 1H), 9.17 (d, J=1.4 Hz, 1H), 8.83 (s, 1H), 8.72 (s, 1H), 8.43 (d, J=5.2 Hz, 1H), 8.33 (s, 1H), 8.28 (dd, J=1.6, 2.6 Hz, 1H), 8.12 (d, J=2.7 Hz, 1H), 7.86 (dd, J=1.3, 5.2 Hz, 1H), 4.07 (s, 3H), 3.70-3.65 (m, 4H), 2.90-2.85 (m, 4H). MS = 416 (MH)+.

Example 341. 6-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile

6-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 6-Amino-nicotinonitrile (33.0 mg, 0.277 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.016 g, 13%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.60 (s, 1H), 9.26 (s, 1H), 8.92-8.80 (m, 3H), 8.75-8.72 (m, 2H), 8.69 (d, J=4.6 Hz, 1H), 8.48 (d, J=5.3 Hz, 1H), 8.28 (d,

J=5.2 Hz, 1H), 8.10 (dd, J=8.9, 2.3 Hz, 1H), 8.00 (dd, J=5.2, 1.3 Hz, 1H), 7.90 (d, J=8.9 Hz, 1H), 4.94-4.89 (m, 1H), 3.78-3.70 (m, 1H), 3.51-3.35 (m, 3H), 2.46-2.40 (m, 1H), 2.35-2.25 (m, 1H). MS = 410 (MH)+.

Example 342. 2-[4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile

342a) 4-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol (500.0 mg, 1.933 mmol) and tert-Butyl 1-Piperazinecarboxylate (432.0 mg, 2.320 mmol) in an analogous manner to [B016]. Product isolated as a yellow foam (0.817 g, 99%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.30 (s, 1H), 8.64-8.60 (m, 2H), 8.38-8.35 (m, 2H), 8.01-7.98 (m, 1H), 4.06-4.01 (m, 4H), 3.67-3.62 (m, 4H), 3.32 (s, 3H), 1.45 (s, 9H). MS = 427 (MH)+.

342b) 2-[4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 2-Amino-isonicotinonitrile (31.0 mg, 0.260 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.015 g, 12%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.44 (s, 1H), 9.36 (s, 1H), 8.90 (br s, 2H), 8.69-8.66 (m, 2H), 8.53-8.48 (m, 2H), 8.36 (s, 1H), 8.04 (d, J=5.7 Hz, 1H), 7.95 (dd, J=5.3, 1.3 Hz, 1H), 7.33 (dd, J=5.1, 1.3 Hz, 1H), 4.18-4.13 (m, 4H), 3.42-3.37 (m, 4H). MS = 410 (MH)+.

Example 343. {2-[2-(4-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(4-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 4-Morpholin-4-yl-pyridin-2-ylamine (47.0 mg, 0.262 mmol)[prepared as described in WO2006/040520] in an analogous manner to Example 303c. Product isolated the free base as a pale yellow solid (0.016 g, 14%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.51 (s, 1H), 9.17 (s, 1H), 8.86 (s, 1H), 8.67-8.52 (m, 2H), 8.35-8.27 (m, 2H), 7.95 (d, J=6.0 Hz, 1H), 7.81-7.78 (m, 1H), 7.30-7.27 (m, 1H), 6.52-6.47 (m, 1H), 4.97-4.75 (m, 1H), 3.77-3.72 (m, 4H), 3.35-3.30 (m, 1H), 3.26-3.22 (m, 4H), 3.06-2.98 (m, 1H), 2.92-2.84 (m, 2H), 2.31-2.21 (m, 1H), 1.93-1.83 (m, 1H). MS = 470 (MH)+.

Example 344. 6-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile

344a) 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol was prepared from 2-Chloro-isonicotinonitrile (0.96 g, 6.9 mmol) and 3-Amino-5-methoxy-isonicotinic acid (0.97 g, 5.8 mmol) in an analogous manner to example 1501a. Product isolated as a tan solid (0.774 g, 46%). ^{1}HNMR (400 MHz, d1-TFA,δ, ppm): 9.24 (s, 1H), 9.11 (d, J=6.2 Hz, 1H), 8.93 (s, 1H), 8.85 (d, J=6.0 Hz, 1H), 8.71 (s, 1H), 4.36 (s, 3H). MS = 289 (MH)+.

344b) R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.50 g, 1.7 mmol) and (R)-3-Amino-pyrrolidine-1-carboxylic acid tert-butyl ester (0.32 mL, 1.9 mmol) in an analogous manner to [B016]. Product isolated as a light brown solid (0.50 g, 63%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.84 (s,1H), 8.61 (d, J=5.0 Hz, 1H), 8.39 (s, 1H), 8.36-8.32 (m, 2H), 8.24-8.17 (m, 1H), 5.09-4.92 (m, 1H), 4.14 (s, 3H), 3.86-3.72 (m, 1H), 3.55-3.32 (m, 3H), 2.37-2.25 (m, 1H), 2.21-2.07 (m, 1H), 1.45-1.38 (m, 9H). MS = 457(MH)+.

344c) 6-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (160.0 mg, 0.3502 mmol) and 6-Amino-nicotinonitrile (50.0 mg, 0.420 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.043 g, 22%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 10.60 (s, 1H), 9.00-8.80 (m, 4H), 8.72 (d, J=2.2 Hz, 1H), 8.48 (d, J=5.3 Hz, 1H), 8.42 (s, 1H), 8.15 (d, J=5.8 Hz, 1H), 8.10 (dd, J=8.9, 2.4 Hz, 1H), 7.97 (dd, J=5.3, 1.5 Hz, 1H), 7.90 (d, J=9.0 Hz, 1H), 5.01-4.93 (m, 1H), 4.17 (s, 3H), 3.75-3.65 (m, 1H), 3.52-3.30 (m, 3H), 2.55-2.45 (m, 1H), 2.29-2.19 (m, 1H). MS = 440 (MH)+.

Example 345. {2-[2-(5-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(5-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 5-Methyl-pyridin-2-ylamine (30.0 mg, 0.277 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.033 g, 27%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.27 (s, 1H), 8.93 (br s, 2H), 8.81-8.77 (m, 1H), 8.76 (d, J=5.6 Hz, 1H), 8.52-8.45 (m, 2H), 8.29 (d, J=5.5 Hz, 1H), 8.20

(s, 1H), 8.08 (br s, 1H), 7.87 (br s, 1H), 7.49 (br s, 1H), 5.00-4.90 (m, 1H), 3.79-3.69 (m, 1H), 3.55-3.35 (m, 3H), 2.47-2.37 (m, 1H), 2.34-2.24 (m, 4H). MS = 399 (MH)+.

Example 346. {2-[2-(5-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(5-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 2-Amino-5-chloropyridine (36.0 mg, 0.280 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.081 g, 65%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.36 (br s, 1H), 9.26 (s, 1H), 8.89 (br s, 2H), 8.74 (d, J=5.6 Hz, 1H), 8.71 (d, J=4.8 Hz, 1H), 8.67 (s, 1H), 8.42 (d, J=5.5 Hz, 1H), 8.34-8.32 (m, 1H), 8.27 (d, J=5.1 Hz, 1H), 7.93 (d, J=5.5 Hz, 1H), 7.88-7.82 (m, 2H), 4.97-4.87 (m, 1H), 3.79-3.70 (m, 1H), 3.55-3.35 (m, 3H), 2.50-2.40 (m, 1H), 2.34-2.24 (m, 1H). MS = 419 (MH)+.

Example 347. 2-[2-(Pyrimidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(Pyrimidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and Pyrimidin-4-ylamine (27.0 mg, 0.284 mmol) in an analogous manner to Example 303c. Product isolated as the trifluoroacetic acid salt as an off-white lyophilate (0.033 g, 28%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 11.07 (br s, 1H), 9.26 (s, 1H), 9.07 (br s, 2H), 8.95 (s, 1H), 8.87 (d, J=5.3 Hz, 1H), 8.84 (s, 1H), 8.73 (d, J=5.6 Hz, 1H), 8.56-8.53 (m, 2H), 8.35 (d, J=5.5 Hz, 1H), 8.10 (d, J=5.2, 1.2 Hz, 1H), 7.97-7.90 (m, 1H), 5.00-4.92 (m, 1H), 3.79-3.69 (m, 1H), 3.55-3.35 (m, 3H), 2.49-2.39 (m, 1H), 2.35-2.25 (m, 1H). MS = 386 (MH)+.

Example 348. 2-(3-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

348a) 2-(3-Cyano-phenyl)-acetamide was prepared from (3-Cyano-phenyl)-acetic acid (1.0 g, 6.2 mmol) in an analogous manner to Example 313a. Product isolated as an off-white solid (0.50 g, 50%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.72-7.69 (m, 2H), 7.61-7.58 (m, 1H), 7.56-7.50 (m, 2H), 6.97 (br s, 1H), 3.47 (s, 2H). MS = 161 (MH)+.

348b) 2-(3-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-

pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 2-(3-Cyano-phenyl)-acetamide (45.0 mg, 0.281 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.125 g, 94%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.97 (s, 1H), 9.24 (s, 1H), 9.12 (s, 1H), 8.90 (br s, 2H), 8.73-8.69 (m, 2H), 8.51 (dd, J=5.1, 0.5 Hz, 1H), 8.25 (dd, J=5.6, 0.7 Hz, 1H), 8.10 (dd, J=5.2, 1.5 Hz, 1H), 7.84-7.82 (m, 1H), 7.78-7.75 (m, 1H), 7.74-7.70 (m, 1H), 7.58 (t, J=7.8 Hz, 1H), 4.94-4.85 (m, 1H), 3.90 (s, 2H), 3.74-3.64 (m, 1H), 3.51-3.33 (m, 3H), 2.47-2.37 (m, 1H), 2.30-2.20 (m, 1H). MS = 451 (MH)+.

Example 349. 2-(4-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

349a) 2-(4-Cyano-phenyl)-acetamide was prepared from (4-Cyano-phenyl)-acetic acid (1.0 g, 6.2 mmol) in an analogous manner to Example 313a. Product isolated as an off-white solid (0.71 g, 71%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 7.77 (d, J=8.3 Hz, 2H), 7.55 (br s, 1H), 7.45 (d, J=8.3 Hz, 2H), 6.98 (br s, 1H), 3.49 (s, 2H). MS = 161 (MH)+.

349b) 2-(4-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (120.0 mg, 0.2811 mmol) and 2-(4-Cyano-phenyl)-acetamide (45.0 mg, 0.281 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as the trifluoroacetic acid salt as a pale orange lyophilate (0.148 g, 93%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.98 (s, 1H), 9.23 (s, 1H), 9.12 (s, 1H), 8.87 (br s, 2H), 8.73-8.68 (m, 2H), 8.51 (dd, J=5.1, 0.6 Hz, 1H), 8.25 (dd, J=5.7, 0.6 Hz, 1H), 8.10 (dd, J=5.1, 1.4 Hz, 1H), 7.83 (d, J=8.4 Hz, 2H), 7.58 (d, J=8.4 Hz, 2H), 4.93-4.84 (m, 1H), 3.92 (s, 2H), 3.73-3.64 (m, 1H), 3.51-3.32 (m, 3H), 2.47-2.36 (m, 1H), 2.30-2.21 (m, 1H). MS = 451 (MH)+.

Example 350. (R)-Pyrrolidin-3-yl-{2-[2-(4-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine

(R)-Pyrrolidin-3-yl-{2-[2-(4-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 4-Trifluoromethyl-pyridin-2-ylamine (46.0 mg, 0.284 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.127 g, 95%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.57 (s, 1H), 9.26 (d, J=0.4 Hz, 1H), 8.94 (br s, 2H), 8.75-8.72 (m, 2H), 8.69 (s, 1H), 8.56 (d,

J=5.1 Hz, 1H), 8.47 (d, J=5.4 Hz, 1H), 8.28 (dd, J=5.7, 0.6 Hz, 1H), 8.26 (s, 1H), 7.97 (dd, J=5.4, 1.5 Hz, 1H), 7.25 (dd, J=5.9, 1.0 Hz, 1H), 4.99-4.90 (m, 1H), 3.80-3.71 (m, 1H), 3.55-3.35 (m, 3H), 2.48-2.40 (m, 1H), 2.34-2.24 (m, 1H). MS = 453 (MH)+.

Example 351. (R)-Pyrrolidin-3-yl-{2-[2-(5-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine

(R)-Pyrrolidin-3-yl-{2-[2-(5-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 5-Trifluoromethyl-pyridin-2-ylamine (46.0 mg, 0.284 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as a trifluoroacetic acid salt as a pale yellow lyophilate (0.102 g, 76%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.64 (s, 1H), 9.27 (d, J=0.6 Hz, 1H), 8.94 (br s, 2H), 8.75-7.73 (m, 3H), 8.66-8.63 (m, 1H), 8.48 (dd, J=5.2, 0.3 Hz, 1H), 8.28 (dd, J=5.6, 0.7 Hz, 1H), 8.08 (dd, J=9.1, 2.5 Hz, 1H), 8.03-7.98 (m, 2H), 4.99-4.90 (m, 1H), 3.80-3.70 (m, 1H), 3.55-3.35 (m, 3H), 2.50-2.40 (m, 1H), 2.34-2.24 (m, 1H). MS = 453 (MH)+.

Example 352. 2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile

352a) 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (2.0 g, 6.9 mmol) and tert-Butyl 1-Piperazinecarboxylate (1.5 g, 8.3 mmol; Supplier = Aldrich) in an analogous manner to [B016]. Product isolated as an off-white solid (1.35 g, 43%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.88 (s, 1H), 8.61 (dd, J=4.9, 0.8 Hz, 1H), 8.39 (s, 1H), 8.34-8.31 (m, 2H), 4.09 (s, 3H), 3.72-3.67 (m, 4H), 3.57-3.52 (m, 4H), 1.44 (s, 9H). MS = 457, 459 (MH)+.

352b) 2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Amino-isonicotinonitrile (31.0 mg, 0.260 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.105 g, 86%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.49 (s, 1H), 8.93 (s, 1H), 8.88 (br s, 2H), 8.64 (s, 1H), 8.51 (dd, J=5.1, 0.6 Hz, 1H), 8.48 (d, J=5.5 Hz, 1H), 8.43 (s, 1H), 8.34 (s, 1H), 7.92 (dd, J=5.4, 1.4 Hz, 1H), 7.34 (dd, J= 5.0, 1.3 Hz, 1H), 4.11 (s, 3H), 3.93-3.88 (m, 4H), 3.37-3.30 (m, 4H). MS = 440 (MH)+.

Example 353. 6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinonitrile

6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinonitrile was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Amino-nicotinonitrile (31.0 mg, 0.260 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as the trifluoroacetic acid salt as pale yellow lyophilate (0.109 g, 89%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.64 (s, 1H), 8.93 (s, 1H), 8.90-8.82 (m, 3H), 8.72 (d, J=2.2 Hz, 1H), 8.49 (d, J=5.4 Hz, 1H), 8.43 (s, 1H), 8.11 (dd, J=8.9, 2.4 Hz, 1H), 7.96 (dd, J=5.2, 1.4 Hz, 1H), 7.92 (d, J=8.9 Hz, 1H), 4.11 (s, 3H), 3.93-3.88 (m, 4H), 3.37-3.31 (m, 4H). MS = 440 (MH)+.

Example 354. {4-[5-Methoxy-4-(4-morpholin-4-yl-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine

354a) 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-(4-morpholin-4-yl-piperidin-1-yl)-pyrido[3,4-d]pyrimidine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (190.0 mg, 0.6581 mmol) and 4-Piperidin-4-yl-morpholine (134.0 mg, 0.7871 mmol) in an analogous manner to [B016]. Product isolated as a red-orange solid (0.146 g, 50%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.84 (s, 1H), 8.60 (dd, J=4.9, 0.6 Hz, 1H), 8.36 (s, 1H), 8.32-8.29 (m, 2H), 4.28 (d, J=11.6 Hz, 2H), 4.08 (s, 3H), 3.60-3.55 (m, 4H), 3.15 (t, J=11.6 Hz, 2H), 2.53-2.46 (m, 5H), 1.96 (d, J=11.3 Hz, 2H), 1.61-1.49 (m, 2H). (400 MHz, CDCl3, δ, ppm): 8.97 (s, 1H), 8.52 (d, J=4.9 Hz, 1H), 8.37 (s, 1H), 8.28 (dd, J=5.2, 1.3 Hz, 1H), 8.21 (s, 1H), 4.36 (d, J=13.2 Hz, 2H), 4.09 (s, 3H), 3.77-3.73 (m, 4H), 3.18-3.09 (m, 2H), 2.63-2.58 (m, 4H), 2.53-2.43 (m, 1H), 2.06 (d, J=12.7 Hz, 2H), 1.74-1.63 (m, 2H). MS = 441, 443 (MH)+.

354b) {4-[5-Methoxy-4-(4-morpholin-4-yl-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-(4-morpholin-4-yl-piperidin-1-yl)-pyrido[3,4-d]pyrimidine (80.0 mg, 0.181 mmol) and Aniline (18.6 µL, 0.204 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.108 g, 97%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.74 (br s, 1H), 9.46 (br s, 1H), 8.87 (s, 1H), 8.39 (s, 1H), 8.31 (d, J=5.4 Hz, 1H), 7.94 (s, 1H), 7.75-7.73 (m, 2H), 7.70 (dd, J=5.3, 1.3 Hz, 1H), 7.31 (t, J=7.6 Hz, 2H), 6.95 (t, J=7.2 Hz, 1H), 4.42 (d, J=12.6 Hz, 2H), 4.12 (s, 3H), 4.04 (d, J=11.7 Hz, 2H), 3.67 (t, J=12.1 Hz, 2H), 3.62-3.54 (m, 1H), 3.51 (d,

J=12.1 Hz, 2H), 3.22-3.10 (m, 4H), 2.25 (d, J=10.4 Hz, 2H), 1.85-1.72 (m, 2H). MS = 498 (MH)+.

Example 355. 2-(4-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

2-(4-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-(4-Cyano-phenyl)-acetamide (45.0 mg, 0.281 mmol) in an analogous manner to Example 303c and Example 1c. Product isolated as the trifluoroacetic acid salt as a pale orange lyophilate (0.102 g, 78%). ^{1}HNMR (400 MHz,d6-DMSO,δ, ppm): 10.99 (s, 1H), 9.08 (s, 1H), 8.90 (s, 1H), 8.83 (br s, 2H), 8.51 (dd, J=5.2, 0.6 Hz, 1H), 8.41 (s, 1H), 8.06 (dd, J=5.1, 1.5 Hz, 1H), 7.83 (d, J=8.4 Hz, 2H), 7.58 (d, J=8.4 Hz, 2H), 4.09 (s, 3H), 3.92 (s, 2H), 3.87-3.83 (m, 4H), 3.31 (br s, 4H). MS = 481 (MH)+.

Example 356. 2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-(3-Cyano-phenyl)-acetamide (45.0 mg, 0.281 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as a pale yellow lyophilate (0.125 g, 96%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.97 (s, 1H), 9.07 (s, 1H), 8.91 (s, 1H), 8.87 (br s, 2H), 8.52 (dd, J=5.1, 0.4 Hz, 1H), 8.41 (s, 1H), 8.06 (dd, J=5.2, 1.4 Hz, 1H), 7.84-7.82 (m, 1H), 7.78-7.74 (m, 1H), 7.73-7.70 (m, 1H), 7.57 (t, J=7.7 Hz, 1H), 4.09 (s, 3H), 3.89 (s, 2H), 3.87-3.83 (m, 4H), 3.31 (br s, 4H). MS = 481 (MH)+.

Example 357. {2-[2-(5-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(5-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2342 mmol) and 5-Morpholin-4-yl-pyridin-2-ylamine (48.0 mg, 0.268 mmol) [prepared as described in Toogood, P. L.; et. al. *J. Med. Chem.* 2005, 48(7), 2388-2406.] in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.103 g, 60%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.27 (s, 1H), 8.93 (br s, 2H), 8.83-8.79 (m, 1H), 8.76 (d, J=5.5 Hz, 1H),

8.14 (d, J=5.9 Hz, 1H), 8.40 (s, 1H), 8.26 (d, J=5.5 Hz, 1H), 8.07-8.01 (m, 1H), 7.94 (d, J=2.9 Hz, 1H), 7.87-7.86 (m, 1H), 7.49-7.40 (m, 1H), 5.00-4.91 (m, 1H), 3.81-3.77 (m, 4H), 3.76-3.69 (m, 1H), 3.55-3.36 (m, 3H), 3.17-3.13 (m, 4H), 2.47-2.37 (m, 1H), 2.33-2.23 (m, 1H). MS = 470 (MH)+.

Example 358. {2-[2-(2-Methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(2-Methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (115.0 mg, 0.2694 mmol) and 2-Methoxy-4-morpholin-4-yl-phenylamine (58.0 mg, 0.278 mmol) [prepared as described in WO2008/051547] in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange-brown lyophilate (0.155 g, 93%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.25 (br s, 1H), 9.27 (s, 1H), 9.08 (br s, 2H), 8.87 (d, J=5.1 Hz, 1H), 8.77 (d, J=5.6 Hz, 1H), 8.30 (d, J=5.3 Hz, 1H), 8.16 (s, 1H), 7.98 (d, J=6.5 Hz, 1H), 7.81 (dd, J=6.6, 1.3 Hz, 1H), 7.31 (d, J=8.5 Hz, 1H), 6.76 (d, J=2.3 Hz, 1H), 6.64 (dd, J=8.8, 2.4 Hz, 1H), 4.94-4.85 (m, 1H), 3.82 (s, 3H), 3.80-3.75 (m, 4H), 3.73-3.63 (m, 1H), 3.55-3.33 (m, 3H), 3.25-3.20 (m, 4H), 2.43-2.34 (m, 1H), 2.31-2.22 (m, 1H). MS = 499 (MH)+.

Example 359. (2-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (115.0 mg, 0.2517 mmol) and 2-Methoxy-4-morpholin-4-yl-phenylamine (55.0 mg, 0.264 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange-brown lyophilate (0.150 g, 92%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.25 (br s, 1H), 9.05 (br s, 2H), 8.93 (s, 1H), 8.47 (s, 1H), 8.13 (s, 1H), 8.00 (d, J=6.6 Hz, 1H), 7.76 (dd, J=6.5, 1.3 Hz, 1H), 7.31 (d, J=8.5 Hz, 1H), 6.76 (d, J=2.4 Hz, 1H), 6.64 (dd, J=8.7, 2.4 Hz, 1H), 4.11 (s, 3H), 3.91-3.86 (m, 4H), 3.81 (s, 3H), 3.80-3.76 (m, 4H), 3.32 (br s, 4H), 3.25-3.21 (m, 4H). MS = 529 (MH)+.

Example 360. {5-Methoxy-2-[2-(2-methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{5-Methoxy-2-[2-(2-methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-

pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Methoxy-4-morpholin-4-yl-phenylamine (55.0 mg, 0.264 mmol;) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange-brown lyophilate (0.057g, 40%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.13 (br s, 1H), 9.21-9.00 (m, 2H), 8.86 (s, 1H), 8.46 (s, 1H), 8.26 (d, J=6.2 Hz, 1H), 8.10 (s, 1H), 7.99 (d, J=6.4 Hz, 1H), 7.74 (dd, J=6.4, 1.2 Hz, 1H), 7.33 (d, J=8.2 Hz, 1H), 6.76 (d, J=2.4 Hz, 1H), 6.63 (dd, J=8.7, 2.4 Hz, 1H), 5.01-4.91 (m, 1H), 4.17 (s, 3H), 3.81 (s, 3H), 3.80-3.75 (m, 4H), 3.69-3.59 (m, 1H), 3.53-3.40 (m, 2H), 3.37-3.26 (m, 1H), 3.25-3.20 (m, 4H), 2.51-2.41 (m, 1H), 2.26-2.16 (m, 1H). MS = 529 (MH)+.

Example 361. (5-Methoxy-2-{2-[4-(tetrahydro-pyran-4-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine

(5-Methoxy-2-{2-[4-(tetrahydro-pyran-4-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-(Tetrahydro-pyran-4-yl)-phenylamine (43.0 mg, 0.243 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic salt as a yellow lyophilate (0.109 g, 81%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.41 (br s, 1H), 8.99 (br s, 1H), 8.88 (br s, 1H), 8.83 (s, 1H), 8.41 (s, 1H), 8.28 (d, J=5.5 Hz, 1H), 8.16 (d, J=6.2 Hz, 1H), 7.93 (s, 1H), 7.69 (dd, J=5.5, 1.2 Hz, 1H), 7.64 d, J=8.5 Hz, 2H), 7.20 (d, J=8.5 Hz, 2H), 5.05-4.95 (m, 1H), 4.16 (s, 3H), 3.98-3.92 (m, 2H), 3.72-3.63 (m, 1H), 3.50-3.28 (m, 5H), 2.76-2.68 (m, 1H), 2.50-2.43 (m, 1H), 2.27-2.17 (m, 1H), 1.73-1.60 (m, 4H). MS = 498 (MH)+.

Example 362. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(tetrahydro-pyran-4-yl)-phenyl]-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(tetrahydro-pyran-4-yl)-phenyl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-(Tetrahydro-pyran-4-yl)-phenylamine (43.0 mg, 0.243 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.099 g, 74%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm,): 9.43 (br s, 1H), 8.95-8.83 (m, 3H), 8.42 (s, 1H), 8.28 (d, J=5.5 Hz, 1H), 7.93 (s, 1H), 7.68 (dd, J=5.4, 1.2 Hz, 1H), 7.64 (d, J=8.4 Hz, 2H), 7.20 (d, J=8.5 Hz, 2H),

4.10 (s, 3H), 3.98-3.92 (m, 2H), 3.90-3.85 (m, 4H), 3.44 (ddd, J=11.2, 11.2, 3.0 Hz, 2H), 3.35-3.29 (m, 4H), 2.76-2.68 (m, 1H), 1.72-1.60 (m, 4H). MS = 498 (MH)+.

Example 363. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-Methyl-pyridin-2-ylamine (27.0 mg, 0.250 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.100 g, 84%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 11.72 (br s, 1H), 9.03-8.90 (m, 3H), 8.55 (d, J=5.5 Hz, 1H), 8.46 (s, 1H), 8.37 (s, 1H), 8.27 (d, J=6.1 Hz, 1H), 8.12 (d, J=5.2 Hz, 1H), 7.27 (s, 1H), 7.14 (d, J=4.5 Hz, 1H), 4.12 (s, 3H), 3.94-3.88 (m, 4H), 3.37-3.30 (m, 4H), 2.47 (s, 3H). MS = 429 (MH)+.

Example 364. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (110.0 mg, 0.2407 mmol) and 5-Methyl-pyridin-2-ylamine (27.0 mg, 0.250 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.122 g, 93%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 11.73 (br s, 1H), 8.98 (br s, 2H), 8.94 (s, 1H), 8.54 (d, J=5.7 Hz, 1H), 8.46 (s, 1H), 8.37 (s, 1H), 8.22 (s, 1H), 8.12-8.08 (m, 1H), 8.00-7.94 (m, 1H), 7.42 (d, J=7.6 Hz, 1H), 4.12 (s, 3H), 3.94-3.88 (m, 4H), 3.37-3.30 (m, 4H), 2.34 (s, 3H). MS = 429 (MH)+.

Example 365. (4-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(4-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-Chloro-pyridin-2-ylamine (32.0 mg, 0.249 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid as a yellow lyophilate (0.107 g, 86%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.56 (br s, 1H), 9.00-8.85 (m, 3H), 8.63 (s, 1H), 8.46 (d, J=5.4 Hz, 1H), 8.43 (s, 1H), 8.29 (d, J=5.6

Hz, 1H), 7.99 (s, 1H), 7.92 (dd, J=5.4, 1.2 Hz, 1H), 7.10 (dd, J=5.6, 1.8 Hz, 1H), 4.10 (s, 1H), 3.94-3.88 (m, 4H), 3.37-3.29 (m, 4H). MS = 449 (MH)+.

Example 366. (5-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(5-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (110.0 mg, 0.2407 mmol) and 2-Amino-5-chloropyridine (32.0 mg, 0.249 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.134 g, 98%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.45 (br s, 1H), 8.93 (s, 1H), 8.87 (br s, 2H), 8.67 (s, 1H), 8.44-8.41 (m, 2H), 8.34-8.32 (s, 1H), 7.90 (d, J=5.4 Hz, 1H), 7.88-7.81 (m, 2H), 4.10 (s, 3H), 3.94-3.87 (m, 4H), 3.37-3.30 (m, 4H). MS = 449 (MH)+.

Example 367. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-Trifluoromethyl-pyridin-2-ylamine (40.0 mg, 0.247 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow solid (0.116 g, 88%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.49 (br s, 1H), 8.93 (s, 1H), 8.87 (br s, 2H), 8.70 (s, 1H), 8.54 (d, J=5.3 Hz, 1H), 8.47 (d, J=5.3 Hz, 1H), 8.42 (s, 1H), 8.30 (s, 1H), 7.91 (dd, J=5.3, 1.3 Hz, 1H), 7.25 (d, J=4.4 Hz, 1H), 4.11 (s, 3H), 3.94-3.88 (m, 4H), 3.37-3.30 (m, 4H). MS = 483 (MH)+.

Example 368. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 5-Trifluoromethyl-pyridin-2-ylamine (40.0 mg, 0.247 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.116 g, 88%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.56 (br s, 1H), 8.94 (s, 1H), 8.88 (br s, 2H), 8.78 (s, 1H), 8.64 (s, 1H), 8.47 (d, J=5.3 Hz, 1H), 8.43 (s, 1H), 8.07 (dd, J=9.0, 2.3 Hz, 1H), 8.01 (d, J=9.0 Hz, 1H),

7.94 (dd, J=5.3, 1.3 Hz, 1H), 4.11 (s, 3H), 3.94-3.88 (m, 4H), 3.37-3.30 (m, 4H). MS = 483 (MH)+.

Example 369. 2-(4-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

369a) 2-(4-Chloro-phenyl)-acetamide was prepared from (4-Chloro-phenyl)-acetic acid (1.0 g, 5.9 mmol) in an analogous manner to Example 313a. Product isolated as a white solid (0.97 g, 97%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.47 (br s, 1H), 7.35 (d, J=8.5 Hz, 2H), 7.27 (d, J=8.5 Hz, 2H), 6.90 (br s, 1H), 3.37 (s, 2H). MS = 170, 172 (MH)+.

369b) 2-(4-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-(4-Chloro-phenyl)-acetamide (42.0 mg, 0.248 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.101 g, 76%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.92 (s, 1H), 9.08 (s, 1H), 8.91 (s, 1H), 8.85 (br s, 2H), 8.51 (dd, J=5.1, 0.5 Hz, 1H), 8.41 (s, 1H), 8.05 (dd, J=5.1, 1.5 Hz, 1H), 7.43-7.37 (m, 4H), 4.09 (s, 3H), 3.88-3.83 (m, 4H), 3.79 (s, 2H), 3.35-3.28 (m, 4H). MS = 490 (MH)+.

Example 370. 2-(3-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

370a) 2-(3-Chloro-phenyl)-acetamide was prepared from (3-Chloro-phenyl)-acetic acid (1.0 g, 5.9 mmol) in an analogous manner to Example 313a. Product isolated as a white solid (0.82 g, 82%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 7.50 (br s, 1H), 7.35-7.27 (m, 3H), 7.23-7.19 (m, 1H), 6.93 (br s, 1H), 3.39 (s, 2H). MS = 170, 172 (MH)+.

370b) 2-(3-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-(3-Chloro-phenyl)-acetamide (42.0 mg, 0.248 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.103 g, 77%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.94 (s, 1H), 9.08 (s, 1H), 8.91 (s, 1H), 8.88 (br s, 2H), 8.51 (dd, J=5.0, 0.5 Hz, 1H), 8.41 (s, 1H), 8.06 (dd, J=5.1, 1.5 Hz, 1H), 7.47-7.45 (m, 1H), 7.41-7.32 (m, 3H), 4.09 (s, 3H), 3.88-3.83 (m, 4H), 3.81 (s, 2H), 3.35-3.29 (m, 4H). MS = 490 (MH)+.

Example 371. N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and Benzeneacetamide (34.0 mg, 0.252 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.120 g, 96%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.90 (s, 1H), 9.09 (s, 1H), 8.91 (s, 1H), 8.87 (br s, 2H), 8.51 (d, J=5.2 Hz, 1H), 8.41 (s, 1H), 8.05 (dd, J=5.0, 1.3 Hz, 1H), 7.40-7.32 (m, 4H), 7.29-7.23 (m, 1H), 4.09 (s, 3H), 3.88-3.83 (m, 4H), 3.78 (s, 2H), 3.35-3.28 (m, 4H). MS = 456 (MH)+.

Example 372. 2-(3-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

2-(3-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-(3-Methoxy-phenyl)-acetamide (43.0 mg, 0.260 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.056 g, 42%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.87 (s, 1H), 9.09 (s, 1H), 8.91 (s, 1H), 8.87 (br s, 2H), 8.51 (dd, J=5.1, 0.6 Hz, 1H), 8.41 (s, 1H), 8.05 (dd, J=5.1, 1.4 Hz, 1H), 7.25 (t, J=7.8 Hz, 1H), 6.97-6.93 (m, 2H), 6.86-6.82 (m, 1H), 4.09 (s, 3H), 3.88-3.83 (m, 4H), 3.78 (s, 3H), 3.74 (s, 2H), 3.35-3.29 (m, 4H). MS = 486 (MH)+.

Example 373. N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(3-trifluoromethyl-phenyl)-acetamide

373a) 2-(3-Trifluoromethyl-phenyl)-acetamide was prepared from (3-Trifluoromethyl-phenyl)-acetic acid (1.0 g, 4.9 mmol) in an analogous manner to Example 313a. Product isolated as white solid (0.88 g, 88%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.63-7.51 (m, 5H), 6.96 (br s, 1H), 3.50 (s, 2H). MS = 204 (MH)+.

373b) N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(3-trifluoromethyl-phenyl)-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-(3-Trifluoromethyl-phenyl)-acetamide (53.0 mg, 0.261 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the

trifluoroacetic acid salt as a yellow lyophilate (0.037 g, 26%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.98 (s, 1H), 9.07 (s, 1H), 8.91 (s, 1H), 8.87 (br s, 2H), 8.52 (dd, J=5.1, 0.4 Hz, 1H), 8.41 (s, 1H), 8.06 (dd, J=5.1, 1.4 Hz, 1H), 7.75 (s, 1H), 7.70-7.57 (m, 3H), 4.09 (s, 3H), 3.92 (s, 2H), 3.88-3.83 (m, 4H), 3.35-3.28 (m, 4H). MS = 524 (MH)+.

Example 374. 2-(4-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

2-(4-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-Methoxyphenylacetamide (43.0 mg, 0.260 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.067 g, 50%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.83 (s, 1H), 9.08 (s, 1H), 8.91 (s, 1H), 8.85 (br s, 2H), 8.50 (dd, J=5.1, 0.6 Hz, 1H), 8.41 (s, 1H), 8.04 (dd, J=5.1, 1.4 Hz, 1H), 7.29 (d, J=8.8 Hz, 2H), 6.90 (d, J=8.8 Hz, 2H), 4.09 (s, 3H), 3.88-3.83 (m, 4H), 3.73 (s, 3H), 3.69 (s, 2H), 3.35-3.29 (m, 4H). MS = 486 (MH)+.

Example 375. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (106.0 mg, 0.2320 mmol) and 6-Morpholin-4-yl-pyridin-3-ylamine (48.0 mg, 0.268 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.148 g, 87%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.52 (br s, 1H), 8.98-8.85 (m, 3H), 8.59 (br s, 1H), 8.43 (s, 1H), 8.26 (d, J=5.3 Hz, 1H), 8.01-7.96 (m, 1H), 7.90 (s, 1H), 7.70 (d, J=5.2 Hz, 1H), 7.09 (br s, 1H), 4.10 (s, 3H), 3.90-3.85 (m, 4H), 3.77-3.72 (m, 4H), 3.48-3.42 (m, 4H), 3.36-3.29 (m, 4H). MS = 500 (MH)+.

Example 376. {2-[2-(Pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{2-[2-(Pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (103.0 mg, 0.2413 mmol) and 3-aminopyridine (27.0 mg, 0.287 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a pale yellow

lyophilate (0.141 g, 95%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.25 (br s, 1H), 9.39 (s, 1H), 9.24 (d, J=0.6 Hz, 1H), 8.97 (br s, 2H), 8.76 (d, J=5.5 Hz, 1H), 8.73 (d, J=5.6 Hz, 1H), 8.51-8.45 (m, 2H), 8.38 (d, J=5.2 Hz, 1H), 8.28 (dd, J=5.6, 0.7 Hz, 1H), 8.07 (s, 1H), 7.93 (dd, J=5.3, 1.2 Hz, 1H), 7.81 (dd, J=8.2, 5.34 Hz, 1H), 5.02-4.93 (m, 1H), 3.78-3.69 (m, 1H), 3.55-3.34 (m, 3H), 2.47-2.37 (m, 1H), 2.32-2.22 (m, 1H). MS = 385 (MH)+.

Example 377. {5-Methoxy-2-[2-(pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{5-Methoxy-2-[2-(pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (107.0 mg, 0.2342 mmol) and 3-aminopyridine (25.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a pale yellow lyophilate (0.063 g, 41%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.15 (br s, 1H), 9.31 (s, 1H), 9.05 (br s, 1H), 8.92 (br s, 1H), 8.84 (s, 1H), 8.48-8.41 (m, 3H), 8.34 (d, J=5.0 Hz, 1H), 8.20 (d, J=6.3 Hz, 1H), 8.03 (s, 1H), 7.87 (d, J=5.3 Hz, 1H), 7.74-7.71 (m, 1H), 5.09-5.00 (m, 1H), 4.17 (s, 3H), 3.74-3.65 (m, 1H), 3.52-3.29 (m, 3H), 2.54-2.44 (m, 1H), 2.27-2.17 (m, 1H). MS = 415 (MH)+.

Example 378. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 3-aminopyridine (25.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis trifluoroacetic acid salt as a yellow lyophilate (0.123 g, 87%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.17 (br s, 1H), 9.33 (s, 1H), 9.02-8.88 (m, 3H), 8.49-8.42 (m, 3H), 8.34 (d, J=4.6 Hz, 1H), 8.03 (s, 1H), 7.87 (dd, J=5.2, 1.3 Hz, 1H), 7.74 (dd, J=8.3, 5.2 Hz, 1H), 4.11 (s, 3H), 3.92-3.86 (m, 4H), 3.37-3.30 (m, 4H). MS = 415 (MH)+.

Example 379. 2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinamide

2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Amino-isonicotinamide (36.0 mg, 0.262 mmol) in an analogous manner to Example

303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.004 g, 2%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.94 (s, 1H), 8.86 (br s, 2H), 8.69 (s, 1H), 8.46 (d, J=5.5 Hz, 1H), 8.44 (s, 1H), 8.41 (d, J=5.3 Hz, 1H), 8.19 (br s, 1H), 8.09 (br s, 1H), 7.95-7.91 (m, 1H), 7.71 (br s, 1H), 7.36-7.33 (m, 1H), 4.11 (s, 3H), 3.93-3.89 (m, 4H), 3.37-3.30 (m, 4H). MS = 458 (MH)+.

Example 380. 6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide

6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Amino-nicotinamide (36.0 mg, 0.262 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.047 g, 37%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.08 (br s, 2H), 8.94 (s, 1H), 8.83 (s, 1H), 8.72 (s, 1H), 8.50 (d, J=5.4 Hz, 1H), 8.45 (s, 1H), 8.26 (br s, 1H), 8.10-7.99 (m, 2H), 7.72 (br s, 1H), 7.47 (br s, 1H), 4.11 (s, 3H), 3.96-3.92 (m, 4H), 3.36-3.29 (m, 4H). MS = 458 (MH)+.

Example 382. (3-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(3-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (110.0 mg, 0.2407 mmol) and 3-Methoxy-4-morpholin-4-yl-phenylamine (55.0 mg, 0.264 mmol) [prepared as described in WO2008/051547] in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.147 g, 95%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.71 (br s, 1H), 9.12-8.95 (m, 2H), 8.91 (s, 1H), 8.43 (s, 1H), 8.25 (d, J=5.3 Hz, 1H), 7.99 (s, 1H), 7.72 (d, J=4.9 Hz, 1H), 7.44 (br s, 1H), 7.25 (d, J=7.5 Hz, 1H), 7.06 (br s, 1H), 4.11 (s, 3H), 3.92-3.86 (m, 4H), 3.84 (s, 3H), 3.82-3.76 (m, 4H), 3.35-3.29 (m, 4H), 3.17-3.00 (m, 4H). MS = 529 (MH)+.

Example 383. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0

mg, 0.2188 mmol) and 2-Methyl-4-morpholin-4-yl-phenylamine (50.0 mg, 0.260 mmol)[prepared as described in WO2008/051547] in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.125 g, 91%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.06 (br s, 1H), 9.07-8.95 (m, 2H), 8.92 (s, 1H), 8.46 (s, 1H), 8.01 (d, J=5.9 Hz, 1H), 7.74 (dd, J=6.3, 1.1 Hz, 1H), 7.27 (d, J=8.7 Hz, 1H), 7.00 (d, J=2.5 Hz, 1H), 6.92 (dd, J=8.8, 2.7 Hz, 1H), 4.11 (s, 3H), 3.89-3.84 (m, 4H), 3.79-3.75 (m, 4H), 3.34-3.27 (m, 4H), 3.20-3.16 (m, 4H), 2.20 (s, 3H). MS = 513 (MH)+.

Example 384. 5-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile

5-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 5-Amino-pyridine-2-carbonitrile (32.0 mg, 0.269 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.093 g, 76%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.24 (s, 1H), 8.95 (d, J=2.4 Hz, 1H), 8.91 (s, 1H), 8.88 (br s, 2H), 8.56 (dd, J=8.7, 2.6 Hz, 1H), 8.47 (d, J=5.4 Hz, 1H), 8.43 (s, 1H), 8.05 (s, 1H), 7.93 (d, J=8.6 Hz, 1H), 7.90 (dd, J=5.4, 1.4 Hz, 1H), 4.11 (s, 3H), 3.91-3.87 (m, 4H), 3.36-3.30 (m, 4H). MS = 440 (MH)+.

Example 385. {5-Methoxy-2-[2-(pyrimidin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine

{5-Methoxy-2-[2-(pyrimidin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (108.0 mg, 0.2364 mmol) and Pyrimidin-5-ylamine (25.0 mg, 0.263 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.029 g, 22%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.77 (s, 1H), 9.22-9.21 (m, 2H), 9.00-8.80 (m, 3H), 8.74 (s, 1H), 8.43-8.40 (m, 2H), 8.18 (d, J=6.3 Hz, 1H), 7.99 (s, 1H), 7.83 (dd, J=5.3, 1.4 Hz, 1H), 5.08-4.98 (m, 1H), 4.17 (s, 3H), 3.74-3.64 (m, 1H), 3.50-3.30 (m, 3H), 2.52-2.44 (m, 1H), 2.28-2.18 (m, 1H). MS = 416 (MH)+.

Example 386. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-5-yl-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-5-yl-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and Pyrimidin-5-ylamine (25.0 mg, 0.263 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.073 g, 62%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.79 (s, 1H), 9.22-9.21 (m, 2H), 8.98-8.95 (m, 3H), 8.74 (s, 1H), 8.43-8.40 (m, 2H), 7.99 (s, 1H), 7.82 (dd, J=5.3, 1.4 Hz, 1H), 4.11 (s, 3H), 3.92-3.86 (m, 4H), 3.37-3.29 (m, 4H). MS = 416 (MH)+.

Example 387. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (102.0 mg, 0.2232 mmol) and 2-Pyridinamine (25.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.056 g, 47%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 11.54 (br s, 1H), 9.05-8.90 (m, 3H), 8.53 (d, J=4.9 Hz, 1H), 8.50-8.45 (m, 2H), 8.39 (d, J=5.2 Hz, 1H), 8.11-8.00 (m, 2H), 7.54 (s, 1H), 7.21 (s, 1H), 4.12 (s, 3H), 3.94-3.89 (m, 4H), 3.37-3.30 (m, 4H). MS = 415 (MH)+.

Example 388. 2-[4-(5-Methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile

388a) 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.25 g, 0.86 mmol) and Morpholine (0.10 mL, 1.1 mmol) in an analogous manner to [B016]. Product isolated as a tan solid (0.269 g, 87%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.87 (s, 1H), 8.60 (dd, J=5.0, 0.9 Hz, 1H), 8.38 (s, 1H), 8.33-8.30 (m, 2H), 4.08 (s, 3H), 3.81-3.71 (m, 8H). MS = 358 (MH)+.

388b) 2-[4-(5-Methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2795 mmol) and 2-Amino-isonicotinonitrile (40.0 mg, 0.336 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.014 g, 9%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.63 (br s, 1H), 8.87 (s, 1H), 8.58

(s, 1H), 8.51 (d, J=5.0 Hz, 1H), 8.47 (d, J=5.4 Hz, 1H), 8.37 (s, 1H), 8.29 (s, 1H), 7.92 (d, J=5.4 Hz, 1H), 7.35 (d, J=4.9 Hz, 1H), 4.09 (s, 3H), 3.82-3.74 (m, 8H). MS = 441 (MH)+.

Example 389. 2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidine (110.0 mg, 0.3074 mmol) and 2-(3-Cyano-phenyl)-acetamide (54.0 mg, 0.337 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.082 g, 44%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.96 (s, 1H), 9.03 (s, 1H), 8.85 (s, 1H), 8.49 (dd, J=5.1, 0.6 Hz, 1H), 8.35 (s, 1H), 8.04 (dd, J=5.1, 1.5 Hz, 1H), 7.84-7.82 (m, 1H), 7.77-7.74 (m, 1H), 7.73-7.70 (m, 1H), 7.57 (t, J=7.8 Hz, 1H), 4.07 (s, 3H), 3.89 (s, 2H), 3.79-3.69 (m, 8H). MS = 482 (MH)+.

Example 390. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,5-trimethoxy-phenyl)-amine

4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]- (3,4,5-trimethoxy-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (106.0 mg, 0.2320 mmol) and 3,4,5-Trimethoxyaniline (48.0 mg, 0.262 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.074 g, 52%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.45 (br s, 1H), 8.98-8.84 (m, 3H), 8.42 (s, 1H), 8.30 (d, J=5.4 Hz, 1H), 7.94 (s, 1H), 7.70 (d, J=5.6 Hz, 1H), 7.13-7.10 (m, 2H), 4.10 (s, 3H), 3.90-3.85 (m, 4H), 3.79 (s, 6H), 3.64 (s, 3H), 3.36-3.29 (m, 4H). MS = 504 (MH)+.

Example 391. N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(4-trifluoromethyl-phenyl)-acetamide

391a) 2-(4-Trifluoromethyl-phenyl)-acetamide was prepared from (4-Trifluoromethyl-phenyl)-acetic acid (1.0 g, 4.9 mmol) in an analogous manner to Example 313a. Product isolated as a white solid (0.92 g, 92%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.66 (d, J=8.1 Hz, 2H), 7.54 (br s, 1H), 7.47 (d, J=8.0 Hz, 2H), 6.96 (br s, 1H), 3.49 (s, 2H). MS = 204 (MH)+.

391b) N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(4-trifluoromethyl-phenyl)-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0

mg, 0.2188 mmol) and 2-(4-Trifluoromethyl-phenyl)-acetamide (54.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.051 g, 36%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.99 (s, 1H), 9.08 (s, 1H), 8.91 (s, 1H), 8.84 (br s, 2H), 8.52 (dd, J=5.1, 0.5 Hz, 1H), 8.41 (s, 1H), 8.06 (dd, J=5.1, 1.4 Hz, 1H), 7.72 (d, J=8.1 Hz, 2H), 7.60 (d, J=8.0 Hz, 2H), 4.09 (s, 3H), 3.92 (s, 2H), 3.87-3.83 (m, 4H), 3.34-3.28 (m, 4H). MS = 524 (MH)+.

Example 392. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-phenyl-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-phenyl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Phenyl-pyridin-3-ylamine (45.0 mg, 0.264 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.086 g, 65%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.82 (s, 1H), 9.01 (d, J=2.3 Hz, 1H), 8.95-8.85 (m, 3H), 8.46-8.40 (m, 3H), 8.06-7.95 (m, 4H), 7.80 (dd, J=5.3, 1.3 Hz, 1H), 7.49 (t, J=7.4 Hz, 2H), 7.42-7.37 (m, 1H), 4.11 (s, 3H), 3.92-3.87 (m, 4H), 3.37-3.30 (m, 4H). MS = 491 (MH)+.

Example 393. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Methyl-pyridin-3-ylamine (29.0 mg, 0.268 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.068 g, 56%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.22 (s, 1H), 9.34 (s, 1H), 8.96 (br s, 2H), 8.91 (s, 1H), 8.46 (d, J=5.4 Hz, 1H), 8.43 (s, 1H), 8.38 (dd, J=8.8, 2.4 Hz, 1H), 8.02 (s, 1H), 7.88 (dd, J=5.3, 1.4 Hz, 1H), 7.73 (d, J=8.8 Hz, 1H), 4.11 (s, 3H), 3.91-3.87 (m, 4H), 3.36-3.30 (m, 4H), 2.61 (s, 3H). MS = 429 (MH)+.

Example 394. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg,

0.2188 mmol) and 5-Amino-2-methoxypyridine (33.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.091 g, 74%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.43 (s, 1H), 9.00-8.85 (m, 3H), 8.48 (d, J=2.8 Hz, 1H), 8.42 (s, 1H), 8.26 (d, J=5.4 Hz, 1H), 8.06 (dd, J=8.8, 2.7 Hz, 1H), 7.89 (s, 1H), 7.69 (dd, J=5.3, 1.1 Hz, 1H), 6.83 (d, J=8.8 Hz, 1H), 4.10 (s, 3H), 3.90-3.86 (m, 4H), 3.84 (s, 3H), 3.35-3.29 (m, 4H). MS = 445 (MH)+.

Example 395. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Trifluoromethyl-pyridin-3-ylamine (43.0 mg, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.084 g, 64%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.09 (s, 1H), 8.96 (d, J=2.5 Hz, 1H), 8.94-8.84 (m, 3H), 8.61 (dd, J=8.7, 2.3 Hz, 1H), 8.46-8.42 (m, 2H), 8.04 (s, 1H), 7.86 (dd, J=5.3, 1.3 Hz, 1H), 7.81 (d, J=8.9 Hz, 1H), 4.11 (s, 3H), 3.93-3.86 (m, 4H), 3.37-3.30 (m, 4H). MS = 483 (MH)+.

Example 396. N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-pyridin-3-yl-acetamide

N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-pyridin-3-yl-acetamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Pyridin-3-yl-acetamide (35.0 mg, 0.257 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.008 g, 6%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.99 (s, 1H), 9.09 (s, 1H), 8.95-8.75 (m, 3H), 8.64 (s, 1H), 8.56 (d, J=4.7 Hz, 1H), 8.51 (d, J=5.1 Hz, 1H), 8.40 (s, 1H), 8.15 (d, J=6.1 Hz, 1H), 8.07 (dd, J=5.2, 1.4 Hz, 1H), 7.93 (d, J=7.7 Hz, 1H), 7.54-7.48 (m, 1H), 4.98-4.90 (m, 1H), 4.15 (s, 3H), 3.49 (s, 2H), 3.70-3.60 (m, 1H), 3.48-3.28 (m, 3H), 2.53-2.43 (m, 1H), 2.25-2.15 (m, 1H). MS = 457 (MH)+.

Example 397. 2-{4-[5-Methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

397a) 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-

d]pyrimidin-4-ol (0.25 g, 0.86 mmol) and 1-Methylpiperazine (0.12 mL, 1.0 mmol) in an analogous manner to [B016]. Product isolated as tan needles (0.283 g, 88%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.85 (s, 1H), 8.60 (d, J=5.1 Hz, 1H), 8.37 (s, 1H), 8.33-8.29 (m, 2H), 4.07 (s, 3H), 3.75-3.70 (m, 4H), 2.52-2.48 (m, 4H), 2.24 (s, 3H). MS = 371, 373 (MH)+.

397b) 2-{4-[5-Methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2697 mmol) and 2-Amino-isonicotinonitrile (39.0 mg, 0.327 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.123 g, 80%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.46 (s, 1H), 9.83 (s, 1H), 8.94 (s, 1H), 8.64 (s, 1H), 8.51 (dd, J=5.0, 0.6 Hz, 1H), 8.49 (d, J=5.3 Hz, 1H), 8.44 (s, 1H), 8.35 (s, 1H), 7.93 (dd, J=5.3, 1.4 Hz, 1H), 7.33 (dd, J= 5.1, 1.4 Hz, 1H), 4.43 (d, J=13.4, 2H), 4.12 (s, 3H), 3.60 (d, J=11.8 Hz, 2H), 3.46 (t, J=12.9 Hz, 2H), 3.30-3.20 (m, 2H), 2.97-2.85 (m, 3H). MS = 454 (MH)+.

Example 398. 2-(3-Chloro-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(3-Chloro-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2697 mmol) and 2-(3-Chloro-phenyl)-acetamide (55.1 mg, 0.325 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate (0.050 g, 29%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.94 (s, 1H), 9.89 (br s, 1H), 9.09 (s, 1H), 8.92 (s, 1H), 8.52 (dd, J=5.1, 0.6 Hz, 1H), 8.42 (s, 1H), 8.07 (dd, J=5.2, 1.5 Hz, 1H), 7.47-7.75 (m, 1H), 7.41-7.32 (m, 3H), 4.37 (d, J=13.9 Hz, 2H), 4.11 (s, 3H), 3.81 (s, 2H), 3.59 (d, J=11.8 Hz, 2H), 3.41 (t, J=13.1 Hz, 2H), 3.29-3.17 (m, 2H), 2.89 (s, 3H). MS = 504, 506 (MH)+.

Example 399. N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-3-yl-acetamide

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-3-yl-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Pyridin-3-yl-acetamide (36.0 mg, 0.264 mmol), in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow

lyophilate (0.115 g, 91%). HNMR (400 MHz, d6-DMSO,δ, ppm): 11.03 (s, 1H), 9.07 (s, 1H), 8.92-8.83 (m, 3H), 8.71 (d, J=1.5 Hz, 1H), 8.64 (dd, J=5.1, 1.2 Hz, 1H), 8.52 (dd, J=5.1, 0.6 Hz, 1H), 8.41 (s, 1H), 8.11-8.05 (m, 2H), 7.68-7.63 (m, 1H), 4.09 (s, 3H), 3.96 (s, 2H), 3.87-3.82 (m, 4H), 3.34-3.28 (m, 4H). MS = 457 (MH)+.

Example 400. N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-4-yl-acetamide

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-4-yl-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Pyridin-4-yl-acetamide (35.0 mg, 0.257 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as an orange lyophilate resin (0.113 g, 90%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 11.06 (s, 1H), 9.07 (s, 1H), 8.90 (s, 1H), 8.86 (br s, 2H), 8.71 (s, 2H), 8.53 (dd, J=5.1, 0.6 Hz, 1H), 8.41 (s, 1H), 8.08 (dd. J=5.2, 1.5 Hz, 1H), 7.71 (br s, 2H), 4.09 (s, 3H), 4.03 (s, 2H), 3.87-3.83 (m, 4H), 3.34-3.28 (m, 4H). MS = 457 (MH)+.

Example 401. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methoxy-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methoxy-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-Methoxy-pyridin-2-ylamine (33.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.098 g, 79%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.00-8.90 (m, 3H), 8.55 (d, J=5.4 Hz, 1H), 8.45 (s, 1H), 8.31 (s, 1H), 8.24 (d, J=6.9 Hz, 1H), 8.12-8.08 (m, 1H), 6.92 (br s, 2H), 4.11 (s, 3H), 4.00 (s, 3H), 3.93-3.88 (m, 4H), 3.37-3.30 (m, 4H). MS = 445 (MH)+.

Example 402. 2-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

402a) 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.40 g, 1.4 mmol) and Piperidin-4-ol (0.17 g, 1.7 mmol) in an analogous manner to [B016]. Product isolated as an orange solid (0.317 g, 62%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.84 (s, 1H), 8.60 (dd, J=4.9, 0.7 Hz, 1H), 8.36 (s, 1H), 8.32-8.29 (m,

2H), 4.81 (d, J=4.1 Hz, 1H), 4.08 (s, 3H), 4.05-3.97 (m, 2H), 3.85-3.77 (m, 1H), 3.45-3.37 (m, 2H), 1.96-1.88 (m, 2H), 1.61-1.51 (m, 2H). MS = 372, 374 (MH)+.

402b) 2-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol (100.0 mg, 0.2689 mmol) and 2-Amino-isonicotinonitrile (39.0 mg, 0.327 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.082 g, 53%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.76 (br s, 1H), 8.84 (s, 1H), 8.58 (s, 1H), 8.52 (d, J=5.2 Hz, 1H), 8.47 (d, J=5.6 Hz, 1H), 8.36 (s, 1H), 8.23 (s, 1H), 7.93 (d, J=5.6 Hz, 1H), 7.37 (d, J=4.3 Hz, 1H), 4.09 (s, 3H), 4.08-4.00 (m, 2H), 3.87-3.80 (m, 1H), 3.50-3.40 (m, 2H), 1.97-1.89 (m, 2H), 1.64-1.54 (m, 2H). MS = 455 (MH)+.

Example 403. 2-(3-Cyano-phenyl)-N-{4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(3-Cyano-phenyl)-N-{4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol (100.0 mg, 0.2689 mmol) and 2-(3-Cyano-phenyl)-acetamide (52.0 mg, 0.325 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.072 g, 43%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.95 (s, 1H), 9.03 (s, 1H), 8.82 (s, 1H), 8.49 (dd, J=5.2, 0.6 Hz, 1H), 8.34 (s, 1H), 8.03 (dd, J=5.2, 1.6 Hz, 1H), 7.84-7.82 (m , 1H), 7.77-7.74 (m, 1H), 7.73-7.70 (m, 1H), 7.57 (t, J=7.8 Hz, 1H), 4.07 (s, 3H), 4.03-3.95 (m, 2H), 3.89 (s, 2H), 3.85-3.77 (m, 1H), 3.45-3.36 (m, 2H), 1.94-1.86 (m, 2H), 1.60-1.50 (m, 2H). MS = 496 (MH)+.

Example 404. 2-(3-Cyano-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide

2-(3-Cyano-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2697 mmol) and 2-(3-Cyano-phenyl)-acetamide (52.0 mg, 0.325 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.044 g, 26%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.97 (s, 1H), 9.79 (br s, 1H), 9.08 (s, 1H), 8.92 (s, 1H), 8.52 (dd, J=5.1, 0.6 Hz, 1H), 8.42 (s, 1H), 8.08 (dd, J=5.1, 1.5 Hz, 1H), 7.84-7.82 (m, 1H), 7.78-7.75 (m, 1H), 7.73-7.70 (m, 1H), 7.58 (t,

J=7.8 Hz, 1H), 4.37 (d, J=13.9 Hz, 2H), 4.11 (s, 3H), 3.89 (s, 2H), 3.59 (d, J=11.0 Hz, 2H), 3.45-3.35 (m, 2H), 3.28-3.18 (m, 2H), 2.91-2.87 (m, 3H). MS = 495 (MH)+.

Example 405. (6-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(6-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Chloro-pyridin-3-ylamine (34.0 mg, 0.264 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.010 g, 9%). MP = 206-208°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.71 (s, 1H), 8.81 (s, 1H), 8.74 (d, J=2.8 Hz, 1H), 8.37-8.32 (m, 3H), 7.92 (s, 1H), 7.75 (dd, J=5.4, 1.1 Hz, 1H), 7.42 (d, J=8.7 Hz, 1H), 4.07 (s, 3H), 3.68-3.63 (m, 4H), 2.90-2.85 (m, 4H). MS = 449, 451 (MH)+.

Example 406. (R)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide

406a) (R)-2-Phenyl-propionamide was prepared from (R)-2-Phenyl-propionic acid (0.941 g, 6.27 mmol) in an analogous manner to Example 313a. Product isolated as a white solid (0.457 g, 48%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.35 (s, 1H), 7.33-7.18 (m, 5H), 6.79 (s, 1H), 3.55 (q, J=7.0 Hz, 1H), 1.30 (d, J=7.0 Hz, 3H). MS = 150 (MH)+.

406b) (R)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and (R)-2-Phenyl-propionamide (45.0 mg, 0.302 mmol) in an analogous manner to Example 303c and Example 4501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.100 g, 78%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.79 (s, 1H), 9.12 (s, 1H), 8.97-8.77 (m, 3H), 8.47 (dd, J=5.3, 0.6 Hz, 1H), 8.41 (s, 1H), 8.15 (d, J=6.0 Hz, 1H), 8.03 (dd, J=5.2, 1.5 Hz, 1H), 7.47-7.43 (m, 2H), 7.37-7.32 (m, 2H), 7.27-7.22 (m, 1H), 5.00-4.90 (m, 1H), 4.16 (s, 3H), 4.09 (q, J=6.9 Hz, 1H), 3.72-3.62 (m, 1H), 3.50-3.30 (m, 3H), 2.53-2.47 (m, 1H), 2.27-2.17 (m, 1H), 1.46 (d, J=7.0, 3H). MS = 470 (MH)+.

Example 407. (S)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide

407a) (S)-2-Phenyl-propionamide was prepared from (S)-2-Phenyl-propionic acid (1.25 g, 8.32 mmol) in an analogous manner to Example 313a. Product isolated as a white solid.

^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.35 (s, 1H), 7.33-7.18 (m, 5H), 6.79 (s, 1H), 3.55 (q, J=7.1 Hz, 1H), 1.30 (d, J=7.1 Hz, 3H).

407b) (S)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide was prepared from (R)-3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and (S)-2-Phenyl-propionamide (45.0 mg, 0.302 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.100 g, 78%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.79 (s, 1H), 9.12 (s, 1H), 8.99-8.79 (m, 3H), 8.47 (dd, J=5.2, 0.6 Hz, 1H), 8.41 (s, 1H), 8.15 (d, J=5.9 Hz, 1H), 8.04 (dd, J=5.2, 1.5 Hz, 1H), 7.47-7.43 (m, 2H), 7.37-7.32 (m, 2H), 7.27-7.22 (m, 1H), 5.00-4.90 (m, 1H), 4.16 (s, 3H), 4.09 (q, J=6.8 Hz, 1H), 3.72-3.62 (m, 1H), 3.50-3.30 (m, 3H), 2.53-2.47 (m, 1H), 2.27-2.17 (m, 1H), 1.46 (d, J=7.0 Hz, 3H). MS = 470 (MH)+.

Example 408. (R)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide

(R)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and (R)-2-Phenyl-propionamide (45.0 mg, 0.302 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.115 g, 89%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.82 (s, 1H), 9.11 (s, 1H), 8.93 (s, 1H), 8.88 (br s, 2H), 8.48 (dd, J=5.1, 0.7 Hz, 1H), 8.42 (s, 1H), 8.04 (dd, J=5.1, 1.4 Hz, 1H), 7.46-7.43 (m, 2H), 7.37-7.33 (m, 2H), 7.27-7.22 (m, 1H), 4.12-4.05 (m, 4H), 3.90-3.86 (m, 4H), 3.36-3.29 (m, 4H), 1.45 (d, J=7.0 Hz, 3H). MS = 470 (MH)+.

Example 409. (S)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide

(S)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and (S)-2-Phenyl-propionamide (45.0 mg, 0.302 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.104 g, 81%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.81 (s, 1H), 9.11 (s, 1H), 8.93 (s, 1H), 8.88 (br s, 2H), 8.48 (dd, J=5.1, 0.5 Hz, 1H), 8.42 (s,

1H), 8.04 (d, J=5.1, 1.4 Hz, 1H), 7.47-7.41 (m, 2H), 7.37-7.32 (m, 2H), 7.27-7.22 (m, 1H), 4.12-4.05 (m, 4H), 3.89-3.84 (m, 4H), 3.36-3.29 (m, 4H), 1.45 (d, J=7.0 Hz, 3H). MS = 470 (MH)+.

Example 410. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (90.0 mg, 0.197 mmol) and 3-Methyl-pyridin-2-ylamine (30.0 mg, 0.277 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow foam (0.062 g, 73%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.97 (s, 1H), 8.81 (s, 1H), 8.52 (s, 1H), 8.35 (dd, J=5.2, 0.5 Hz, 1H), 8.32 (s, 1H), 8.15 (dd, J=4.7, 1.4 Hz, 1H), 7.80 (dd, J=5.2, 1.4 Hz, 1H), 7.59-7.55 (m, 1H), 6.94 (dd, J=7.3, 5.0 Hz, 1H), 4.07 (s, 3H), 3.68-3.64 (m, 4H), 2.90-2.85 (m, 4H), 2.32 (s, 3H). MS = 429 (MH)+.

Example 411. (3-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(3-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (90.0 mg, 0.197 mmol) and 3-Fluoro-pyridin-2-ylamine (31.0 mg, 0.276 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.110 g, 84%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.34 (br s, 1H), 8.97-8.79 (m, 4H), 8.48-8.44 (m, 2H), 8.27 (d, J=4.8 Hz, 1H), 8.04 (dd, J=5.6, 1.2 Hz, 1H), 7.86-7.80 (m, 1H), 7.21-7.16 (m, 1H), 4.11 (s, 3H), 3.94-3.88 (m, 4H), 3.37-3.30 (m, 4H). MS = 433 (MH)+.

Example 412. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-piperazin-1-ylpyridin-3-yl)-amine

4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-piperazin-1-yl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (106 mg, 0.232 mmol) and 4-(5-Amino-pyridin-2-yl)-piperazine-1-carboxylic acid tert-butyl ester (73.0 mg, 0.262 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a brown lyophilate (0.107 g, 63%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.28 (s, 1H), 8.95-8.85 (m, 3H), 8.73 (br s, 2H), 8.51 (d,

J=2.8 Hz, 1H), 8.42 (s, 1H), 8.25 (d, J=5.4 Hz, 1H), 8.03 (dd, J=9.1, 2.8 Hz, 1H), 7.59 (s, 1H), 7.66 (dd, J=5.4, 1.2 Hz, 1H), 6.97 (d, J=9.2 Hz, 1H), 4.10 (s, 3H), 3.90-3.85 (m, 4H), 3.65-3.60 (m, 4H), 3.36-3.29 (m, 4H), 3.25-3.19 (m, 4H). MS = 499 (MH)+.

Example 413. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-methyl-4-(4-methyl-piperazin-1-yl)-phenyl]-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-methyl-4-(4-methyl-piperazin-1-yl)-phenyl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (102.0 mg, 0.2232 mmol) and 2-Methyl-4-(4-methyl-piperazin-1-yl)-phenylamine (54.0 mg, 0.263 mmol)[prepared as described in WO2008/051547] in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a brown lyophilate (0.128 g, 75%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.00-9.30 (m, 2H), 9.07 (br s, 2H), 8.90 (s, 1H), 8.44 (s, 1H), 8.06 (d, J=5.9 Hz, 1H), 7.95 (s, 1H), 7.70 (d, J=5.7 Hz, 1H), 7.34 (d, J=8.7 Hz, 1H), 7.02 (d, J=2.3 Hz, 1H), 6.94 (dd, J=8.7, 2.4 Hz, 1H), 4.11 (s, 3H), 3.95-3.80 (m, 6H), 3.55 (d, J=11.5 Hz, 2H), 3.35-3.28 (m, 4H), 3.23-3.12 (m, 2H), 2.99 (t, J=13.8 Hz, 2H), 2.89 (s, 3H), 2.21 (s, 3H). MS = 526 (MH)+.

Example 414. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-piperidin-4-yl-1H-pyrazol-4-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-piperidin-4-yl-1H-pyrazol-4-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-(4-Amino-pyrazol-1-yl)-piperidine-1-carboxylic acid tert-butyl ester (70.0 mg, 0.263 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a brown lyophilate (0.123 g, 78%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.40 (br s, 1H), 9.00 (br s, 2H), 8.90 (s, 1H), 8.75-8.65 (m, 1H), 8.50-8.37 (m, 2H), 8.25 (d, J=5.6 Hz, 1H), 8.10 (s, 1H), 7.84 (s, 1H), 7.62 (d, J=5.5 Hz, 1H), 7.55 (s, 1H), 4.54-4.44 (m, 1H), 4.10 (s, 3H), 3.90-3.85 (m, 4H), 3.47-3.40 (m, 2H), 3.36-3.30 (m, 4H), 3.15-3.02 (m, 2H), 2.23-2.06 (m, 4H). MS = 487 (MH)+.

Example 415. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Methyl-pyridin-2-ylamine (30.0 mg, 0.277 mmol) in an analogous

manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.095 g, 80%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.96-8.87 (m, 3H), 8.56 (br s, 1H), 8.53 (d, J=5.6 Hz, 1H), 8.45 (s, 1H), 8.05-8.00 (m, 1H), 7.85 (br s, 1H), 7.45-7.39 (m, 1H), 7.04-6.99 (m, 1H), 4.11 (s, 3H), 3.93-3.88 (m, 4H), 3.37-3.30 (m, 4H). MS = 429 (MH)+.

Example 416. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (104.0 mg, 0.2276 mmol) and 5-Methyl-pyridin-3-ylamine (30.0 mg, 0.277 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.123 g, 99%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.13 (br s, 1H), 9.17 (br s, 1H), 8.95-8.85 (m, 3H), 8.46 (d, J=5.4 Hz, 1H), 8.43 (s, 1H), 8.30 (s, 1H), 8.24 (s, 1H), 8.02 (s, 1H), 7.87 (dd, J=5.4, 1.3 Hz, 1H), 4.11 (s, 3H), 3.91-3.86 (m, 4H), 3.36-3.30 (m, 4H), 2.43 (s, 3H). MS = 429 (MH)+.

Example 417. (5-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(5-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 5-Chloro-pyridin-3-ylamine (35.0 mg, 0.272 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a pale yellow lyophilate (0.112 g, 90%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.88 (s, 1H), 8.91 (s, 1H), 8.84 (br s, 2H), 8.69 (d, J=2.3 Hz, 1H), 8.64 (t, J=2.2 Hz, 1H), 8.45-8.42 (m, 2H), 8.13 (d, J=2.2 Hz, 1H), 7.99 (s, 1H), 7.82 (dd, J=5.3, 1.3 Hz, 1H), 4.11 (s, 3H), 3.91-3.86 (m, 4H), 3.36-3.30 (m, 4H). MS = 406, 408 (MH)+.

Example 418. (2-Fluoro-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

418a) 2-Fluoro-4-morpholin-4-yl-phenylamine was prepared from 4-(3-Fluoro-4-nitro-phenyl)-morpholine (0.52 g, 2.3 mmol) [prepared as described in Quan, M. L.; et. al. J. Med. Chem. 2005, 48, 1729-1744.] in an analogous manner to Example 10b. Product isolated as a pale pink solid (0.40 g, 88%). ^{1}HNMR 400 MHz, d6-DMSO, δ, ppm): 6.71-

6.63 (m, 2H), 6.53 (dd, J=8.5, 2.3 Hz, 1H), 4.56 (br s, 2H), 3.71-3.67 (m, 4H), 2.93-2.89 (m, 4H). MS =197 (MH)+.

418b) (2-Fluoro-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (105.0 mg, 0.2298 mmol) and 2-Fluoro-4-morpholin-4-yl-phenylamine (52.0 mg, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as an orange lyophilate (0.120 g, 70%). ^{1}HNMR (400 MHz,d6-DMSO,δ, ppm): 9.27 (br s, 1H), 8.96-8.89 (m, 3H), 8.43 (s, 1H), 8.16 (d, J=5.7 Hz, 1H), 7.94 (s, 1H), 7.70 (dd, J=5.6, 1.1 Hz, 1H), 7.61 (t, J=9.2 Hz, 1H), 6.93 (dd, J=14.1, 2.5 Hz, 1H), 6.82 (dd, J=8.9, 2.3 Hz, 1H), 4.10 (s, 3H), 3.90-3.85 (m, 4H), 3.77-3.73 (m, 4H), 3.34-3.28 (m, 4H), 3.17-3.08 (m, 4H). MS = 517 (MH)+.

Example 419. 3-Fluoro-4-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile

3-Fluoro-4-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 4-Amino-3-fluoro-benzonitrile (36.0 mg, 0.264 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.019 g, 19%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.58 (d, J=2.5 Hz, 1H), 8.91 (s, 1H), 8.85-8.70 (m, 2H), 8.45 (m, 2H), 8.30 (s, 1H), 7.89 (dd, J=5.3, 1.3 Hz, 1H), 7.83 (dd, J=11.7, 1.9 Hz, 1H), 7.66-7.62 (m, 1H), 4.10 (s, 3H), 3.91-3.87 (m, 4H), 3.33-3.30 (m, 4H). MS = 457 (MH)+.

Example 420. 4-Fluoro-3-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile

420a) A 100 mL round bottom flask equipped with a large magnetic stir bar, reflux condenser and nitrogen inlet adapter was charged with 4-Fluoro-3-nitro-benzonitrile (1.0 g, 6.0 mmol), Ammonium chloride (1.6 g, 30 mmol), Ethanol (20 mL, 300 mmol) and Water (10 mL, 600 mmol). To the suspension was added powdered Iron (1.1 g, 20 mmol). The suspension was stirred vigorously to allow iron to disperse into the suspension without clinging to the stir bar. The mixture was kept under an atmosphere of Nitrogen. An induction period (~20 minutes) was observed before the reaction began to darken to a rusty brown color and maintain a mild exotherm from 23°C to 26°C over the course of three hours. After 3 hours, the reaction was complete by HPLC. The reaction was filtered

through a plug of diatomaceous earth. The filter pad was rinsed with methanol (~100 mL). The filtrate was evaporated to dryness. The solid was triturated with dichloromethane (~100 mL) and filtered. The filtrate was evaporated. 3-Amino-4-fluoro-benzonitrile was isolated as a brown solid (0.78 g, 95%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.19 (dd, J=11.5, 8.3 Hz, 1H), 7.09 (dd, J=8.3, 2.1 Hz, 1H), 6.96 (ddd, J=8.3, 4.3, 2.1 Hz, 1H), 5.69 (br s, 2H). MS = 137 (MH)+.

420b) 4-Fluoro-3-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 3-Amino-4-fluoro-benzonitrile (36.0 mg, 0.264 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.096g). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.41 (d, J=2.0 Hz, 1H), 8.99-8.85 (m, 1H), 8.93-8.84 (m, 3H), 8.44-8.41 (m, 2H), 8.22 (s, 1H), 7.84 (dd, J=5.3, 1.4 Hz, 1H), 7.53-7.46 (m, 2H), 4.11 (s, 3H), 3.92-3.87 (m, 4H), 3.36-3.30 (m, 4H). MS = 457 (MH)+.

Example 421. (2,6-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2,6-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,6-Difluoro-phenylamine (30.0 µL, 0.279 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.132 g, 88%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.91-8.80 (m, 4H), 8.41 (s, 1H), 8.18 (d, J=5.6 Hz, 1H), 7.82 (s, 1H), 7.69-7.66 (m, 1H), 7.33-7.25 (m, 1H), 7.21-7.12 (m, 2H), 4.10 (s, 3H), 3.89-3.84 (m, 4H), 3.35-3.27 (m, 4H). MS = 450 (MH)+.

Example 422. (2-Fluoro-6-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2-Fluoro-6-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-Fluoro-6-methyl-phenylamine (33.0 mg, 0.264 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.099 g, 67%). ^{1}HNMR (400 MHz, d6-

DMSO,δ, ppm): 8.98-8.83 (m, 4H), 8.42 (s, 1H), 8.14 (d, J=5.5 Hz, 1H), 7.75 (br s, 1H), 7.65 (d, J=5.3 Hz, 1H), 7.26-7.10 (m, 3H), 4.10 (s, 3H), 3.88-3.82 (m, 4H), 3.36-3.27 (m, 4H), 2.25 (s, 3H). MS = 446 (MH)+.

Example 423. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-2-yl-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-2-yl-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2-amino-pyrimidine (25.0 mg, 0.263 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.009 g, 10%). MP = 200-203°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.94 (s, 1H), 9.31 (s, 1H), 8.39 (s, 1H), 8.59 (d, J=4.8 Hz, 2H), 8.44-8.41 (m, 1H), 8.33 (s, 1H), 7.90 (dd, J=5.2, 1.5 Hz, 1H), 7.00 (t, J=4.8 Hz, 1H), 4.07 (s, 3H), 3.71-3.66 (m, 4H), 2.92-2.87 (m, 4H). MS = 416 (MH)+.

Example 424. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-pyridin-3-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (108.0 mg, 0.2364 mmol) and 5-Methoxy-pyridin-3-ylamine (33.0 mg, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.104 g, 99%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.84 (s, 1H), 8.91 (s, 1H), 8.85 (br s, 2H), 8.62 (s, 1H), 8.44-8.41 (m, 2H), 8.10 (t, J=2.2 Hz, 1H), 7.99 (s, 2H), 7.81 (d, J=5.3 Hz, 1H), 4.11 (s, 3H), 3.91-3.86 (m, 7H), 3.36-3.30 (m, 4H). MS = 445 (MH)+.

Example 425. (S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol

425a) (S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1000.0 mg, 3.4639 mmol) and (S)-Piperidin-3-ol; hydrochloride (570.0 mg, 4.142 mmol) in an analogous manner to [B016]. Product isolated as a yellow foam (0.747 g, 58%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.83 (s, 1H), 8.60 (dd, J=5.0, 0.6 Hz, 1H), 8.35 (s, 1H), 8.32-8.29 (m, 2H), 4.88 (d, J=3.9 Hz, 1H), 4.14-4.05 (m, 4H), 3.95-3.89 (m, 1H),

3.69-3.61 (m, 1H), 3.48-3.38 (m, 1H), 3.09 (dd, J=12.4, 8.3 Hz, 1H), 1.96-1.84 (m, 2H), 1.62-1.40 (m, 2H). MS = 372, 374 (MH)+.

425b) (S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol was prepared from (S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol (101.0 mg, 0.2716 mmol) and Aniline (30.0 µL, 0.329 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.102 g, 69%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.60 (br s, 1H), 8.81 (s, 1H), 8.35 (s, 1H), 8.27 (d, J=5.6 Hz, 1H), 7.94 (s, 1H), 7.72-7.68 (m, 3H), 7.33 (t, J=7.7 Hz, 2H), 6.99 (t, J=6.8 Hz, 1H), 4.11-4.04 (m, 5H), 3.97-3.90 (m, 1H), 3.70-3.62 (m, 1H), 3.49-3.40 (m, 1H), 3.11 (dd, J=12.8, 8.3 Hz, 1H), 1.98-1.85 (m, 2H), 1.65-1.43 (m, 2H). MS = 429 (MH)+.

Example 426. 2-{4-[4-((S)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

2-{4-[4-((S)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile was prepared from (S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol (109.0 mg, 0.2932 mmol) and 2-Amino-isonicotinonitrile (39.0 mg, 0.327 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.121 g, 72%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.60 (br s, 1H), 8.83 (s, 1H), 8.61 (s, 1H), 8.52 (d, J=5.2 Hz, 1H), 8.46 (d, J=5.4 Hz, 1H), 8.35 (s, 1H), 8.26 (s, 1H), 7.91 (d, J=5.1 Hz, 1H), 7.34 (d, J=4.9 Hz, 1H), 4.15-4.05 (m, 5H), 4.00-3.92 (m, 1H), 3.70-3.62 (m, 1H), 3.52-3.40 (m, 1H), 3.11 (dd, J=12.7, 8.3 Hz, 1H), 1.98-1.87 (m, 2H), 1.67-1.43 (m, 2H). MS = 455 (MH)+.

Example 427. 1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol

1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol (104.0 mg, 0.2797 mmol) and Aniline (30.0 µL, 0.329 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.093 g, 61%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.66 (br s, 1H), 8.82 (s, 1H), 8.36 (s, 1H), 8.25 (d, J=5.6 Hz, 1H), 7.96 (s, 1H), 7.72-7.67 (m, 3H), 7.34 (t, J=7.8 Hz, 2H), 7.02 (t, J=7.2 Hz, 1H), 4.08 (s, 3H), 4.05-3.97 (m, 2H), 3.87-3.79 (m, 1H), 3.47-3.39 (m, 2H), 1.96-1.88 (m, 2H), 1.63-1.52 (m, 2H). MS = 429 (MH)+.

Example 428. (R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol

428a) (R)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1000.0 mg, 3.4639 mmol) and (R)-Piperidin-3-ol; hydrochloride (570.0 mg, 4.142 mmol) in an analogous manner to [B016]. Product isolated as a tan solid (0.561 g, 44%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.83 (s, 1H), 8.60 (dd, J=5.0, 0.5 Hz, 1H), 8.35 (s, 1H), 8.32-8.29 (m, 2H), 4.88 (d, J=3.9 Hz, 1H), 4.15-4.05 (m, 4H), 3.95-3.88 (m, 1H), 3.70-3.60 (m, 1H), 3.47-3.37 (m, 1H), 3.09 (dd, J=12.7, 8.3 Hz, 1H), 1.96-1.84 (m, 2H), 1.60-1.40 (m, 2H). MS = 372, 374 (MH)+.

Example 429. 2-{4-[4-((R)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

2-{4-[4-((R)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile was prepared from (R)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol (105.0 mg, 0.2824 mmol) and 2-Amino-isonicotinonitrile (39.0 mg, 0.327 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.013 g, 8%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.60 (br s, 1H), 8.83 (s, 1H), 8.61 (s, 1H), 8.52 (d, J=5.1 Hz, 1H), 8.46 (d, J=5.7 Hz, 1H), 8.35 (s, 1H), 8.26 (s, 1H), 7.91 (d, J=5.4 Hz, 1H), 7.34 (d, J=5.3 Hz, 1H), 4.14-4.04 (m, 4H), 4.00-3.92 (m, 1H), 3.70-3.62 (m, 1H), 3.51-3.41 (m, 1H), 3.12 (dd, J=12.9, 8.2 Hz, 1H), 1.98-1.88 (m, 2H), 1.65-1.43 (m, 2H). MS= 455 (MH)+.

Example 430. [5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine

430a) (S)-2-{[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-methyl}-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1000.0 mg, 3.4639 mmol) and (S)-2-Aminomethyl-pyrrolidine-1-carboxylic acid tert-butyl ester (840.0 mg, 4.194 mmol) in an analogous manner to [B016]. Product isolated as a yellow foam (0.817 g, 50%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.87-8.25 (m, 6H), 4.30-4.22 (m, 1H), 4.14 (s, 3H), 4.01-3.91 (m, 1H), 3.72-3.50 (m, 1H), 3.37-3.27 (m, 1H), 2.03-1.78 (m, 5H), 1.45-1.10 (m, 9H). MS = 471, 473 (MH)+.

430b) [5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine was prepared from (S)-2-{[2-(2-Chloro-pyridin-4-yl)-5-

methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-methyl}-pyrrolidine-1-carboxylic acid tert-butyl ester (108.0 mg, 0.2293 mmol) and Aniline (25.0 µL, 0.274 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.109 g, 87%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.42 (br s, 1H), 8.97 (br s, 1H), 8.82 (s, 1H), 8.64 (t, J=5.7 Hz, 1H), 8.54 (br s, 1H), 8.40 (s, 1H), 8.31 (d, J=5.4 Hz, 1H), 7.94 (s, 1H), 7.75-7.70 (m, 3H), 7.31 (t, J=7.7 Hz, 2H), 6.95 (t, J=7.4 Hz, 1H), 4.15 (s, 3H), 4.12-3.85 (m, 3H), 3.34-3.14 (m, 2H), 2.20-1.74 (m, 4H). MS = 428 (MH)+.

Example 431. [5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-1-pyrrolidin-2-ylmethyl-amine

431a) (R)-2-{[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-methyl}-pyrrolidine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1000.0 mg, 3.4639 mmol) and (R)-2-Aminomethyl-pyrrolidine-1-carboxylic acid tert-butyl ester (840.0 mg, 4.194 mmol) in an analogous manner to [B016]. Product isolated as a yellow foam (0.869 g, 53%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.86-8.25 (m, 6H), 4.31-4.21 (m, 1H), 4.14 (s, 3H), 4.00-3.90 (m, 1H), 3.72-3.50 (m, 1H), 3.36-3.28 (m, 1H), 2.02-1.78 (m, 5H), 1.45-1.10 (m, 9H). LC/MS = 471, 473 (MH)+.

431b) [5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-1-pyrrolidin-2-ylmethyl-amine was prepared from (R)-2-{[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-methyl}-pyrrolidine-1-carboxylic acid tert-butyl ester (105.0 mg, 0.2230 mmol) and Aniline (25.0 µL, 0.274 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.117 g, 97%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.42 (br s, 1H), 8.97 (br s, 1H), 8.82 (s, 1H), 8.64 (t, J=5.9 Hz, 1H), 8.53 (br s, 1H), 8.40 (s, 1H), 8.31 (d, J=5.4 Hz, 1H), 7.94 (s, 1H), 7.75-7.70 (m, 3H), 7.31 (t, J=7.5 Hz, 2H), 6.95 (t, J=7.4 Hz, 1H), 4.15 (s, 3H), 4.12-3.85 (m, 3H), 3.34-3.15 (m, 2H), 2.20-1.74 (m, 4H). MS = 428 (MH)+.

Example 432. 2-{4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol

432a) 2-{4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1000.0 mg, 3.4639 mmol) and 2-Piperazin-1-yl-ethanol (550.0 mg, 4.225 mmol) in an analogous manner to Example 303c and Example 1501c. Product

isolated as a yellow solid (0.414 g, 30%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.84 (s, 1H), 8.60 (dd, J=5.1, 0.7 Hz, 1H), 8.36 (s, 1H), 8.32-8.29 (m, 2H), 4.46 (t, J=5.4 Hz, 1H), 4.07 (s, 3H), 3.75-3.70 (m, 4H), 3.58-3.52 (m, 2H), 2.63-2.58 (m, 4H), 2.46 (t, J=6.2 Hz, 2H). LC/MS = 401, 403 (MH)+.

Example 433. {1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol

433a) {1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1000.0 mg, 3.4639 mmol) and Azetidin-3-yl-methanol; hydrochloride (550.0 mg, 4.450 mmol) in an analogous manner to [B016]. Product isolated as a tan solid (0.925 g, 75%). ^{1}HNMR (400 MHz,d6-DMSO,δ, ppm): 8.80 (s, 1H), 8.59 (dd, J=4.8, 1.1 Hz, 1H), 8.33-8.29 (m, 3H), 4.83 (t. J=5.5 Hz, 1H), 4.60-4.53 (m, 1H), 4.41-4.34 (m, 1H), 4.27-4.21 (m, 1H), 4.16-4.10 (m, 1H), 4.06 (s, 3H), 3.59 (t, J=5.7 Hz, 2H), 2.85-2.75 (m, 1H). MS = 358, 360 (MH)+.

433b) {1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol was prepared from {1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol (114.0 mg, 0.3186 mmol) and Aniline (31.0 µL, 0.340 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.117 g, 69%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.65 (br s, 1H), 8.79 (s, 1H), 8.33 (s, 1H), 8.25 (d, J=5.5 Hz, 1H), 7.97 (s, 1H), 7.72-7.67 (m, 3H), 7.34 (t, J=7.8 Hz, 2H), 7.01 (t, J=7.3 Hz, 1H), 4.61-4.11 (m, 4H), 4.07 (s, 3H), 3.60 (d, J=6.2 Hz, 2H), 2.87-2.76 (m, 1H). MS = 415 (MH)+.

Example 434. {(R)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol

434a) (R)-4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-2-hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.00 g, 3.46 mmol) and (R)-2-Hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (0.90 g, 4.2 mmol) in an analogous manner to [B016]. Product isolated as an off-white solid (1.23 g, 72%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.86 (s, 1H), 8.60 (d, J=5.4 Hz, 1H), 8.38 (s, 1H), 8.36-8.32 (m, 2H), 4.78 (t, J=5.2 Hz, 1H), 4.48 (d, J=12.7 Hz, 1H), 4.17-4.11 (m, 1H), 4.09 (s, 3H), 4.06-3.99 (m, 1H), 3.88-3.80 (m, 1H), 3.47-3.35 (m, 3H), 3.29-3.21 (m, 2H), 1.42 (s, 9H). LC/MS = 487, 489 (MH)+.

434b) {(R)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol was prepared from (R)-4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-2-hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (104.0 mg, 0.2136 mmol) and Aniline (23.0 µL, 0.252 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow foam (0.033 g, 34%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (s, 1H), 8.81 (s, 1H), 8.33 (s, 1H), 8.30 (d, J=5.3 Hz, 1H), 7.89 (s, 1H), 7.77-7.73 (m, 2H), 7.66 (dd, J=5.3, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.71 (t, J=5.5 Hz, 1H), 4.24-4.15 (m, 2H), 4.07 (s, 3H), 3.44-3.36 (m, 2H), 3.16-3.02 (m, 2H), 2.88-2.78 (m, 3H). MS = 444 (MH)+.

Example 435. (R)-7-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one

(R)-7-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one was a byproduct from Example 434. Product isolated as the free base as a yellow foam (0.023 g, 23%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (s, 1H), 8.87 (s, 1H), 8.38 (s, 1H), 8.32 (d, J=5.2 Hz, 1H), 7.91 (s, 1H), 7.77-7.74 (m, 2H), 7.69 (dd, J=5.3, 1.4 Hz, 1H), 7.31-7.26 (m, 2H), 6.93-6.88 (m, 1H), 4.50-4.39 (m, 2H), 4.29 (d, J=13.1 Hz, 1H), 4.12-4.03 (m, 6H), 3.77 (dd, J=13.2, 2.1 Hz, 1H), 3.17-3.06 (m, 2H). MS = 470 (MH)+.

Example 436. (±)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

436a) To a solution of 3,6-Dihydro-2H-pyridine-1-carboxylic acid benzyl ester (1.16 g, 5.34 mmol) [prepared as described in Solares, F. L.; et. al. *Tetrahedron* 2006, 62, 3284-3291]in Acetone (4 mL,) and Water (4 mL,) was added N-Methylmorpholine N-oxide (0.88 g, 7.5 mmol) followed by 2.5 wt% (w/v) OsO4 in t-BuOH(2.5:97.5, Osmium tetraoxide:tert-Butyl alcohol, 0.8 mL, 0.06 mmol). The mixture was stirred at room temperature for 1 hour. Reaction was complete by LC/MS. Saturated aqueous sodium thiosulfate (50 mL) was added and mixture was stirred for 5 minutes then extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over sodium sulfate, filtered and evaporated to a red-brown oil. The recovered oil was purified via chromatography using an ISCO apparatus (silica gel column (24 g) and 2:1 Ethyl Acetate:Hexane). (±)-cis-3,4-Dihydroxy-piperidine-1-carboxylic acid benzyl ester was isolated as a pale yellow oil(1.13 g, 84%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 7.43-7.27 (m, 5H), 5.05 (s, 2H), 4.66 (d, J=4.1 Hz, 1H), 4.55 (d, J=3.7 Hz, 1H), 3.75-3.64 (m, 1H), 3.51-3.18 (m, 5H), 1.69-1.60 (m, 1H), 1.52-1.43 (m, 1H). MS = 274 (M+Na)+.

436b) A Paar bottle (500 mL) was charged with 10% Palladium on Carbon (50% Wet)(5:45:50, Palladium:carbon black:Water, 1.0 g, 0.47 mmol) followed by a solution of (±)-cis-3,4-Dihydroxy-piperidine-1-carboxylic acid benzyl ester (1.13 g, 4.50 mmol) in 2:1 Ethyl Acetate:Methanol(50 mL). The reaction mixture was degassed and charged with Hydrogen (50 psi). The mixture was shaken on a Paar apparatus for 4 hours. The reaction mixture was degassed and kept under an atmosphere of Nitrogen. The mixture was filtered through a plug of diatomaceous earth and rinsed with dichloromethane. The filtrate was evaporated. (±)-cis-Piperidine-3,4-diol was isolated as a pale yellow oil (0.569 g, 100%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 4.11 (br s, 3H), 3.57-3.53 (m, 1H), 3.46-3.42 (m, 1H), 2.79-2.67 (m, 2H), 2.57-2.49 (m, 1H), 2.47-2.37 (m, 1H), 1.61-1.51 (m, 1H), 1.47-1.39 (m, 1H). MS = 118 (MH)+.

436c) (±)-cis-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.00 g, 3.46 mmol) and (±)-cis-Piperidine-3,4-diol (0.56 g, 4.8 mmol) in analogous manner to [B016]. Product isolated as a pale yellow solid (0.927 g, 69%). ^{1}HNMR (400 MHz,d6-DMSO,δ, ppm): 8.82 (s, 1H), 8.60 (dd, J=5.0, 0.5 Hz, 1H), 8.35 (s, 1H), 8.32-8.29 (m, 2H), 4.65-4.61 (m, 2H), 4.07 (s, 3H), 3.94 (br s, 1H), 3.83-3.74 (m, 2H), 3.65-3.53 (m, 3H), 1.94-1.85 (m, 1H), 1.73-1.65 (m, 1H). MS = 388, 390 (MH)+.

436d) (±)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from (±)-cis-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol (100.0 mg, 0.2578 mmol) and Aniline (29.0 µL, 0.318 mmol) in an analogous manner to Example 303c. Product isolated as the free base as a yellow solid (0.039 g, 34%). MP = 241-243°C. ^{1}HNMR (400 MHz,d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.79 (s, 1H), 8.32-8.29 (m, 2H), 7.90 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.3, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.64-4.60 (m, 2H), 4.07 (s, 3H), 3.98-3.88 (m, 1H), 3.85-3.72 (m, 2H), 3.66-3.53 (m, 3H), 1.97-1.87 (m, 1H), 1.76-1.66 (m, 1H). MS = 445 (MH)+.

Example 437. (±)-trans-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

437a) (±)-trans-Piperidine-3,4-diol was prepared from (±)-trans-3,4-Dihydroxy-piperidine-1-carboxylic acid benzyl ester (1.0 g, 4.0 mmol) [prepared as described in Solares, F. L.; et. al. *Tetrahedron* 2006, 62, 3284-3291] in an analogous manner to Example 436a. Product isolated as a pale yellow oil (0.451 g, 97%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 4.59 (br s, 2H), 4.09 (br s, 1H), 3.20-3.13 (m, 1H), 3.11-3.04 (m, 1H), 2.88 (ddd,

J=4.4, 12.1, 1.2 Hz, 1H), 2.77 (dddd, J=12.6, 4.1, 4.1, 1.2 Hz, 1H), 2.35 (dddd, J=14.1, 11.3, 2.9 Hz, 1H), 2.15 (dd, J=12.2, 9.1 Hz, 1H), 1.71 (dddd, J=12.6, 3.8, 3.8, 3.8 Hz, 1H), 1.25-1.15 (m, 1H). MS = 118 (MH)+.

437b) (±)-trans-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.00 g, 3.46 mmol) and (±)-trans-Piperidine-3,4-diol (0.46 g, 3.9 mmol) in an analogous manner to [B016]. Product isolated as a tan solid (0.700 g, 52%). MP = 213-216°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.83 (s, 1H), 8.61 (dd, J=5.0, 0.6 Hz, 1H), 8.36 (s, 1H), 8.32-8.29 (m, 2H), 5.00 (d, J=4.1 Hz, 1H), 4.94 (d, J=4.2 Hz, 1H), 4.11-4.03 (m, 4H), 4.00-3.90 (m, 1H), 3.59-3.47 (m, 2H), 3.44-3.37 (m, 1H), 3.16 (dd, J=13.1, 7.9 Hz, 1H), 2.07-1.99 (m, 1H), 1.54-1.44 (m, 1H). MS = 388, 390 (MH)+.

437c) desired (±)-trans-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from (±)-trans-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol (100.0 mg, 0.2578 mmol) and Aniline (29.0 µL, 0.318 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as tan foam (0.1126 g, 98%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.80 (s, 1H), 8.33 (s, 1H), 8.30 (d, J=5.4 Hz, 1H), 7.90 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.3, 1.3 Hz, 1H), 7.40-7.36 (m, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 5.00 (d, J=4.1 Hz, 1H), 4.94 (d, J=4.2 Hz, 1H), 4.10-4.04 (m, 4H), 3.98 (d, J=13.4 Hz, 1H), 3.55-3.46 (m, 1H), 3.40 (dddd, J=7.7, 7.7, 4.2, 4.2 Hz, 1H), 3.13 (dd, J=13.0, 7.7 Hz, 1H), 2.09-2.00 (m, 1H), 1.57-1.46 (m, 1H). MS = 445 (MH)+.

Example 438. 4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-one

438a) 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-one was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.0 g, 3.5 mmol) and Piperazin-2-one (0.42 g, 4.2 mmol) in an analogous manner to [B016]. Product isolated as a tan solid (1.12 g, 87%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.89 (s, 1H), 8.63-8.60 (m, 1H), 8.41 (s, 1H), 8.34-8.32 (m, 2H), 8.15 (s, 1H), 4.23 (s, 2H), 4.10 (s, 3H), 3.95-3.90 (m, 2H), 3.43-3.39 (m, 2H). LC/MS = 371, 373 (MH)+.

438b) 4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-one was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-one (100.0 mg, 0.2697 mmol) and Aniline (30.0 µL, 0.329 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as

the trifluoroacetic acid salt as a yellow lyophilate (0.022 g, 19%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.66 (br s, 1H), 8.87 (s, 1H), 8.40 (s, 1H), 8.27 (d, J=5.5 Hz, 1H), 8.18 (s, 1H), 7.97 (s, 1H), 7.74-7.69 (m, 3H), 7.34 (t, J=7.7 Hz, 2H), 7.00 (t, J=7.0 Hz, 1H), 4.23 (s, 2H), 4.10 (s, 3H), 3.92-3.87 (m, 2H), 3.46-3.41 (m, 2H). MS = 428 (MH)+.

Example 439. (2,3-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2,3-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,3-Difluoro-phenylamine (27.0 µL, 0.266 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.125 g, 84%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.24 (s, 1H), 8.91 (s, 1H), 8.86 (br s, 2H), 8.42 (s, 1H), 8.33 (d, J=5.4 Hz, 1H), 8.10 (s, 1H), 8.07-8.03 (m, 1H), 7.78 (dd, J=5.3, 1.4 Hz, 1H), 7.19-7.11 (m, 1H), 7.06-6.98 (m, 1H), 4.10 (s, 3H), 3.91-3.86 (m, 4H), 3.36-3.29 (m, 4H). MS = 450 (MH)+.

Example 440. (2,5-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2,5-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,5-Difluoro-phenylamine (27.0 µL, 0.268 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.036 g, 24%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.25 (s, 1H), 8.91 (s, 1H), 8.89 (br s, 2H), 8.45-8.38 (m, 3H), 8.21 (s, 1H), 7.81 (dd, J=5.3, 1.4 Hz, 1H), 7.31-7.24 (m, 1H), 6.80-6.74 (m, 1H), 4.11 (s, 3H), 3.92-3.87 (m, 4H), 3.36-3.30 (m, 4H). MS = 450 (MH)+.

Example 441. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,4,6-Trifluoro-phenylamine (39.0 mg, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.092 g, 60%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm):

8.93 (br s, 2H), 8.90 (s, 1H), 8.82 (s, 1H), 8.42 (s, 1H), 8.17 (dd, J=5.4, 0.5 Hz, 1H), 7.83 (s, 1H), 7.68 (dd, J=5.3, 1.4 Hz, 1H), 7.34-7.23 (m, 2H), 4.10 (s, 3H), 3.90-3.84 (m, 4H), 3.35-3.29 (m, 4H). MS = 468 (MH)+.

Example 442. ((R)-4-{2-[2-(2,6-Difluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-piperazin-2-yl)-methanol

((R)-4-{2-[2-(2,6-Difluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-piperazin-2-yl)-methanol was prepared from (R)-4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-2-hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2054 mmol) and 2,6-Difluoro-phenylamine (32.0 mg, 0.248 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a tan foam (0.066 g, 66%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.80 (s, 1H), 8.76 (s, 1H), 8.32 (s, 1H), 8.15 (d, J=5.3 Hz, 1H), 7.77 (s, 1H), 7.64 (d, J-5.2, 1.3 Hz, 1H), 7.31-7.10 (m, 3H), 4.70 (t, J=5.5 Hz, 1H), 4.21-4.12 (m, 2H), 4.06 (s, 3H), 3.42-3.35 (m, 2H), 3.15-3.00 (m, 2H), 2.86-2.77 (m, 3H). MS = 480 (MH)+.

Example 443. 3-Hydroxymethyl-1-[5-methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol

443a) To a cooled solution of 4-Oxo-piperidine-3-carboxylic acid ethyl ester; hydrochloride (5.0 g, 24 mmol) and Sodium bicarbonate (4.40 g, 52.4 mmol) in Water (50 mL) at 5°C was added Benzyl chloroformate (3.40 mL, 23.8 mmol) dropwise. The mixture was stirred at room temperature overnight. Saturated aqueous sodium carbonate (10 mL) was added and stirred for 30 minutes. The reaction mixture was extracted dichloromethane (3 x 30 mL). The combined organic layer was dried over magnesium sulfate, filtered and evaporated. The crude material was purified via chromatography using an ISCO apparatus (silica gel column 120 g and 10%→50% Ethyl Acetate:hexane). 4-Oxo-piperidine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester was isolated as a clear oil (7.30 g, 100%). ^{1}HNMR (400 MHz, CDCl3,δ, ppm): 12.07 (s, 1H), 7.43-7.29 (m, 5H), 5.20-5.15 (m, 2H), 4.24 (q, J=7.2 Hz, 2H), 4.14 (br s, 2H), 3.65 (t, J=5.9 Hz, 2H), 2.39 (br s, 2H), 1.31 (t, J=7.2 Hz, 3H). MS = 328 (M+Na)+.

443b) Sodium borohydride (4.5 g, 120 mmol) was added in 0.5g portions over 1 hour to a stirred solution of 4-Oxo-piperidine-1,3-dicarboxylic acid 1-benzyl ester 3-ethyl ester (3.0 g, 9.8 mmol) in Methanol (30 mL) under an atmosphere of Nitrogen at room temperature. Gas evolution and exotherm was noted during each addition. The slow portionwise addition kept reaction temperatures below 25°C during the course of additions. The

mixture was stirred for 1 hour at room temperature then slowly warmed. The reaction was refluxed for 4 hours, cooled to room temperature and stirred overnight. A 1:1 mixture of water:methanol (100 mL) was added dropwise to the reaction over 1 hour. No exotherm or gas evolution was noted. The mixture was stirred for 4 hours. The methanol was evaporated under reduced pressure. Methanol (50 mL) was added and the white suspension was heated at reflux for 30 minutes. The methanol was evaporated under reduced pressure. This was repeated twice. The mixture was evaporated to a white oily solid. The solid was triturated with dichloromethane (3 x 50 mL) and decanted. The combined organic was dried over magnesium sulfate, filtered and evaporated. 4-Hydroxy-3-hydroxymethyl-piperidine-1-carboxylic acid benzyl ester was isolated as a clear oil (0.655 g, 25%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 7.41-7.28 (m, 5H), 5.13-5.00 (m, 2H), 4.70-4.56 (m, 1H), 4.50-4.39 (m, 1H), 4.09-3.60 (m, 3H), 3.47-2.58 (m, 4H), 1.80-1.20 (m, 3H). MS = 288 (M+Na)+.

443c) 3-Hydroxymethyl-piperidin-4-ol was prepared from 4-Hydroxy-3-hydroxymethyl-piperidine-1-carboxylic acid benzyl ester (0.655 g, 2.47 mmol) in an analogous manner to Example 436b. Product isolated as a viscous oil (0.324 g, 100%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 4.60-3.18 (m, 7H), 3.3-2.78 (m, 1H), 2.70-2.56 (m, 1H), 2.43-2.10 (m, 1H), 1.74-1.18 (m, 3H).

443d) 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-3-hydroxymethyl-piperidin-4-ol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.70 g, 2.4 mmol) and 3-Hydroxymethyl-piperidin-4-ol (0.324 g, 2.47 mmol) in an analogous manner to [B016]. Product isolated as a pale yellow foam (0.342 g, 35%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.83 (d, J=5.4 Hz, 1H), 8.61-5.85 (m, 1H), 8.35 (d, J=6.2 Hz, 1H), 8.33-8.29 (m, 2H), 4.78-4.69 (m, 1H), 4.58-4.46 (m, 1H), 4.36-3.70 (m, 6H), 3.56-3.12 (m, 4H), 2.02-1.45 (m, 3H). MS = 402, 404 (MH)+.

443e) 3-Hydroxymethyl-1-[5-methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-3-hydroxymethyl-piperidin-4-ol (100.0 mg, 0.2488 mmol) and Aniline (28.0 µL, 0.307 mmol) in an analogous manner to Example 303c and Example 1501c. Product was isolated as the free base as a mixture of enantiomers as a yellow foam (0.071 g, 62%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (d, J=3.0 Hz, 1H), 8.80 (d, J=4.5 Hz, 1H), 8.34-8.29 (m, 2H), 7.90 (s, 1H), 7.75 (d, J=7.7 H, 2H), 7.68 (dd, J=5.3, 1.2 Hz, 1H), 7.31-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.79-4.69 (m, 1H), 4.55-

4.43 (m, 1H), 4.30-3.70 (m, 6H), 3.56-3.25 (m, 3H), 3.19-2.91 (m, 1H), 2.04-1.50 (m, 3H). MS = 459 (MH)+.

Example 444. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (121.0 mg, 0.2648 mmol) and 2,3,6-Trifluoro-phenylamine (33.9 μL, 0.320 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.155 g, 84%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.07 (s, 1H), 8.94-8.84 (m, 3H), 8.42 (s, 1H), 8.21 (d, J=5.3 Hz, 1H), 7.89 (s, 1H), 7.72 (dd, J=5.3, 1.4 Hz, 1H), 7.33 (dddd, J=9.7, 9.7, 9.7, 4.9 Hz, 1H), 7.21 (dddd, J=9.6, 4.7, 4.7, 2.2 Hz, 1H), 4.10 (s, 3H), 3.91-3.84 (m, 4H), 3.36-3.28 (m, 4H). MS = 468 (MH)+.

Example 445. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (124.0 mg, 0.2714 mmol) and 2-(trifluoromethyl)-Benzenamine (40.0 μL, 0.318 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.134 g, 69%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.00-8.85 (m, 4H), 8.42 (d, J=2.3 Hz, 1H), 8.19 (dd, J=5.4, 1.4 Hz, 1H), 7.99 (s, 1H), 7.80-7.66 (m, 4H), 7.44-7.37 (m, 1H), 4.11 (s, 3H), 3.90-3.84 (m, 4H), 3.35-3.28 (m, 4H). MS = 482 (MH)+.

Example 446. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (140.0 mg, 0.3064 mmol) and 3-(trifluoromethyl)-Benzenamine (46.2 μL, 0.370 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.179 g, 98%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.76 (s, 1H), 8.93-8.83 (m, 3H), 8.42 (s, 1H), 8.41 (d, J=5.4 Hz, 1H), 8.34 (s, 1H), 7.97 (s, 1H), 7.92 (d, J=8.3 Hz, 1H), 7.78 (dd, J=5.3, 1.3 Hz, 1H), 7.52 (t, J=7.9

Hz, 1H), 7.23 (d, J=7.6 Hz, 1H), 4.11 (s, 3H), 3.91-3.86 (m, 4H), 3.36-3.30 (m, 4H). MS = 482 (MH)+.

Example 447. (6-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(6-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Fluoro-pyridin-2-ylamine (30.0 mg, 0.268 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as an off-white solid (0.003 g, 2%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.15 (s, 1H), 8.81 (s, 1H), 8.74 (s, 1H), 8.40 (d, J=5.1 Hz, 1H), 8.32 (s, 1H), 7.88-7.81 (m, 2H), 7.75 (dd, J=8.1, 2.6 Hz, 1H), 6.59 (dd, J=7.7, 2.3 Hz, 1H), 4.07 (s, 3H), 3.71-3.66 (m, 4H), 2.90-2.85 (m, 4H). MS = 433 (MH)+.

Example 448. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (124.0 mg, 0.2714 mmol) and 6-Methoxy-pyridin-2-ylamine (40.0 mg, 0.322 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as an off-white solid (0.098 g, 80%). MP = 189-191°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.79 (s, 1H), 9.04 (s, 1H), 8.73 (s, 1H), 8.37 (d, J=5.2 Hz, 1H), 8.31 (s, 1H), 7.79 (dd, J=5.2, 1.4 Hz, 1H), 7.58 (t, J=7.9 Hz, 1H), 7.16 (d, J=7.8 Hz, 1H), 6.30 (d, J=7.7 Hz, 1H), 4.07 (s, 3H), 4.04 (s, 3H), 3.67-3.62 (m, 4H), 2.89-2.84 (m, 4H). MS = 445 (MH)+.

Example 449. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 6-Trifluoromethyl-pyridin-2-ylamine (43.0 mg, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as off-white solid (0.005 g, 5%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.34 (s, 1H), 8.80-8.78 (m, 2H), 8.42 (d, J=4.7 Hz, 1H), 8.32 (s, 1H), 8.08 (d, J=8.1 Hz, 1H), 7.94 (t,

J=8.1 Hz, 1H), 7.89 (dd, J=5.1, 1.3 Hz, 1H), 7.36 (d, J=7.4 Hz, 1H), 4.07 (s, 3H), 3.68-3.63 (m, 4H), 2.90-2.85 (m, 4H). MS = 483 (MH)+.

Example 450. (2-Fluoro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2-Fluoro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (124.0 mg, 0.2714 mmol) and 2-Fluoro-pyridin-3-ylamine (40.0 mg, 0.357 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.156 g, 86%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.26 (s, 1H), 8.91 (br s, 3H), 8.86 (ddd, J=10.0, 8.0, 1.7 Hz, 1H), 8.42 (s, 1H), 8.36 (dd, J=5.5 Hz, 1H), 8.19 (s, 1H), 7.81 (dd, J=5.3, 1.3 Hz, 1H), 7.77 (ddd, J=4.6, 1.5, 1.5 Hz, 1H), 7.32 (ddd, J=7.9, 4.8, 0.9 Hz, 1H), 4.11 (s, 3H), 3.93-3.87 (m, 4H), 3.36-3.30 (m, 4H). MS = 433 (MH)+.

Example 451. (2-Fluoro-3-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2-Fluoro-3-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (111.0 mg, 0.2429 mmol) and 2-Fluoro-3-methyl-phenylamine (36.0 mg, 0.288 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the tris-trifluoroacetic acid salt as a yellow lyophilate (0.146 g, 76%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.04 (br s, 1H), 8.90 (s, 1H), 8.87 (br s, 2H), 8.42 (s, 1H), 8.28 (d, J=5.3 Hz, 1H), 8.06 (s, 1H), 7.98 (t, J=7.8 Hz, 1H), 7.73 (dd, J=5.3, 1.3 Hz, 1H), 7.05 (t, J=7.8 Hz, 1H), 6.93 (t, J=7.2 Hz, 1H), 4.10 (s, 3H), 3.91-3.86 (m, 4H), 3.35-3.29 (m, 4H), 2.28 (d, J=1.8 Hz, 3H). MS = 446 (MH)+.

Example 452. (2-Fluoro-3-trifluoromethyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2-Fluoro-3-trifluoromethyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (102.0 mg, 0.2232 mmol) and 2-Fluoro-3-trifluoromethyl-phenylamine (48.0 mg, 0.268 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.050 g, 30%). ^{1}HNMR (400 MHz, d6-

DMSO,δ, ppm): 9.32 (s, 1H), 8.91 (s, 1H), 8.85 (br s, 2H), 8.63 (ddd, J=7.8, 7.8, 2.3 Hz, 1H), 8.42 (s, 1H), 8.35 (d, J=5.3 Hz, 1H), 8.14 (s, 1H), 7.81 (dd, J=5.3, 1.4 Hz, 1H), 7.39-7.30 (m, 2H), 4.11 (s, 3H), 3.92-3.86 (m, 4H), 3.36-3.29 (m, 4H). MS = 500 (MH)+.

Example 453. (2,4-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2,4-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,4-Difluoro-phenylamine (27.0 μL, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.059 g, 39%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.03 (s, 1H), 8.90 (s, 1H), 8.87 (br s, 2H), 8.42 (s, 1H), 8.27 (d, J=5.3 Hz, 1H), 8.10 (ddd, J=9.3, 9.3, 6.3 Hz, 1H), 8.00 (s, 1H), 7.72 (dd, J=5.4, 1.3 Hz, 1H), 7.31 (ddd, J=11.5, 9.0, 2.9 Hz, 1H), 7.11-7.04 (m, 1H), 4.10 (s, 3H), 3.90-3.85 (m, 4H), 3.35-3.29 (m, 4H). MS = 450 (MH)+.

Example 454. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,4-trifluoro-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,4-trifluoro-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,3,4-Trifluoro-phenylamine (28.0 μL, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.104 g, 68%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.21 (s, 1H), 8.95-8.85 (m, 3H), 8.42 (s, 1H), 8.30 (d, J=5.3 Hz, 1H), 8.04 (s, 1H), 7.99-7.91 (m, 1H), 7.77 (dd, J=5.3, 1.3 Hz, 1H), 7.33-7.24 (m, 1H), 4.10 (s, 1H), 3.91-3.86 (m, 4H), 3.36-3.29 (m, 4H). MS = 468 (MH)+.

Example 455. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,5-trifluoro-phenyl)-amine

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,5-trifluoro-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2188 mmol) and 2,4,5-Trifluoro-phenylamine (39.0 mg, 0.265 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the bis-trifluoroacetic acid salt as a yellow lyophilate (0.027 g, 17%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm):

9.21 (s, 1H), 8.91 (s, 1H), 8.86 (br s, 2H), 8.54 (ddd, J=13.6, 8.5, 8.5 Hz, 1H), 8.42 (s, 1H), 8.36 (d, J=5.4 Hz, 1H), 8.14 (s, 1H), 7.79 (dd, J=5.3, 1.4 Hz, 1H), 7.60 (ddd, J=10.9, 10.9, 7.7 Hz, 1H), 4.10 (s, 3H), 3.91-3.86 (m, 4H), 3.36-3.29 (m, 4H). MS = 468 (MH)+.

Example 456. (3S,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol or (3R,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

(3S,4S)- or (3R,4R)- 1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from (±)-trans-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol (67.52 mg) via super critical fluid chiral chromatography using Chiralcel OJ-H (10 x 250 mm) column using 30% MeOH (w/ 0.1% diethylamine modifier):70% CO2 eluent at 6.0 mL/min over 4 injections of 150 µL, T=35°C, P=120 bar, UV = 220 nm. Product isolated as the initial peak as a yellow solid (0.0166 g, 24%). Purity: >99% ee @ 100% purity. RT: 8.6 min, ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (s, 1H), 8.80 (s, 1H), 8.33 (s, 1H), 8.31 (d, J=5.4 Hz, 1H), 7.90 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.3, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 5.01-4.98 (m, 1H), 4.94 (d, J=4.1 Hz, 1H), 4.11-3.94 (m, 5H), 3.55-3.38 (m, 3H), 3.16-3.10 (m, 1H), 2.08-2.00 (m, 1H), 1.57-1.47 (m, 1H). MS = 445 (MH)+.

Example 457. (3R,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol or (3S,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

(3R,4R)- or (3S,4S)- 1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from (±)-trans-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol (67.52 mg) via super critical fluid chiral chromatography using Chiralcel OJ-H (10 x 250 mm) column using 30% MeOH (w/ 0.1% diethylamine modifier):70% CO2 eluent at 6.0 mL/min over 4 injections of 150 µL, T=35°C, P=120 bar, UV = 220 nm. Product isolated as the secondary peak as a yellow solid (0.0209 g, 31%). Purity: >97.6% ee @ 98% purity. RT: 12.98 min. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.80 (s, 1H), 8.33 (s, 1H), 8.31 (d, J=5.2 Hz, 1H), 7.90 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.4, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 5.02-4.98 (m, 2H), 4.11-3.93 (m, 5H), 3.55-3.37 (m, 3H), 3.16-3.10 (m, 1H), 2.08-2.00 (m, 1H), 1.57-1.47 (m, 1H). MS = 445 (MH)+.

Example 458. 3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-propionamide

458a) 3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-propionamide was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.00 g, 3.46 mmol) and 3-Amino-propionamide; hydrochloride (0.52 g, 4.2 mmol) in an analogous manner to [B016]. Product isolated as a tan solid (0.303 g, 24%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.93 (t, J=5.5 Hz, 1H), 8.79 (s, 1H), 8.61-8.58 (m, 1H), 8.35 (s, 1H), 8.34-8.32 (m, 2H), 7.50 (br s, 1H), 7.00 (br s, 1H), 4.11 (s, 3H), 3.94-3.87 (m, 2H), 2.57-2.52 (m, 2H). MS = 359, 361 (MH)+.

458b) 3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-propionamide was prepared from 3-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ylamino]-propionamide (100.0 mg, 0.2787 mmol) and Aniline (30.0 µL, 0.329 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.043 g, 28%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.55 (br s, 1H), 8.88 (t, J=5.4 Hz, 1H), 8.77 (s, 1H), 8.34 (s, 1H), 8.26 (d, J=5.4 Hz, 1H), 7.96 (s, 1H), 7.74-7.69 (m, 3H), 7.50 (s, 1H), 7.33 (t, J=7.9 Hz, 2H), 7.04-6.95 (m, 2H), 4.12 (s, 3H), 3.95-3.89 (m, 2H), 2.58-2.53 (m, 2H). MS = 416 (MH)+.

Example 459. [4-(5-Methoxy-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine

459a) 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-piperidin-1-yl-pyrido[3,4-d]pyrimidine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.0 g, 3.5 mmol) and Piperidine (0.41 mL, 4.2 mmol) in an analogous manner to [B016]. Product isolated as a yellow-orange solid (0.61 g, 49%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 8.83 (s, 1H), 8.59 (d, J=5.0 Hz, 1H), 8.35 (s, 1H), 8.31-8.28 (m, 2H), 4.08 (s, 3H), 3.71-3.65 (m, 4H), 1.75-1.65 (m, 6H). MS = 356, 358 (MH)+.

459b) [4-(5-Methoxy-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-4-piperidin-1-yl-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2810 mmol) and Aniline (31.0 µL, 0.340 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.075 g, 64%). MP = 221-223°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (s, 1H), 8.80 (s, 1H), 8.32 (s, 1H), 8.30 (d, J=5.2 Hz, 1H), 7.90 (s, 1H), 7.77-7.73 (m, 2H), 7.66 (dd, J=5.2, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.08 (s, 3H), 3.70-3.65 (m, 4H), 1.75-1.67 (m, 6H). MS = 413 (MH)+.

Example 460. {4-[4-(4,4-Difluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine

460a) 2-(2-Chloro-pyridin-4-yl)-4-(4,4-difluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.0 g, 3.5 mmol) and 4,4-Difluoro-piperidine; hydrochloride (0.66 g, 4.2 mmol) in an analogous manner to [B016]. Product isolated as an orange solid (0.806 g, 59%). ^{1}HNMR (400 MHz, d6-DMSO, δ, ppm): 8.90 (s, 1H), 8.61 (dd, J=4.9, 0.8 Hz, 1H), 8.41 (s, 1H), 8.34-8.31 (m, 2H), 4.10 (s, 3H), 3.84-3.79 (m, 4H), 2.26-2.14 (m, 4H). MS =392, 394 (MH)+.

460b) {4-[4-(4,4-Difluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine was prepared from 2-(2-Chloro-pyridin-4-yl)-4-(4,4-difluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2552 mmol) and Aniline (28.0 µL, 0.307 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as an orange solid (0.027 g, 23%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.87 (s, 1H), 8.38 (s, 1H), 8.32 (d, J=5.2 Hz, 1H), 7.92 (s, 1H), 7.78-7.74 (m, 2H), 7.68 (dd, J=5.3, 1.4 Hz, 1H), 7.31-7.25 (m, 2H), 6.93-6.88 (m, 1H), 4.10 (s, 3H), 3.82-3.78 (m, 4H), 2.27-2.15 (m, 4H). MS = 449 (MH)+.

Example 461. 1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile

461a) 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.0 g, 3.5 mmol) and Piperidine-4-carbonitrile (0.46 g, 4.2 mmol) in an analogous manner to [B016]. Product isolated as an orange solid (0.80 g, 61%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.87 (s, 1H), 8.61 (dd, J=5.0, 0.7 Hz, 1H), 8.39 (s, 1H), 8.34-8.31 (m, 2H), 4.10 (s, 3H), 3.96-3.88 (m, 2H), 3.57-3.49 (m, 2H), 3.25-3.17 (m, 1H), 2.14-2.05 (m, 2H), 1.96-1.86 (m, 2H). MS = 381, 383 (MH)+.

461b) 1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile (100.0 mg, 0.2626 mmol) and Aniline (29.0 µL, 0.318 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.090 g, 77%). MP = 242-244°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.84 (s, 1H), 8.36 (s, 1H), 8.31 (d, J=5.2 Hz, 1H), 7.91 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.4, 1.4 Hz, 1H), 7.31-7.26 (m, 2H), 6.93-6.88 (m, 1H), 4.09 (s, 3H), 3.96-3.88 (m, 2H), 3.56-3.48 (m, 2H), 3.26-3.19 (m, 1H), 2.15-2.06 (m, 2H), 1.98-1.88 (m, 2H). MS = 438 (MH)+.

Example 462. {4-[4-(4-Fluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine

462a) 2-(2-Chloro-pyridin-4-yl)-4-(4-fluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidine was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (1.0 g, 3.5 mmol) and 4-Fluoro-piperidine; hydrochloride (0.58 g, 4.2 mmol) in an analogous manner to [B016]. Product isolated as an orange solid (0.61 g, 47%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.87 (s, 1H), 8.61 (dd, J=4.9, 0.7 Hz, 1H), 8.38 (s, 1H), 8.33-8.30 (m, 2H), 5.08-4.90 (m, 1H), 4.09 (s, 3H), 3.83-3.68 (m, 4H), 2.16-2.00 (m, 2H), 1.97-1.85 (m, 2H). MS = 374, 376 (MH)+.

462b) {4-[4-(4-Fluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine was prepared from 2-(2-Chloro-pyridin-4-yl)-4-(4-fluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidine (100.0 mg, 0.2675 mmol) and Aniline (30.0 µL, 0.329 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.057 g, 49%). MP = 202-205°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.83 (s, 1H), 8.35 (s, 1H), 8.31 (d, J=5.3 Hz, 1H), 7.91 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.3, 1.3 Hz, 1H), 7.31-7.25 (m, 2H), 6.92-6.87 (m, 1H), 5.10-4.90 (m, 1H), 4.09 (s, 3H), 3.84-3.67 (m, 4H), 2.17-2.02 (m, 2H), 1.98-1.85 (m, 2H). MS = 431 (MH)+.

Example 463. (3R,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol or (3S,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

(3R,4S)- or (3S,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from (±)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol via super critical fluid chiral chromatography was performed using a Chiralpak AD-H (10 x 250 mm) column using 40% MeoH (w/ 0.1% diethylamine modifier):60% CO2 eluent at 6.0 mL/min over 2 injections of 400 µL, T=35°C, P=120 bar, UV = 220 nm. Product isolated as the initial peak as a yellow solid (0.0254 g, 38%). Purity: >99% ee @ 100% purity. RT: 9.4 min. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.79 (s, 1H), 8.32-8.29 (m, 2H), 7.90 (s, 1H), 7.77-7.73 (m, 2H), 7.67 (dd, J=5.3, 1.4 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.63 (br s, 2H), 4.07 (s, 3H), 4.00-3.88 (m, 1H), 3.84-3.72 (m, 2H), 3.65-3.52 (m, 3H), 1.97-1.88 (m, 1H), 1.75-1.68 (m, 1H). MS = 445 (MH)+.

Example 464. (3S,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol or (3R,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

(3S,4R)- or (3R,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol was prepared from (±)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol via super critical fluid chiral chromatography was performed using a Chiralpak AD-H (10 x 250 mm) column using 40% MeOH (w/ 0.1% diethylamine modifier):60% CO2 eluent at 6.0 mL/min over 2 injections of 400 µL, T=35°C, P=120 bar, UV = 220 nm. Product isolated as the secondary peak as a yellow solid (0.0255 g, 38%). Purity: >99% ee @ 100% Purity. RT: 8.6 min. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.32 (s, 1H), 8.79 (s, 1H), 8.32-8.29 (m, 2H), 7.90 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.2, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.64 (br s, 2H), 4.07 (s, 3H), 3.99-3.73 (m, 3H), 3.65-3.54 (m, 3H), 1.97-1.87 (m, 1H), 1.76-1.66 (m, 1H). MS = 445 (MH)+.

Example 465. {(R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol

465a) {(R)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.50 g, 1.7 mmol) and (R)-3-Hydroxymethyl-pyrrolidine-1-carboxylic acid tert-butyl ester (0.42 g, 2.1 mmol) [deprotected with 1:1 trifluoroacetic acid:methylene chloride before addition] in an analogous manner to [B016]. Product isolated as a yellow foam (0.186 g, 28%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.78 (s, 1H), 8.59 (dd, J=5.0, 0.6 Hz, 1H), 8.34 (s, 1H), 8.32-8.29 (m, 2H), 4.72 (br s, 1H), 4.07 (s, 3H), 3.90-3.37 (m, 6H), 2.37 (br s, 1H), 1.99 (br s, 1H), 1.68 (br s, 1H). MS = 372, 374 (MH)+.

465b) {(R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol was prepared from {(R)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol (186.0 mg, 0.5002 mmol) and Aniline (55.0 µL, 0.604 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.091 g, 42%). MP = 208-209°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (s, 1H), 8.75 (s, 1H), 8.30 (s, 1H), 8.29 (d, J=5.2 Hz, 1H), 7.90 (s, 1H), 7.78-7.74 (m, 2H), 7.68 (dd, J=5.3, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.91-6.86 (m, 1H), 4.73 (br s, 1H), 4.07 (s, 3H), 3.88-3.35 (m, 6H), 2.37 (br s, 1H), 2.00 (br s, 1H), 1.70 (br s, 1H). MS = 429 (MH)+.

Example 466. {(S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol

466a) desired {(S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.50 g, 1.7 mmol) and (S)-3-Hydroxymethyl-pyrrolidine-1-carboxylic acid tert-butyl ester (0.42 g, 2.1 mmol) [deprotected with 1:1 trifluoroacetic acid:methylene chloride before addition] in an analogous manner to [B016]. Product isolated as a yellow resin (0.185g, 29%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.78 (s, 1H), 8.59 (d, J=5.0 Hz, 1H), 8.34 (s, 1H), 8.32-8.29 (m, 2H), 4.72 (br s, 1H), 4.07 (s, 3H), 3.90-3.35 (m, 6H), 2.42 (br s, 1H), 1.99 (br s, 1H), 1.70 (br s, 1H). MS= 372, 374 (MH)+.

466b) {(S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol was prepared from {(S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol (185.0 mg, 0.4976 mmol) and Aniline (55.0 µL, 0.604 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow foam (0.093 g, 43%). MP = 210-211°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.31 (s, 1H), 8.75 (s, 1H), 8.30 (s, 1H), 8.29 (d, J=5.3 Hz, 1H), 7.90 (s, 1H), 7.78-7.74 (m, 2H), 7.68 (dd, J=5.3, 1.4 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.86 (m, 1H), 4.73 (br s, 1H), 4.07 (s, 1H), 3.88-3.35 (m, 6H), 2.37 (br s, 1H), 2.00 (br s, 1H), 1.71 (br s, 1H). MS = 429 (MH)+.

Example 467. (meso)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azepane-4,5-diol

467a) To a round bottom flask equipped a stir bar and a reflux condenser containing But-3-enylamine (0.58 g, 8.1 mmol) and Tetrahydrofuran (50 mL) was added 4-Bromo-but-1-ene (1.0 g, 7.4 mmol) and the mixture was heated at 60°C for 18 hours. The mixture was cooled to room temperature. Triethylamine (1.1 mL, 8.1 mmol) was added followed Di-tert-Butyldicarbonate (1.8 g, 8.1 mmol). The suspension was stirred at room temperature for 1 hour. The suspension was filtered through a plug of diatomaceous earth and the filtrate was evaporated to a yellow suspension. To the residue was added methanol (40 mL) followed by 1N aqueous Sodium hydroxide (5 mL). The mixture was stirred for 1 hour. The resulting suspension was filtered through a plug of diatomaceous earth. The filtrate was evaporated. The residue was purified via chromatography using an ISCO apparatus (silica gel column 24g 0%→5% Ethyl Acetate:Hexane). Di-but-3-enyl-carbamic acid tert-butyl ester was isolated as clear oil (0.304 g, 18%). ^{1}HNMR (400 MHz,

CDCl3,δ, ppm): 5.83-5.70 (m, 2H), 5.10-4.99 (m, 4H), 3.23 (br s, 4H), 2.31-2.24 (m, 4H), 1.46 (s, 9H). MS = 248 (M+Na)+.

467b) To a solution of Di-but-3-enyl-carbamic acid tert-butyl ester (0.30 g, 1.3 mmol) in dry Toluene (30 mL) under an atmosphere of Nitrogen was added (1,3-Bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(o-isopropoxyphenylmethylene)ruthenium (45.0 mg, 0.0717 mmol). The mixture was heated at 50°C for 5 hours. The mixture was cooled to room temperature and stirred overnight. The volatiles were evaporated. The residue was triturated with hexane (30 mL) and the suspension was filtered through a plug of diatomaceous earth. The filtrate was evaporated. The residue was purified via chromatography using an ISCO apparatus (silica gel column 24 g with 0%→5% Ethyl Acetate:Hexane). 2,3,6,7-Tetrahydro-azepine-1-carboxylic acid tert-butyl ester was isolated as a clear oil (0.166 g, 63%). ^{1}HNMR (400 MHz, CDCl3,δ, ppm): 5.79-5.66 (m, 2H), 3.50-3.38 (m, 4H), 2.28 (br s, 4H), 1.47 (s, 9H). MS = 220 (M+Na)+.

467c) (meso)- cis-4,5-Dihydroxy-azepane-1-carboxylic acid tert-butyl ester was prepared from 2,3,6,7-Tetrahydro-azepine-1-carboxylic acid tert-butyl ester (0.166 g, 0.841 mmol) in an analogous manner to Example 436a. Product isolated as an off-white solid (0.151g, 77%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 4.48 (d, J=4.3 Hz, 2H), 3.67-3.60 (m, 2H), 3.45-3.32 (m, 2H), 3.19-3.05 (m, 2H), 1.84-1.73 (m, 2H), 1.64-1.52 (m, 2H), 1.38 (s, 9H). MS = 254 (M+Na)+.

467d) (meso)-cis-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-azepane-4,5-diol was prepared from 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (0.20 g, 0.69 mmol), and (meso)-cis-4,5-Dihydroxy-azepane-1-carboxylic acid tert-butyl ester (0.15 g, 0.65 mmol) [deprotected with 1:1 trifluoroacetic acid:methylene chloride before addition] in an analogous manner to [B016]. Product isolated as an orange resin (0.115 g, 44%). ^{1}HNMR (400 MHz,d6-DMSO,δ, ppm): 8.77 (s, 1H), 8.59 (dd, J=4.8, 1.0 Hz, 1H), 8.32-8.28 (m, 3H), 4.45-4.42 (m, 2H), 4.04 (s, 3H), 3.88-3.60 (m, 6H), 2.10-2.00 (m, 2H), 1.86-1.77 (m, 2H). MS = 402, 404 (MH)+.

467e) (meso)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azepane-4,5-diol was prepared from (meso)-cis-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-azepane-4,5-diol (115.0 mg, 0.2862 mmol) and Aniline (33.0 µL, 0.362 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow foam (0.033 g, 25%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.29 (s, 1H), 8.74 (s, 1H), 8.29 (d, J=5.2 Hz, 1H), 8.26 (s, 1H),

7.90 (s, 1H), 7.77-7.74 (m, 2H), 7.67 (dd, J=5.3, 1.3 Hz, 1H), 7.30-7.25 (m, 2H), 6.92-6.87 (m, 1H), 4.45 (d, J=4.2 Hz, 2H), 4.05 (s, 3H), 3.87-3.60 (m, 6H), 2.12-2.02 (m, 2H), 1.87-1.78 (m, 2H). MS = 459 (MH)+.

Example 468. 1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol

1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol (90.0 mg, 0.242 mmol) and 6-Fluoro-pyridin-2-ylamine (33.0 mg, 0.294 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow foam (0.048g, 35%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.43 (br s, 1H), 8.83 (s, 1H), 8.71 (s, 1H), 8.43 (d, J=5.3 Hz, 1H), 8.36 (s, 1H), 7.92-7.85 (m, 2H), 7.69-7.65 (m, 1H), 6.65 (dd, J=7.9, 2.2 Hz, 1H), 4.11-4.01 (m, 5H), 3.87-3.80 (m, 1H), 3.51-3.42 (m, 2H), 1.97-1.89 (m, 2H), 1.64-1.54 (m, 2H). MS = 448 (MH)+.

Example 469. 1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol

1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol was prepared from 1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol (90.0 mg, 0.242 mmol) and 6-Methoxy-pyridin-2-ylamine (36.0 mg, 0.290 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow foam (0.031 g, 27%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.45 (br s, 1H), 8.86 (s, 1H), 8.78 (s, 1H), 8.43 (d, J=5.6 Hz, 1H), 8.36 (s, 1H), 7.90 (d, J=6.0 Hz, 1H), 7.69 (t, J=7.9 Hz, 1H), 7.05 (d, J=8.0 Hz, 1H), 6.44 (d, J=8.0 Hz, 1H), 4.10-3.98 (m, 8H), 3.87-3.80 (m, 1H), 3.48-3.39 (m, 2H), 1.97-1.89 (m, 2H), 1.63-1.53 (m, 2H). MS = 460 (MH)+.

Example 470. ((S)-1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol

((S)-1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol was prepared from {(S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol (90.0 mg, 0.242 mmol) and 6-Fluoro-pyridin-2-ylamine (40.0 mg, 0.357 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.026 g, 19%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.43 (br s, 1H), 8.79 (s, 1H), 8.68 (s, 1H), 8.43 (d, J=5.5 Hz, 1H), 8.37 (s, 1H), 7.92-7.85 (m,

2H), 7.68 (d, J=7.9 Hz, 1H), 6.65 (d, J=8.0 Hz, 1H), 4.09 (s, 3H), 3.92-3.40 (m, 6H), 2.45-2.30 (m, 1H), 2.08-1.98 (m, 1H), 1.80-1.65 (m, 1H). MS = 448 (MH)+.

Example 471. ((S)-1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol

((S)-1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol was prepared from {(S)-1-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol (90.0 mg, 0.242 mmol) and 6-Methoxy-pyridin-2-ylamine (45.0 mg, 0.362 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the trifluoroacetic acid salt as a yellow lyophilate (0.044 g, 31%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 10.44 (br s, 1H), 8.86 (s, 1H), 8.73 (s, 1H), 8.43 (d, J=5.6 Hz, 1H), 8.36 (s, 1H), 7.91 (d, J=5.0 Hz, 1H), 7.68 (t, J=8.2 Hz, 1H), 7.03 (d, J=8.0 Hz, 1H), 6.44 (d, J=7.8 Hz, 1H), 4.08 (s, 3H), 4.04 (s, 3H), 3.90-3.35 (m, 6H), 2.45-2.30 (m, 1H), 2.05-1.95 (m, 1H), 1.77-1.64 (m, 1H). MS = 460 (MH)+.

Example 473. 2-(4-Cyano-phenyl)-N-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide

2-(4-Cyano-phenyl)-N-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2141 mmol) and 2-(4-Cyano-phenyl)-acetamide (50.0 mg, 0.312 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a tan solid (0.094 g, 89%). MP = 200-203°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.05 (s, 1H), 8.97 (s, 1H), 8.49 (dd, J=5.1, 0.6 Hz, 1H), 8.09 (s, 1H), 8.04 (dd, J=5.2, 1.4 Hz, 1H), 7.84-7.81 (m, 2H), 7.60-7.57 (m, 2H), 3.91 (s, 2H), 3.85-3.45 (m, 4H), 2.83 (m, 4H), 2.63-2.55 (m, 1H), 1.28-1.22 (m, 2H), 1.04-0.99 (m, 2H). LC/MS = 491 (MH)+.

Example 474. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2141 mmol) and 2-Methyl-4-morpholin-4-yl-phenylamine (61.0 mg, 0.317 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as an orange-brown solid (0.085 g, 75%). MP = 214-220°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.93 (s, 1H), 8.23 (s, 1H), 8.14 (d, J=5.3 Hz, 1H), 8.07 (s, 1H),

7.58 (s, 1H), 7.52 (dd, J=5.2, 1.3 Hz, 1H), 7.28 (d, J=8.6 Hz, 1H), 6.86 (d, J=2.7 Hz, 1H), 6.79 (dd, J=8.6, 2.8 Hz, 1H), 3.80-3.50 (m, 8H), 3.10-3.06 (m, 4H), 2.81 (br s, 4H), 2.64-2.56 (m, 1H), 2.19 (s, 3H), 1.27-1.21 (m, 2H), 1.04-0.99 (m, 2H). LC/MS = 523 (MH)+.

Example 475. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (107.0 mg, 0.2291 mmol) and 6-Morpholin-4-yl-pyridin-3-ylamine (57.0 mg, 0.318 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a yellow solid (0.103 g, 87%). MP = 217-219°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.08 (s, 1H), 8.96 (s, 1H), 8.45 (d, J=2.6 Hz, 1H), 8.24 (d, J=5.4 Hz, 1H), 8.09 (s, 1H), 7.99 (dd, J=9.1, 2.7 Hz, 1H), 7.81 (s, 1H), 7.62 (dd, J=5.3, 1.3 Hz, 1H), 6.85 (d, J=9.1 Hz, 1H), 3.90-3.50 (m, 8H), 3.37-3.34 (m, 4H), 2.86 (br s, 4H), 2.66-2.58 (m, 1H), 1.29-1.23 (m, 2H), 1.05-1.00 (m, 2H). LC/MS = 510 (MH)+.

Example 476. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2141 mmol) and 3-aminopyridine (30.0 mg, 0.319 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a pale yellow solid (0.067 g, 74%). MP = 226-228°C. ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 9.55 (s, 1H), 8.98 (s, 1H), 8.87 (d, J=2.5 Hz, 1H), 8.35 (d, J=5.4 Hz, 1H), 8.32-8.28 (m, 1H), 8.12-8.09 (m, 2H), 7.95 (s, 1H), 7.75 (dd, J=5.3, 1.2 Hz, 1H), 7.30 (dd, J=8.4, 4.7 Hz, 1H), 3.96-3.46 (m, 4H), 2.87 (br s, 4H), 2.66-2.58 (m, 1H), 1.30-1.23 (m, 2H), 1.06-1.01 (m, 2H). LC/MS = 425.0 (MH)+.

Example 477. (2-Chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

(2-Chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2141 mmol) and o-Chloroaniline (52.0 uL, 0.315 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as an orange foam

(0.086 g, 88%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.97 (s, 1H), 8.68 (s, 1H), 8.26 (d, J=5.3 Hz, 1H), 8.09 (s, 1H), 8.04-8.00 (m, 2H), 7.72 (dd, J=5.3, 1.4 Hz, 1H), 7.48 (dd, J=8.0, 1.5 Hz, 1H), 7.34-7.29 (m, 1H), 7.09-7.04 (m, 1H), 3.96-3.46 (m, 4H), 2.86 (br s, 4H), 2.65-2.57 (m, 1H), 1.29-1.23 (m, 2H), 1.05-1.00 (m, 2H). LC/MS = 458.0 (MH)+.

Example 478. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-3-yl)-amine

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-3-yl)-amine was prepared from 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100.0 mg, 0.2141 mmol) and 4-Methyl-pyridin-3-ylamine (34.0 mg, 0.314 mmol) in an analogous manner to Example 303c and Example 1501c. Product isolated as the free base as a pale yellow foam (0.070 g, 74%). ^{1}HNMR (400 MHz, d6-DMSO,δ, ppm): 8.98 (s, 1H), 8.81 (s, 1H), 8.64 (s, 1H), 8.22 (d, J=5.4 Hz, 1H), 8.16 (d, J=4.9 Hz, 1H), 8.11 (s, 1H), 7.87 (s, 1H), 7.67 (dd, J=5.2, 1.3 Hz, 1H), 7.25 (d, J=4.9 Hz, 1H), 3.95-3.45 (m, 4H), 2.93 (br s, 4H), 2.65-2.59 (m, 1H), 2.28 (s, 3H), 1.29-1.23 (m, 2H), 1.06-1.01 (m, 2H). LC/MS = 439.2 (MH)+.

Example 481. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine

481a) 3-Bromo-5-fluoro-isonicotinic acid tert-butyl ester (1.9 g, 6.9 mmol), cyclopropyltrifluoroborate (1.18 g, 7.97 mmol), palladium acetate (81.3 mg, 0.36 mmol), butyl-ditricyclo[3.3.1.1(3,7)]decan-1-yl-phosphane (194.8 mg, 0.54 mmol), and cesium carbonate (7 g, 21.7 mmol) was heated at 85 °C in toluene (35 mL)/water (4 mL) overnight, under nitrogen. Cooled, partitioned between ether and water. Organic extracts dried ($MgSO_4$), filtered, solvent evaporated; product isolated by flash chromatography (ISCO, Silica gel, EtOAc/Hexanes 0 - 10 %; 2nd fraction is product): 3-cyclopropyl-5-fluoro-isonicotinic acid tert-butyl ester (50% yield).

481b) 3-Cyclopropyl-5-fluoro-isonicotinic acid tert-butyl ester (700.0 mg, 2.95 mmol) was treated with trifluoroacetic acid (2.0 mL, 26.0 mmol) in methylene chloride (5 mL) at 25 °C overnight. Solvent was evaporated, and the crude residue was dried on high vacuum, and then used without further purification: 3-cyclopropyl-5-fluoro-isonicotinic acid; compound with trifluoro-acetic acid (quant.).

481c) 3-Cyclopropyl-5-fluoro-isonicotinic acid; compound with trifluoro-acetic acid (995 mg, 3.37 mmol) and 2-chloro-isonicotinamidine; hydrochloride (1.3 g, 6.7 mmol) were treated with N,N,N',N'-tetramethyl-O-(7-azabenzotriazol-1-yl)uronium

hexafluorophosphate (1.35 g, 3.54 mmol) and N,N-diisopropylethylamine (3.5 mL, 20.2 mmol) in N,N-dimethylformamide (14 mL) at room temperature overnight. The reaction mixture was partitioned between DCM and water, organic layer washed extensively with water, dried ($MgSO_4$), solvent evaporated when a precipitate formed. Trituration from ether followed by filtration afforded N-[(2-chloro-pyridin-4-yl)-imino-methyl]-3-cyclopropyl-5-fluoro-isonicotinamide, which was used in the next step without further purification.

481d) N-[(2-Chloro-pyridin-4-yl)-imino-methyl]-3-cyclopropyl-5-fluoro-isonicotinamide (solid product from step c) and cesium carbonate (1.4 g, 4.2 mmol) were mixed in N,N-dimethylacetamide (17 mL). The reaction was microwaved on 300 watts, 120°C for 20 minutes. Reaction mixture was diluted with ice/water and neutralized with AcOH to pH 5 at 0 °C, and the precipitate was collected by filtation, washed with water and dried: 2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-3H-pyrido[3,4-d]pyrimidin-4-one (33% yield over 2 steps).

481e) A suspension of 2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-3H-pyrido[3,4-d]pyrimidin-4-one (0.85 g, 2.8 mmol), triethylamine (1.3 mL, 9.3 mmol) and 4-dimethylaminopyridine (43.0 mg, 0.352 mmol) in N,N-dimethylformamide (10 mL, 100 mmol) was treated with 2,4,6-triisopropylbenzenesulfonyl chloride (0.98 g, 3.2 mmol) and the mixture was stirred at room temperature for 1 hour. tert-Butyl-1-piperazinecarboxylate (0.65 g, 3.5 mmol) was added and the mixture was stirred at room temperature overnight. Water (40 mL) was added and the mixture was stirred vigorously for 1 hour. The suspension was filtered, rinsed with water and dried. The solid was dissolved in DCM, the solution was dried ($MgSO_4$), filtered and the solvent was evaporated under vacuum. The product was isolated by flash chromatography (Isco, Silica Gel, 20%→100% Ethyl Acetate/Hexane): 4-[2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester, tan solid (1.03 g).

481f) A reaction tube was charged with 4-[2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (200 mg, 0.428 mmol), aniline (43.9 µL, 0.482 mmol), palladium acetate (16 mg, 0.07 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (38.8 mg, 0.067 mmol), and cesium carbonate (366 mg, 1.125 mmol) in 1,4-dioxane (2 mL). The tube was evacuated and back-filled with nitrogen three times, and then flushed with argon, capped, and heated at 100°C for 3 h. The reaction mixture was cooled to room temperature and partitioned between ether and water. The organic extracts were dried ($MgSO_4$), then the solvent was

evaporated under reduced pressure. The product was used in the next step without further purification. The crude product obtained in step 1 was treated with trifluoroacetic acid (1.48 mL, 19.2 mmol) in methylene chloride (5.92 mL) at room temperature until reaction was complete (by hplc); approx. 1h. The volatiles were evporated under reduced pressure and the product was isolated by reverse phase chromatography (Gilson) followed by neutralization by cation-exchange column (Strata, from Phenomenex) filtration and releasing with methanolic ammonia: [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine (133 mg, 73% yield over 2 steps); bright yellow solid; MP: 221-226 C; ^{1}H-NMR ($CDCl_3$) δ: 9.11 (s, 1H), 8.36 (d, J = 5.2 Hz, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.80 (dd, J = 5.2; 1.3 Hz, 1H), 7.45 (d, J = 8.3 Hz, 2H), 7.37 (dd, J = 8.4; 8.4 Hz, 2H), 7.07 (t, J = 8.4 Hz, 1H), 6.68 (br s, 1H), 3.75 (br s, 4H), 3.01 (m, 4H), 269 (m, 1H), 1.59 (water and exhcangeable NH), 1.26 (m, 2H), 1.00 (m, 2H); LC/MS (ESI+): 424.17 (M+H).

Example 482. 2-{4-[5-Cyclopropyl-4-(4-hydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

This product was prepared from 2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-3H-pyrido[3,4-d]pyrimidin-4-one according to a procedure similar to Example 481e,f: white solid; ^{1}H NMR (dmso-d_6) δ: 10.40 (s, 1H), 8.98 (s, 1H), 8.64 (br s, 1H), 8.49 (dd, J = 6.0; 0.4 Hz, 1H), 8.45 (d, J = 5.2 Hz, 1H), 8.37 (br s, 1H), 8.10 (s, 1H), 7.88 (dd, J = 5.2; 1.4 Hz, 1H), 7.30 (dd, J = 6.0; 1.4 Hz, 1H), 7.81 (br s, 1H), 4.11 (m, 2H), 3.80 (br s, 1H), 3.50 (br s, 2H), 2.60 (br s, 1H), 1.90 (m, 2H), 1.52 (br s, 1H), 1.26 (m, 2H), 1.04 (m, 2H); LC/MS (ESI+): 465.2 (M+H).

Example 483. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine

This product was prepared from 2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-3H-pyrido[3,4-d]pyrimidin-4-one according to a procedure similar to Example 481e,f: yellow lyophilate; ^{1}H NMR (dmso-d_6) δ: 10.40 (s, 1H), 9.08 (s, 1H), 9.03 (br s, 2H), 8.81 (s, 1H), 8.45 (d, J = 5.3 Hz, 1H), 8.20 (s, 1H), 7.92 (m, 1H), 7.86 (m, 1H), 7.69 (m, 1H), 6.65 (m, 1H),3.97 (br s, 4H), 3.34 (br s, 4H), 2.69 (m, 1H), 1.27 (m, 2H), 1.09 (m, 2H); LC/MS (ESI+): 443.2 (M+H).

Example 484. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine

This product was prepared from 4-[2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester according to a procedure similar to Example 481f: off-white foam; ^{1}H-NMR ($CDCl_3$) δ: 9.12 (s, 1H), 8.39 (d, J = 5.3 Hz, 1H), 8.23 (m, 1H), 8.05 (s, 1H), 7.93 (s, 1H), 7.85 (m, 1H), 7.14 (m, 2H), 6.97 (m, 2H), 6.86 (br s, 1H), 3.76 (br s, 4H), 3.03 (m, 4H), 2.69 (m, 1H), 1.93 (br s, water and exch. protons), 1.27 (m, 2H), 1.01 (m, 2H); LC/MS (ESI+): 442.1 (M+H).

Example 485. (±)-2-{4-[5-Cyclopropyl-4-cis-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

This product was prepared from 2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-3H-pyrido[3,4-d]pyrimidin-4-one according to a procedure similar to Example 481e,f: tan solid; ^{1}H-NMR ($CDCl_3$) δ: 9.18 (s, 1H), 8.52 (s, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.39 (m, 2H), 8.15 (m, 2H), 7.93 (m, 1H), 7.04 (m, 1H), 3.95 (m, 7H), 2.78 (br s, 1H), 2.60 (m, 1H), 1.87 (m, 2H), 1.63 (br s, water), 1.27 (m, 2H), 1.01 (m, 2H); LC/MS (ESI+): 481.0 (M+H).

Example 486. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-o-tolyl-amine

This product was prepared from 4-[2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester according to a procedure similar to Example 481f: yellow foam; ^{1}H-NMR ($CDCl_3$) δ: 9.08 (s, 1H), 8.33 (d, J = 5.2 Hz, 1H), 8.02 (s, 1H), 7.81 (s, 1H), 7.76 (m, 1H), 7.60 (m, 1H), 7.24 (m, 2H), 7.08 (m, 1H), 6.54 (br s, 1H), 3.72 (br s, 4H), 2.97 (m, 4H), 2.67 (m, 1H), 3.04 (s, 3H), 1.95 (br s, NH), 1.25 (m, 2H), 0.99 (m, 2H); LC/MS (ESI+): 438.1 (M+H).

Example 487. 2-{4-[5-Cyclopropyl-4-((3R,4S)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

This product was obtained by separation of enantiomers (SCF chiral chromatography) of racemic Example 485.

Example 488. 2-{4-[5-Cyclopropyl-4-((3S,4R)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

This product was obtained by separation of enantiomers (SCF chiral chromatography) of racemic Example 485. It is the optical antipode of Example 487.

Example 489. 4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-N-(1-phenylpyrazol-4-yl)pyridin-2-amine: A tube was charged with 4-[2-(2-chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (131.4 mg, 0.2877 mmol), 1-phenyl-1H-pyrazol-4-ylamine (55.0 mg, 0.346 mmol),

Palladium Acetate (7.9 mg, 0.035 mmol), 9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (21.0 mg, 0.0364 mmol), cesium carbonate (144.6 mg, 0.4438 mmol) and 1,4-dioxane (1 mL). The tube was evacuated and back flushed with nitrogen. The tube was sealed and the reaction mixture was heated at 90°C for 18 hours. The mixture was cooled to room temperature and diluted with water (10 mL). The suspension was stirred for 15 minutes, filtered, rinsed with water and dried by suction to yield a dark solid.

The dark solid was suspended in methylene chloride (3 mL) and stirred at room temperature. Trifluoroacetic Acid (1 mL, 20 mmol) was added dropwise and the mixture was stirred at room temperature for 1 hour. The volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus with 5%→30% acetonitrile: water (w/ 0.1% TFA as modifier) solvent gradient. The desired fractions were combined, frozen and lyophilized. The recovered lyophilate was consistent for desired 4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-N-(1-phenylpyrazol-4-yl)pyridin-2-amine (14mg, 10%). ^{1}H NMR (DMSO-d_6): δ-8.91 (bs, 1H), 8.71 (bs, 3H), 8.41 (s, 1H), 8.34 (d, 1H, J=5.43Hz), 7.88 (s, 1H), 7.84 (s, 1H), 7.83 (dd, 2H, JJ=1.09, 8.69Hz), 7.66 (dd, 1H, JJ= 1.30, 5.65), 7.47-7.53 (m, 2H), 7.25-7.31 (m, 1H), 4.10 (s, 3H), 3.88 (bs, 4H), 3.33 (bs, 4H). LCMS (ESI+) 480.3 (M+H).

Example 490. (2,3-Dimethyl-2H-indazol-6-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3, 4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine: A tube was charged with 4-[2-(2-chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (131.4 mg, 0.2877 mmol), 2,3-dimethyl-2H-indazol-6-ylamine (55.7 mg, 0.346 mmol), palladium acetate (7.9 mg, 0.035 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (21.0 mg, 0.0364 mmol), cesium carbonate (144.6 mg, 0.4438 mmol) and 1,4-dioxane (1 mL). The tube was evacuated and back flushed with nitrogen. The tube was sealed and the reaction mixture was heated at 90°C for 18 hours. The mixture was cooled to room temperature and diluted with water (10 mL). The suspension was stirred for 15 minutes, filtered, rinsed with water and dried by suction to yield a dark solid.

The dark solid was suspended in methylene chloride (3 mL, 40 mmol) and stirred at room temperature. Trifluoroacetic Acid (1 mL, 20 mmol) was added dropwise and the mixture was stirred at room temperature for 1 hour. The volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus with 5%→30%

acetonitrile: water (w/ 0.1% TFA as modifier) solvent gradient. The desired fractions were combined, frozen and lyophilized. The recovered lyophilate was consistent for desired (2,3-dimethyl-2H-indazol-6-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3, 4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine (38mg, 27%).

^{1}H NMR (DMSO-d_6): δ-9.50 9bs, 1H), 8.91 (bs, 3H), 8.42 (s, 1H), 8.36 (d, 1H, J=5.19Hz), 8.24 (bs, 1H), 8.01 (bs, 1H), 7.72 (dd, 1H, J=1.20, 5.28Hz), 7.58 (d, 1H, J=9.07Hz), 7.06 (dd, 1H, JJ=1.65, 8.87Hz), 4.10 (s, 3H), 3.99 (s, 3H0, 3.89 (bs, 4H), 3.33 (bs, 3H), 2.57 (s, 3H). LCMS (ESI+) 482.1 (M+H).

Example 491. [1-(2-Fluoro-phenyl)-1H-pyrazol-4-yl]-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3, 4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

A tube was charged with 4-[2-(2-chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (131.4 mg, 0.2877 mmol), 1-(2-fluoro-phenyl)-1H-pyrazol-4-ylamine (61.2 mg, 0.346 mmol), palladium acetate (7.9 mg, 0.035 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (21.0 mg, 0.0364 mmol), cesium carbonate (144.6 mg, 0.4438 mmol) and 1,4-dioxane (1 mL). The tube was evacuated and backflushed with nitrogen. The tube was sealed and the reaction mixture was heated at 90°C for 18 hours. The mixture was cooled to room temperature and diluted with water (10 mL). The suspension was stirred for 15 minutes, filtered, rinsed with water and dried by suction to yield a dark solid.

The dark solid was suspended in methylene chloride (3 mL) and stirred at room temperature. Trifluoroacetic Acid (1 mL, 20 mmol) was added dropwise and the mixture was stirred at room temperature for 1 hour. The volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus with 5%→30% acetonitrile: water (w/ 0.1% TFA as modifier) solvent gradient. The desired fractions were combined, frozen and lyophilized. The recovered lyophilate was consistent for desired [1-(2-fluoro-phenyl)-1H-pyrazol-4-yl]-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3, 4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine (12mg, 8.4%)

^{1}H NMR (DMSO-d_6): δ-9.51 (bs, 1H), 8.90 (bs, 3H), 8.59 (d, 1H, J=3.17Hz), 8.41 (s, 1H), 8.33 (d, 1H, J=5.50Hz), 7.83-7.88 (m, 3H), 7.69 (dd, 1H, J=1.33, 5.50Hz), 7.33-7.51 (m, 3H), 4.10 (s, 3H), 3.88 (bs, 4H), 3.33 (bs, 4H). LCMS (ESI+) 490.1 (M+H). HPLC >95% pure (retaintion time =1.7 min. in G method).

Example 492. [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin- 2-yl]-(1-phenyl-1H-pyrazol-4-yl)-amine.

A tube was charged with 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (403.0 mg, 0.8631 mmol), 1-Phenyl-1H-pyrazol-4-ylamine (165.0 mg, 1.036 mmol), Palladium Acetate (24 mg, 0.10 mmol), 9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (63.1 mg, 0.109 mmol), Cesium Carbonate (433.8 mg, 1.331 mmol) and 1,4-Dioxane (4 mL). The tube was evacuated and backflushed with nitrogen. The tube was sealed and the reaction mixture was heated at 90°C for 18 hours. The mixture was cooled to room temperature and diluted with water (10 mL). The suspension was stirred for 15 minutes, filtered, rinsed with water and dried by suction to yield a dark solid.

The dark solid was suspended in methylene chloride (8 mL) and stirred at room temperature. Trifluoroacetic Acid (4 mL, 50 mmol) was added dropwise and the mixture was stirred at room temperature for 1 hour. The volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus with 5%→30% acetonitrile: water (w/ 0.1% TFA as modifier) solvent gradient. The desired fractions were combined, frozen and lyophilized. The recovered lyophilate was consistent for desired [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin- 2-yl]-(1-phenyl-1H-pyrazol-4-yl)-amine (10mg, 4%).

^{1}H NMR (DMSO-d_6): δ-9.40 (s, 1H), 8.97 (s, 1H), 8.7 (s, 1H), 8.35 (d, 1H, J=5.65Hz), 8.09 (s, 1H), 7.78-7.85 (m, 4H), 7.63 (dd, 1H, J=1.42, 5.34Hz), 7.49 (t, 2H, J=8.37Hz), 7.27 (t, 1H, J=7.48Hz), 3.52-3.88 (bm, 4H), 2.58-2.85 (bm, 5H), 1.20-1.32 (m, 2H), 1.00-1.06 (m, 2H). LCMS (ESI+) 490.19 (M+H). HPLC >95% pure (retaintion time =1.8 min. in G method).

Example 493. [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin- 2-yl]-(2,3-dimethyl-2H-indazol-6-yl)-amine

A tube was charged with 4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (241.2 mg, 0.5166 mmol), 2,3-Dimethyl-2H-indazol-6-ylamine (100.0 mg, 0.6203 mmol), Palladium Acetate (14 mg, 0.063 mmol), 9,9-Dimethyl-4,5-bis(diphenylphosphino)xanthene (37.8 mg, 0.0653 mmol), Cesium Carbonate (259.6 mg, 0.7968 mmol) and 1,4-Dioxane (2 mL). The tube was evacuated and backflushed with nitrogen. The tube was sealed and the reaction mixture was heated at 90°C for 18 hours. The mixture was cooled to room temperature and diluted with water (10 mL). The suspension was stirred for 15 minutes, filtered, rinsed with water and dried by suction to yield a brown solid.

The dark solid was suspended in Methylene chloride (5 mL, 70 mmol) and stirred at room temperature. Trifluoroacetic Acid (2 mL, 30 mmol) was added dropwise and the mixture was stirred at room temperature for 1 hour. The volatiles were evaporated. The residue was purified via reverse phase chromatography using a Gilson apparatus with 5%→30% Acetonitrile: Water (w/ 0.1% TFA as modifier) solvent gradient. The desired fractions were combined, frozen and lyophilized. The recovered lyophilate was consistent with [4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin- 2-yl]-(2,3-dimethyl-2H-indazol-6-yl)-amine (60mg, 24%).

^{1}H NMR (DMSO-d_6): δ-9.32 (s, 1H), 8.96 (s, 1H), 8.35 (d, 1H, J=5.25Hz), 8.28 (bs, 1H), 8.08 (s, 1H), 7.95 (bs, 1H), 7.68 (dd, 1H, J=1.36, 5.45Hz), 7.52 (d, 1H, J=8.95Hz), 7.04 (dd, 1H, J=1.56, 8.95Hz), 3.97 (s, 3H), 2.53-2.70 (m,5H), 2.45 (bs, 4H), 2.45 (s, 3H), 1.21-1.29 (m, 2H), 1.00-1.06 (m, 2H). LCMS (ESI+) 492.20 (M+H). HPLC >95% pure (retaintion time =1.7 min. in G method).

Example 494. Phenyl-[4-(4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine. Following a procedure similar to 303c, 4-[2-(2-Chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (180 mg, 0.42 mmol), and Aniline (51.1 uL, 0.561 mmol)were converted to the title compound 35.28 mgs, 22% yield. LC/MS = 384.2 (M+H)+

Example 495. [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin- 2-yl]-(2-fluoro-pyridin-3-yl)-amine: A tube was charged with 4-[2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (100 mg, 0.214 mmol), 2-fluoro-pyridin-3-ylamine (46.2 mg, 0.412 mmol), palladium acetate (12.0 mg, 0.053 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (34.0 mg, 0.058 mmol), cesium carbonate (120 mg, 0.368 mmol) and 1,4-dioxane (0.7 mL, 8 mmol). The tube was evacuated and backflushed with nitrogen. The tube was sealed and the reaction mixture was heated at 100°C for 3h. The mixture was cooled to room temperature and diluted with dichloromethane (10 mL) and filtered through celite. The filtrate was evaporated to a dark resin.

The brown resin was dissolved in methylene chloride (0.7 mL, 10 mmol) and trifluoroacetic acid (0.7 mL, 9 mmol) was added. The mixture was stirred for 1 hour at room temperature and concentrated. The residue was purified via reverse phase chromatography using a Gilson apparatus. The desired fractions were loaded onto a SCX cartridge and rinsed with methanol and the product was released with 2M ammonia in

methanol. The ammonia filtrate was evaporated and placed under high vacuum for 2 hours. The recovered yellow solid (35 mg, 37%) was consistent for the title compound. 1H NMR (300MHz, DMSO-d6): 9.26 (s, 1H), 8.98 (s, 1H), 8.88 (t, J=9Hz, 1H), 8.34 (d, J=5Hz, 1H), 8.18 (s, 1H), 8.10 (s, 1H), 7.79 (d, J=5Hz, 1H), 7.75 (d, J=4Hz, 1H), 7.31 (m, 1H), 3.72 (m, 4H), 2.88 (br s, 4H), 2.62 (m, 1H), 1.26 (d, J=8Hz, 2H), 1.04 (d, J=5Hz, 2H), MS: 433 (M+H).

Example 496. [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-isoxazol-3-yl)-amine

4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester (75 mg, 0.16 mmol), 5-methyl-isoxazol-3-ylamine (32.2 mg, 0.3283 mmol), bis(dibenzylideneacetone)palladium(0) (5 mg, 0.0085 mmol), XANTPHOS (10 mg, 0.171 mmol), and lithium hexamethylsilazide (55 mg, 0.328 mmol) were combined in tetrahydrofuran (3 mL), degassed with Argon and subjected to reaction in a microwave at 120C for six hours. Additional palladium, isoxazole, and silazide were added and the microwave temperature was raised to 150C for an additional six hours. The reaction was concentrated and purification was effected via reverse phase chromatography to afford the title compound (2 mg, 3%). MS: 419.23 (M+H).

Example 497. 2-[2-(3-Piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol. Following a procedure similar to Example 303c, 2-(2-Chloro-pyridin-4-yl)- pyrido[3,4-d]pyrimidin-4- ol (67 mg, 0.26 mmol) and 4-(3-Amino-phenyl)-piperazine- 1-carboxylic acid tert-butyl ester (1.1 eq) were converted to the title compound isolated as the bis-TFA salt (21 mg, 13%). LC/MS: M+H+ = 400.

Example 498. 2-[2-(3-Piperazin-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin- 4-ol. Following a procedure similar to Example 303c, 2-(2-Chloro-pyridin-4-yl)- pyrido[3,4-d]pyrimidin-4- ol (143 mg, 0.56 mmol) and 4-(3-Amino-benzyl)-piperazine- 1-carboxylic acid tert-butyl ester (1.1 eq) were converted to the title compound isolated as the bis TFA salt (51.4 mg, 14%). LC/MS: M+H+ = 414.

Example 499. 2-[2-(1-Piperidin-4-ylmethyl-1H-pyrazol-4-ylamino)-pyridin-4-yl]-pyrido[3, 4-d]pyrimidin-4-ol. Following a procedure similar to Example 303c, 2-(2-Chloro-pyridin-4-yl)- pyrido[3,4-d]pyrimidin-4- ol (145 mg, 0.56 mmol) and 4-(4-Amino-pyrazol-1-ylmethyl)- piperidine-1-carboxylic acid tert-butyl ester (1.1 eq) were converted to the title compound isolated as the bis TFA salt (20.56 mg, 6%). LC/MS: M+H+ = 403.

Example 500. {5-Methoxy-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4- d]pyrimidin-4-yl}-methyl-amine. Following a procedure similar to Example 303b, 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin- 4-ol (362 mgs, 1.25 mmol) and methylamine•HCl (1.1 eq) were converted to [2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-methyl- amine (64% yield) which was converted using a procedure analogous to Example 497 to the title compound islated as a bis TFA salt (14 mgs, 5% yield), LC/MS: M+H+ = 443.25

Example 501. (5-Methoxy-2-{2-[4-(2-pyrrolidin-1-yl-ethoxy)-phenylamino]-pyridin-4-yl}- pyrido[3,4-d]pyrimidin-4-yl)-methyl-amine. Following a procedure analogous to Example 500, 4-(2-Pyrrolidin-1-yl-ethoxy)- phenylamine (44 mg, 0.21 mmol) was converted to t he title compound isolated as the bis-TFA salt (6.35 mgs, 5% yield) LC/MS: M+H+ = 472.

Example 502. {5-Methoxy-2-[2-(3-piperidin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine. Following a procedure analogous to Example 500, 4-(3-Amino-phenyl)-piperidine-1-carboxylic acid tert-butyl ester (0.1468 g, 0.5312 mmol) was converted to the title compound isolated as a bis-TFA salt (23.61 mgs, 7% yield). LC/MS: M+H+ = 442.

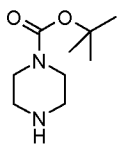
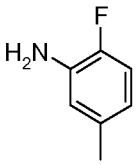
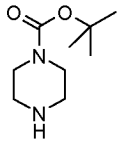
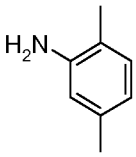
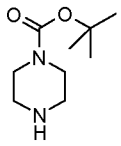
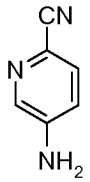
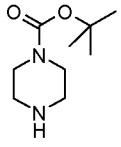
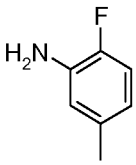
Example 503. [4-(5-Methoxy-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1- yl-phenyl)-amine

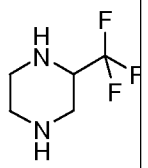
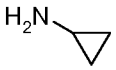
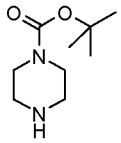
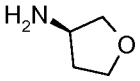
503a) 2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol (208 mg, 0.720 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (221.1 mg, 0.7301 mmol), Triethylamine (0.31 mL, 2.2 mmol), and 4-Dimethylaminopyridine (8.8 mg, 0.072 mmol) in N,N-Dimethylformamide (2 mL, 30 mmol) were stirred at room temperature for 1h, Hydrazine hydrate (0.05410 g, 1.081 mmol) was added and the reaction was stirred overnight. The product precipitated and was triturated from ether.Taking on without further purification.

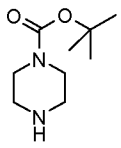
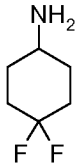
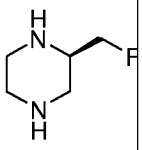
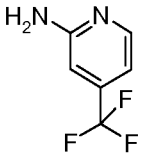
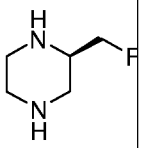
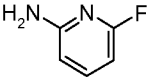
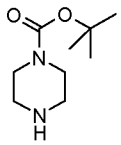
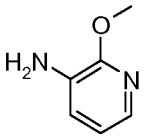
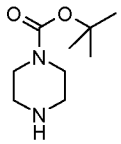
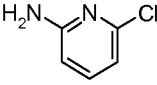
503b) [2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-hydrazine (0.218 g, 0.720 mmol) was treated with 1,4-Dioxane (5.0 mL, 65 mmol) and Water (0.6 mL, 30 mmol) and then Silver(I) Oxide (334 mg, 1.44 mmol) and stirred at room temperature. After 1.5 h, LC/MS indicated major product (M+H)+ = 273. Filtered off silver salts and concentrated and put on high vac. Purified by ISCO chomatography 12g SiO2, gradient elution 0% to 100% EA/hexane over 13 minutes to give 2-(2-Chloro-pyridin-4-yl)- 5-methoxy-pyrido[3,4-d]pyrimidine

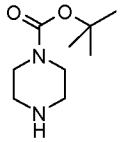
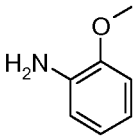
503c) Using a procedure analogous to Example 497 to the title compound 2-(2-Chloro-pyridin-4-yl)- 5-methoxy-pyrido[3,4-d]pyrimidine (31 mgs, 0.11 mmol) was converted to the title compound (6.37 mgs, 13% yield). LC/MS: M+H+ = 414.

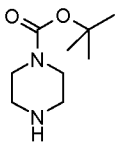
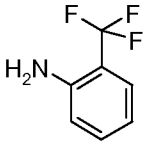
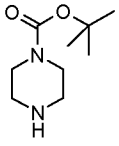
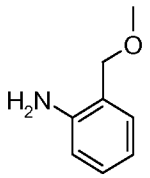
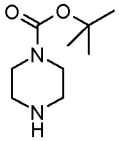
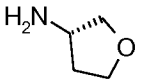
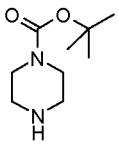
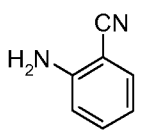
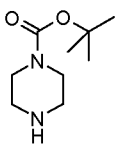
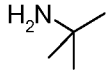
The following compounds were synthesised according to the general synthesis shown in scheme [B4]

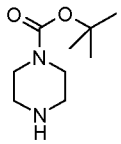
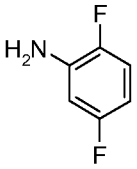
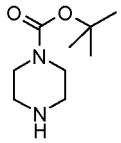
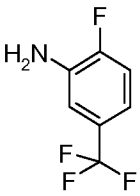
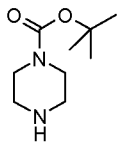
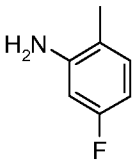
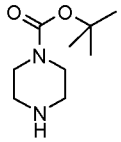
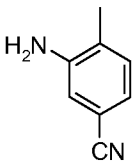
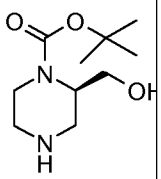
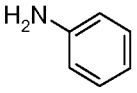
Ex	Amine 1	Amine 2	Analysis		Name
			LCMS	NMR	
504			method 5: RT: 2.87min, MI: 456 [M+H]	(DMSO, 500 MHz) 9.04 (1H, s), 8.30 (1H, d), 8.17 (1H, s), 8.05 (1H, s), 7.94 (1H, d), 7.73 (1H, d), 7.13 (1H, d), 6.87(1H, m), 3.90 (4H, very broad s), 3.31 (4H, broad s), 2.68 (1H, m), 2.29 (3H, s), 1.25 (2H ,m), 1.06 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methyl-phenyl)-amine
505			method 5: RT: 2.20min, MI: 452 [M+H]	(DMSO,500 MHz) 9.07 (1H, s), 8.19 (1H, s), 8.14 (1H, d), 7.98 (1H, s), 7.73 (1H, d), 7.33 (1H, s), 7.22 (1H, d), 7.03 (1H, d), 3.89 (4H, very broad s), 3.30 (4H, broad s), 2.48 (1H, m), 2.29 (3H, s), 2.20 (3H, s), 1.25 (2H, m), 1.07 (2H,m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-dimethyl-phenyl)-amine
506			method 5: RT: 5.19min, MI: 450 [M+H]	(DMSO) 10.27ppm (s, 1H), 9.06ppm (s, 1H), 8.95ppm (d, 1H), 8.58ppm (dd, 1H), 8.48ppm (d, 1H), 8.19ppm (s, 1H), 8.06ppm (s, 1H), 7.91ppm (m, 2H), 3.85ppm (s, 4H), 3.90ppm (broad s, 4H), 2.68ppm (m, 1H), 1.27ppm (m, 2H), 1.09ppm (m, 2H). A second set of piperazine 4H is suspected to be running under the DMSO water peak at 3.33ppm.	5-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile
507			method 5: RT: 2.10min, MI: 426 [M+H]	1H NMR (DMSO, 500 MHz) 9.08 (1H, s), 8.78 (1H, s), 8.47 (1H, d), 8.31 (1H, m), 8.19 (1H, s), 8.16 (1H, d), 7.94 (2H, dd), 3.93 (4H, very broad s), 3.31 (4H, br s), 2.68 (1H, m), 1.26-1.24 (2H, m), 1.08-1.05 (2H, m).	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine

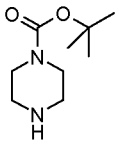
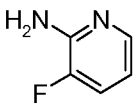
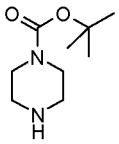
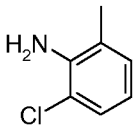
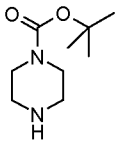
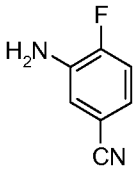
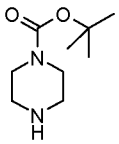
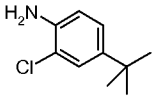
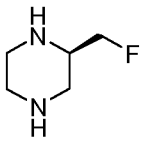
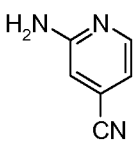
508			method 5: RT 3.28 min, MI: 456.17 [M+H]	1H NMR (DMSO, 500MHz) 8.99 (1H, s), 8.15 (1H, d), 8.10 (1H, s), 7.64 (1H, s), 7.49 (1H, d), 6.98 (1H, s), 4.56-4.25 (1H, m, br), 3.95 (1H, d, br), 3.65 (s, br, 4H), 3.03 (4H, s, br), 1.28-1.22 (3H, m, br), 1.05-1.01 (2H, m, br), 0.73 (2H, d, br), 0.47 (2H, s, br).	Cyclopropyl-{4-[5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine
509			method 5: RT 1.73 min: , MI: 418.19 [M+H]	1H NMR (DMSO, 500MHz) 8.99 (1H, s), 8.13 (1H, d), 8.12 (1H, s), 7.58 (1H, s), 7.45 (1H, d), 7.05 (1H, d), 4.43 (1H, m, br), 3.91-3.82 (2H, m), 3.80 (4H, m, br), 3.75-3.70 (1H, m), 3.54 (1H, dd), 3.20 (4H, m, br), 2.70-2.67 (1H, m), 2.21-2.14 (1H, m), 1.85-1.79 (1H, m), 1.24-1.22 (2H, m), 1.05-1.04 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(R)-tetrahydro-furan-3-yl-amine

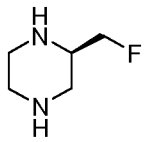
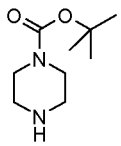
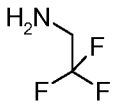
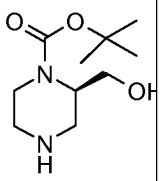
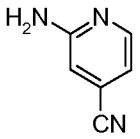
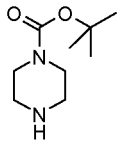
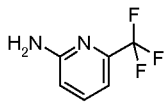
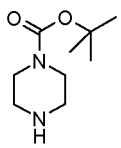
510			method 5: RT: 2.37 min,MI:466.20 [M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.11 (1H, d), 8.06 (1H, s), 7.54 (1H, s), 7.41 (1H, d), 6.80 (1H, d), 4.02-3.97 (1H, m, br), 3.79-3.54 (4H, m, br), 2.84 (4H, m, 2.62-2.59 (1H, m), 2.10-1.89 (6H, m, br), 1.59-1.53 (2H, m, br), 1.26-1.22 (2H, m), 1.02-0.99 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,4-difluoro-cyclohexyl)-amine
511			method 5: RT: 2.31 min,MI: 525 [M+H]	1H NMR (DMSO, 500MHz) 9.00 (1H, s), 8.68 (1H, s), 8.50 (1H, m), 8.45 (1H, m), 8.32 (1H, m), 8.11 (1H, s), 7.89 (1H, d), 7.85 (1H, m), 4.47 (1H, d), 4.38 (1H, d), 4.30 (1H, m), 4.16 (1H, m), 3.32 (1H, m), 3.22 (2H, m), 3.13 (2H, m), 2.62 (1H, m), 1.26-1.24 (2H, m), 1.05-1.03 (2H, m)	{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-trifluoromethyl-pyridin-2-yl)-amine
512			method 5: RT: 2.31 min,MI: 525 [M+H]	1H NMR (DMSO, 500MHz) 9.00 (1H, s), 8.68 (1H, s), 8.50 (1H, m), 8.45 (1H, m), 8.32 (1H, m), 8.11 (1H, s), 7.89 (1H, d), 7.85 (1H, m), 4.47 (1H, d), 4.38 (1H, d), 4.30 (1H, m), 4.16 (1H, m), 3.32 (1H, m), 3.22 (2H, m), 3.13 (2H, m), 2.62 (1H, m), 1.26-1.24 (2H, m), 1.05-1.03 (2H, m)	{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine
513			455.2 (M+H)	($CDCl_3$) 9.12 (d, J = 1.6 Hz, 1H), 8.70 (dd, J = 8.0; 1.5 Hz, 1H), 8.40 (d, J = 4.4 Hz, 1H), 8.06 (s, 1H), 7.89 (s, 1H), 7.83 (dd, J = 5.2; 1.3 Hz, 1H), 7.75 (m, 1H), 7.19 (s, 1H), 6.92 (m, 1H), 4.07 (s, 3H), 3.77 (br s, 4H), 3.04 (m, 4H), 2.70 (m, 1H), 1.84 (exch. protons), 1.27 (m, 2H), 1.01 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-pyridin-3-yl)-amine
514			459.1 (M+H)	(dmso-d6) 10.24 (s, 1H), 8.98 (s, 1H), 8.75 (s, 1H), 8.41 (d, J = 5.2 Hz, 1H), 8.10 (s, 1H), 7.88 (m, 1H), 7.82 (m, 1H), 7.74 (m, 1H), 6.97 (d, J = 7.5	(6-Chloro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-

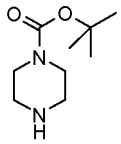
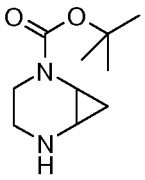
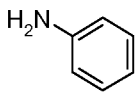
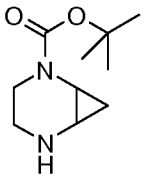
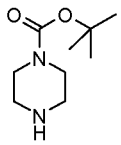
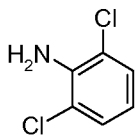
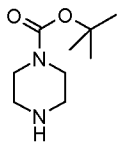
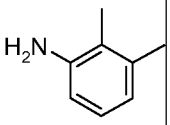
				Hz, 1H), 3.75 (br m, 4H), 2.86 (br m, 4H), 2.62 (m, 1H), 1.25 (m, 2H), 1.03 (m, 2H)	pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
515			454.2 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-phenyl)-amine

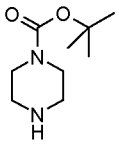
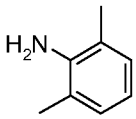
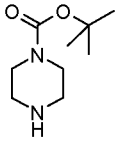
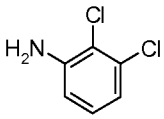
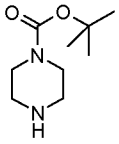
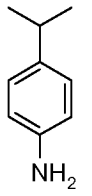
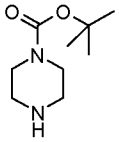
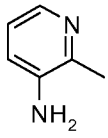
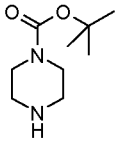
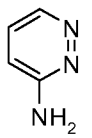
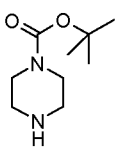
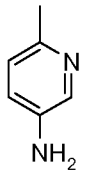
516			492.1 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine
517			468.2 (M+H)+	(CDCl$_3$) 9.11 (s, 1H), 8.37 (dd, J = 5.3; 0.4 Hz, 1H), 8.04 (s, 1H), 7.96 (s, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.79 (dd, J = 5.3; 1.3 Hz, 1H), 7.72 (br s, 1H), 7.35 (m, 1H), 7.27 (m, 1H), 7.01 (m, 1H), 4.57 (s, 2H), 3.75 (br s, 4H), 3.43 (s, 3H), 3.01 (m, 4H), 2.69 (m, 1H), 2.04 (br s, exch. protons), 1.26 (m, 2H), 1.00 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxymethyl-phenyl)-amine
518			method 5: RT:2.27 min,MI: 418.17 M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.11 (1H, d), 8.06 (1H, s), 7.56 (1H, s), 7.43 (1H, dd), 7.01 (1H, d), 4.45-4.39 (1H, m), 3.90-3.53 (4H, s, br), 3.89 (1H, dd), 3.85 (1H, q), 3.75-3.70 (1H, m), 3.55 (1H, dd), 3.15 (2H, d), 2.85 (4H, s, br), 2.62-2.61 (1H, m), 2.20-2.16 (1H, m), 1.85-1.80 (1H, m), 1.26-1.22 (2H, m), 1.02-1.01 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(S)-tetrahydro-furan-3-yl-amine
519			449.1 (M+H)+	(CDCl$_3$) 9.14 (m, 2H), 8.42 (d, J = 1.4 Hz, 1H), 8.07 (s, 1H), 7.93 (d, J = 8.1 Hz, 1H), 7.84 (dd, J = 8.1; 5.9 Hz, 1H), 7.68 (m, 2H), 7.39 (m, 2H), 3.82 (m, 4H), 3.05 (m, 4H), 2.71 (m, 1H), 1.7 (br s, exch. H's), 1.28 (m, 2H), 1.02 (m, 2H)	2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile
520			method 5: RT: 3.73 min,MI:404.	1H NMR (DMSO, 500MHz) 8.92 (1H, s), 8.07 (2H, dd), 7.56 (1H, s), 7.35 (1H, s), 6.47 (1H, s), 3.75-3.54 (4H, m, br), 2.83 (4H, m, br), 2.62 (1H, m, br), 1.41 (9H, s), 1.24	tert-Butyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-

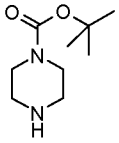
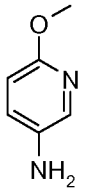
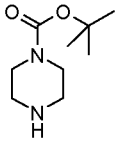
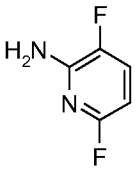
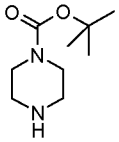
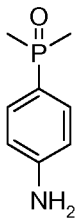
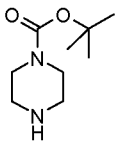
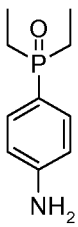
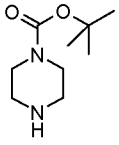
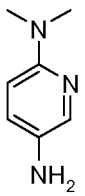
			30 [M+H]	(2H, m, br), 1.00 (2H, m, br).	yl]-amine
521			method 5: RT: 3.90 min,MI: 460 [M+H]	1H NMR (DMSO, 500MHz) 9.25 (1H, s), 9.05 (1H, s), 8.97 (1H, s, br), 8.39 (1H, d), 8.24 (1H, s), 8.17 (1H, s), 7.78 (1H, d), 7.28 (1H, m), 6.76 (1H, m), 3.96-3.88 (4H, s,br), 3.31 (4H, s, br), 2.65 (1H, m), 1.28-1.25 (2H, m), 1.08-1.05 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-difluoro-phenyl)-amine
522			method 5: RT:4.02 min,MI: 510 [M+H]	1H NMR (DMSO, 500MHz) 9.37 (1H, s), 9.06 (1H, s), 8.97 (1H, s br), 8.41 (1H, d), 8.23 (1H, s), 8.18 (1H, s), 7.84 (1H, d), 7.47 (1H, m), 7.32 (1H, m), 3.96-3.88 (4H, s br), 3.31 (4H, s br), 2.65 (1H, m), 1.28-1.25 (2H, m), 1.08-1.05 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-trifluoromethyl-phenyl)-amine
523			method 5: RT:3.80 min,MI: 466 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 8.97 (1H, s br), 8.28 (1H, d), 8.18 (1H, s), 8.05 (1H, s), 7.81 (1H, s), 7.75 (1H, d), 7.23 (1H, d), 6.81 (1H, d), 3.96-3.88 (4H, s br), 3.31 (4H, s br), 2.66 (1H, m), 2.27 (3H,s), 1.28-1.25 (2H, m), 1.08-1.05 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-2-methyl-phenyl)-amine
524				1H NMR (DMSO, 500MHz) 9.06 (1H, s), 8.96 (1H, s br), 8.78 (1H, s), 8.36 (1H, s), 8.33 (1H, d), 8.18 (1H, s), 8.06 (1H, s), 7.78 (1H, d), 7.43 (1H, m), 3.96-3.88 (4H, s br), 3.31 (4H, s br), 2.68 (1H, m), 2.38 (3H, s), 1.28-1.25 (2H, m), 1.08-1.05 (2H, m)	3-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-4-methyl-benzonitrile
525			method 5: RT: 3.20 min,MI: 480 [M+H]	1H NMR (DMSO, 500MHz) 9.30 (1H, s), 9.01 (1H, s), 8.32 (1H, d), 8.16 (1H, s), 7.91 (1H, s), 7.75 (1H, d), 7.70 (1H, d), 7.28 (2H, m), 6.90 (1H, m), 4.43 (4H, m), 4.05 (2H, m), 3.67 (1H, m), 3.48 (1H, m), 3.21 (1H, m), 2.53 (1H, m), 1.28-1.25 (2H, m), 1.3-1.01 (2H, m)	7-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one

526			method 5: RT: 2.33 min,MI:443 [M+H]	1H NMR (DMSO, 500MHz) 11.53 (1H, s), 9.11 (1H, s), 8.92 (1H, s), 8.55 (1H, d), 8.30 (1H, d), 8.24 (1H, s), 8.21 (1H, dd), 7.98 (1H, m), 7.31 (1H, m), 4.01(4H, s), 3.30 (4H, s), 2.68 (1H, m), 1.28 (2H, m), 1.10 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-pyridin-2-yl)-amine
527			method 5: RT: 5.3 min,MI: 472 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 9.02-8.90 (2H, broad s), 8.19 (1H, s), 8.14(1H, d), 7.75 (1H, s), 7.69 (1H, d), 7.45 (1H, d), 7.34(1H, d), 7.27 (1H, m), 3.89 (4H, s), 3.31 (4H, s), 2.67(1H, m), 1.26 (2H, m), 1.07 (2H, m).	(2-Chloro-6-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
528			method 5: RT: 3.68 min,MI:467 [M+H]	1H NMR (DMSO, 500MHz) 9.41 (1H, s), 9.05 (1H, s), 8.98 (1H, d), 8.43(1H, d), 8.23 (1H, s), 8.18 (1H, s), 7.86 (1H, d), 7.49 (1H, m), 3.94 (4H, s), 3.33 (4H, s), 2.69 (1H, m),1.26 (2H, m), 1.08 (2H, m).	3-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-4-fluoro-benzonitrile
529			method 5: RT: 4.21 min,MI:514 [M+H]	1H NMR (DMSO, 500MHz) 9.06 (1H, s), 9.01-8.90 (2H, broad s), 8.24 (1H, d), 8.19 (1H, s), 8.01 (1H, s), 7.84 (1H, d), 7.75 (1H, dd), 7.48 (1H, d), 7.39 (1H, dd), 3.91 (4H, s), 3.32 (4H, s), 2.68 (1H, m), 1.31 (9H, s), 1.24 (2H, m), 1.08 (2H, m).	(4-tert-Butyl-2-chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
530			method 5: RT: 2.13 min,MI: 482 [M+H]	1H NMR (DMSO, 500MHz) 10.00 (1H, s), 9.06 (1H, s), 8.61 (1H, s), 8.48 (2H, m), 8.31 (1H, s), 7.93 (1H, d), 7.26 (1H, d), 4.44 (2H, m), 4.06 (2H, m), 3.77 (1H, m), 3.35 (4H, m), 2.68 (1H, m), 1.28-1.25 (2H, m), 1.02-0.99 (2H, m)	2-{4-[5-Cyclopropyl-4-((R)-3-fluoro methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile

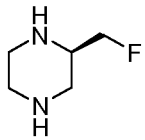
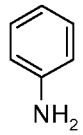
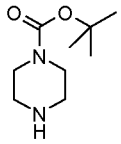
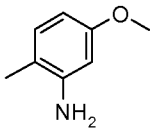
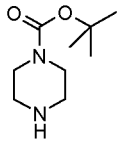
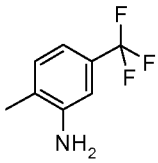
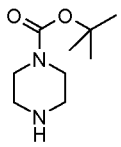
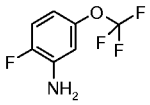
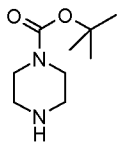
531			method 5: RT: 2.54 min,MI: 475 [M+H]	1H NMR (DMSO, 500MHz) 9.22 (1H, s), 8.98 (1H, s), 8.86 (1H, m), 8.33 (1H, d), 8.15 (1H, s), 8.13(1H, s), 8.11 (1H, s), 7.79 (1H, d), 7.74 (1H, d), 7.30 (1H, m), 4.50 (1H, d), 4.40 (1H, d), 4.17 (1H, m), 3.34 (2H, m), 3.21 (2H, m), 2.99 (2H, m), 2.53 (1H, m), 1.26-1.24 (2H, m), 1.05-1.03 (2H, m).	{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-pyridin-3-yl)-amine
532			method 5: RT: 2.75 min,MI:430.26 [M+H]	1H NMR (DMSO, 500MHz) 8.94 (1H, s), 8.16 (1H, d), 8.07 (1H, s), 7.8 (1H, s), 7.54 (1H, dd), 7.40 (1H, t), 4.24-4.20 (2H, m), 3.86-3.51 (4H, m, br), 2.84 (4H, m, br), 2.63-2.57 (1H, m), 1.25-1.23 (2H, m), 1.02-1.01 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-ethyl)-amine
533			method 5: RT: 2.99 min,MI:506 [M+H]	1H NMR (DMSO, 500MHz) 10.00 (1H, s), 9.06 (1H, s), 8.61 (1H, s), 8.48 (2H, m), 8.31 (1H, s), 7.93 (1H, d), 7.26 (1H, d), 4.44 (2H, m), 4.06 (2H, m), 3.77 (1H, m), 3.35 (4H, m), 2.68 (1H, m), 1.28-1.25 (2H, m), 1.02-0.99 (2H, m)	2-{4-[5-Cyclopropyl-4-(3-oxo-tetrahydro-oxazolo[3,4-a]pyrazin-7-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile
534			method 5: RT: 3.4 min,MI:493 [M+H]	1H NMR (DMSO, 500MHz) 10.53 (1H, s), 8.96 (1H, s), 8.82 (1H, s), 8.43 (1H, m), 8.10 (2H, m), 7.38 (3H, m), 3.81 (4H, m), 2.89 (4H, m), 2.54 (1H, m), 1.27 (2H, m), 1.04 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine
535			method 5: RT: 3.81 min,MI:443 [M+H]	1H NMR (DMSO, 500MHz) 9.90 (1H, s), 8.98 (1H, s), 8.59 (1H, t), 8.48-8.44(1H, td), 8.42 (1H, d), 8.20 (1H, s), 8.07 (1H, d), 7.98 (1H, s), 7.82 (1H, dd), 2.89 (4H, s), 2.63(1H, m), 1.27 (2H, m),	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-

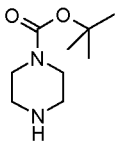
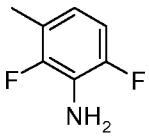
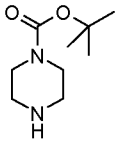
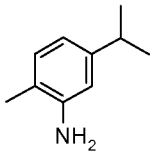
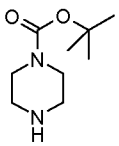
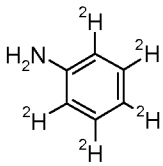
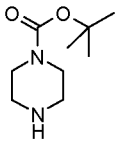
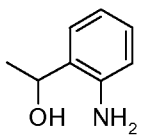
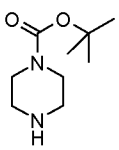
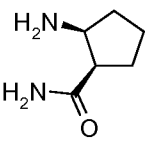
				1.40 (2H, m).	pyridin-3-yl)-amine
536			method 5: RT: 3.31 min,MI:493 [M+H]	1H NMR (DMSO, 500MHz) 8.98 (1H, s), 8.83 (1H, s), 8.44 (1H, d), 8.28 (1H, d), 8.20 (1H, d), 8.10 (1H, s), 8.04 (1H, s), 7.75 (1H, d), 7.69-7.66 (1H, q), 3.42 (4H, broad s), 2.87 (1H, s), 2.62 (1H, m), 1.27 (2H, m), 1.04 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-pyridin-3-yl)-amine
537			436.1		{4-[5-Cyclopropyl-4-(2,5-diaza-bicyclo[4.1.0]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
538			472.1		{4-[5-Cyclopropyl-4-(2,5-diaza-bicyclo[4.1.0]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
539			492.1 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-dichloro-phenyl)-amine
540			452.2 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dimethyl-phenyl)-amine

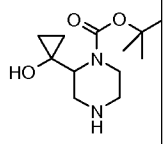
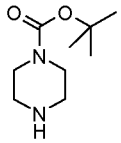
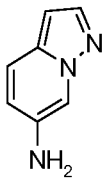
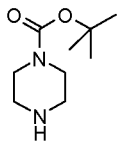
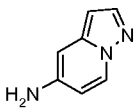
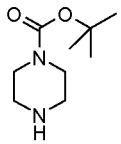
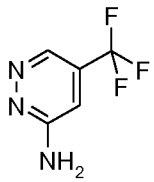
541			452.2 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-dimethyl-phenyl)-amine
542			492.1 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dichloro-phenyl)-amine
543			466.30 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dichloro-phenyl)-amine
544			439.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-pyridin-3-yl)-amine
545			426.15 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridazin-3-yl-amine
546			439.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-

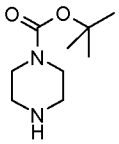
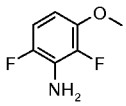
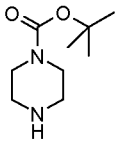
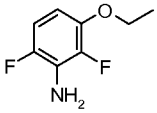
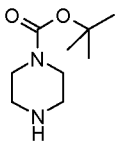
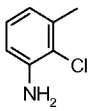
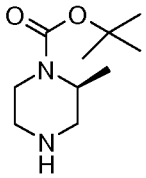
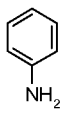
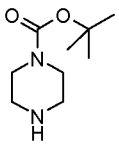
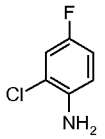
					yl]-(6-methyl-pyridin-3-yl)-amine
547			455.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine
548			461.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,6-difluoro-pyridin-2-yl)-amine
549			500.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(dimethyl-phosphinoyl)-phenyl]-amine
550			528.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(diethyl-phosphinoyl)-phenyl]-amine
551			468.25 (M+H)		N^5-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-N^2,N^2-dimethyl-pyridine-2,5-

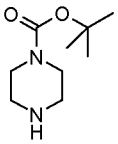
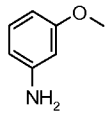
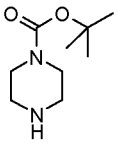
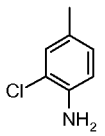
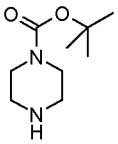
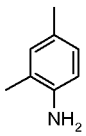
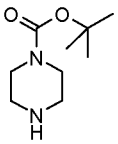
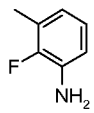
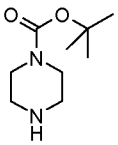
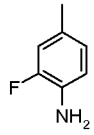
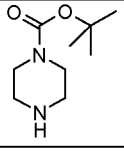
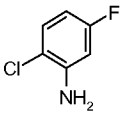
					diamine

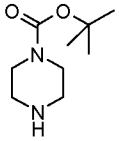
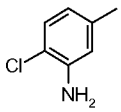
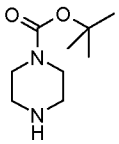
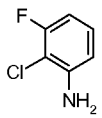
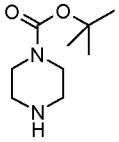
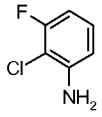
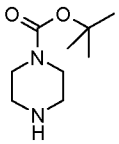
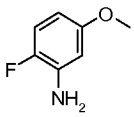
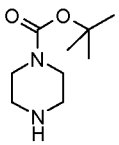
552			method 5: RT: 2.16 min,MI: 456 [M+H]	1H NMR (DMSO, 500MHz) 9.30 (1H, s), 8.98 (1H,s), 8.31 (1H, d), 8.11 (1H, s), 7.90 (1H, s), 7.75 (1H, d), 7.66 (1H, d), 7.27 (2H, m), 6.89 (1H, m), 4.46 (1H, d), 4.38 (1H, d), 4.13 (2H, m), 3.34 (2H, m), 3.00 (3H, m), 2.68 (1H, m), 1.28-1.25 (2H, m), 1.08-1.05 (2H, m)	{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
553			method 5: RT: 3.74 min,MI: 468 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 8.91 (1H, s br), 8.19 (2H, dd), 7.97 (1H, s), 7.72 (1H, d), 7.26 (1H, s), 7.21 (1H, dd), 6.73 (1H, d), 3.99-3.88 (4H, s br), 3.73 (3H, s), 3.30 (4H, s br), 2.62 (1H, m, br), 2.19 (3H, s), 2.20 (3H, s), 1.25-1.23 (2H, m), 1.08-1.05 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-2-methyl-phenyl)-amine
554			method 5: RT: 2.92 min,MI:506 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 8.98 (1H, s br), 8.28 (1H, dd), 8.22 (1H, s), 8.18 (1H, s), 8.06 (1H, s), 7.78 (1H, d), 7.49 (1H, d), 7.36 (1H, d), 3.96-3.88 (4H, s br), 3.30 (4H, s br), 2.68 (1H, m), 2.37 (3H, s), 1.26-1.23 (2H, m), 1.08-1.05 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-5-trifluoromethyl-phenyl)-amine
555			method 5: RT: 3.30 min,MI: 526 [M+H]	1H NMR (DMSO, 500MHz) 9.32 (1H, s), 9.05 (1H, s), 8.92 (1H, s br), 8.62 (1H, m), 8.40 (1H, d), 8.23(1H, s), 8.18 (1H, s), 8.06 (1H, s), 7.83 (1H, d), 7.49 (1H, d), 7.36 (1H, m), 3.96-3.88 (4H, s br), 3.33 (4H, s br), 2.68 (1H, m), 1.26-1.23 (2H, m), 1.08-1.05 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-trifluoromethoxy-phenyl)-amine
556			method 5: RT:2.35 min,MI: 520 [M+H]	1H NMR (DMSO, 500MHz) 9.44 (1H, s), 9.08 (1H, s), 9.04 (1H,s), 8.97 (1H, s br), 8.43 (1H, dd), 8.24 (1H, s), 8.20 (1H, s), 7.87 (1H, d), 7.56 (1H, d), 3.96-3.88 (4H, s br), 3.35 (4H, s br), 3.24 (3H, s), 2.69 (1H, m), 1.28-1.25 (2H, m), 1.08-1.05 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methanesulfonyl-phenyl)-amine

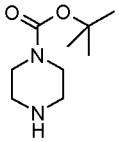
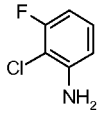
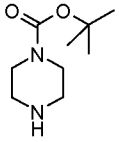
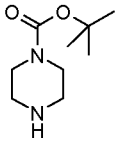
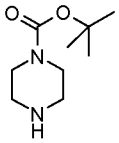
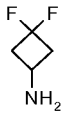
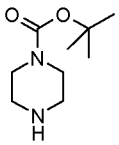
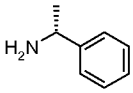
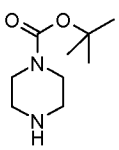
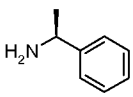
557			method 5: RT: 2.37 min,MI: 474 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 8.93 (1H, s br), 8.83 (1H, s), 8.18 (1H, s), 7.82 (1H, s), 7.15(1H, m), 7.06 (1H, m), 3.87 (4H, s br), 3.31 (4H, s br), 2.69 (1H, m), 2.24 (3H, s), 1.26-1.24 (2H, m), 1.07-1.05 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-3-methyl-phenyl)-amine
558			method 5: RT: 4.08 min,MI: 480 [M+H]	1H NMR (DMSO, 500MHz) 9.02 (1H, s), 8.93 (1H, s br), 8.17 (2H, dd), 7.90 (1H, s), 7.71 (1H, s), 7.38 (1H, s), 7.23 (1H, dd), 7.02 (1H, m), 4.02-3.88 (4H, s br), 3.30 (4H, s br), 2.87 (1H, m, br), 2.63-2.57 (1H, m), 2.20 (3H, s), 1.25-1.23 (2H, m), 1.20 (6H, m), 1.06-1.02 (2H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-isopropyl-2-methyl-phenyl)-amine
559			method 5: RT:2.01 min,MI: 429 [M+H]	1H NMR (DMSO, 500MHz) 9.45 (1H, s, br), 9.05 (1H,s), 8.90 (1H, s,br), 8.32 (1H,d), 8.18(1H, s), 7.82 (1H, s), 7.15 (1H, m), 7.06 (1H, m), 3.87 (4H, s,br), 3.31 (4H, s, br), 2.69 (1H, m), 2.24 (3H,s), 1.26-1.24 (2H, m), 1.07-1.05 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pent-deuterio-phenyl-amine
560			450.2 (M-OH)+	(CDCl3) 9.07 (s, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.00 (br s, 2H), 7.91 (s, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.75 (dd, J = 5.3; 1.2 Hz, 1H), 7.30 (m, 2H), 7.05 (m, 1H), 5.09 (q, J = 6.6 Hz, 1H), 3.73 (br s, 4H), 2.97 (m, 4H), 2.66 (m, 1H), 2.17 (br s, OH, exch. NH), 1.61 (d, J = 6.6 Hz, 3H), 1.24 (m, 2H), 0.98 (m, 2H)	1-{2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-phenyl}-ethanol
561			459.25 (M+H)+	(dmso-d6; note: a minor rotamer also observed) 10.85 (s, 1H), 9.17 (br s, exch. 3H), 9.08 (s, 1H), 8.53 (d, J = 5.2 Hz, 1H), 8.19 (s, 1H), 8.10 (dd, J = 5.2; 1.4 Hz, 1H), 8.04 (br s, 3H), 4.19 (br s, large exch. H's signal), 3.91 (m, 4H), 3.35 (br s, 4H), 3.08 (m, 1H), 2.70 (m, 1H), 2.24 (m,	(1R,2S)-2-Amino-cyclopentane-carboxylic acid [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-

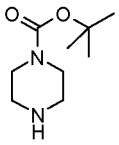
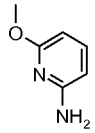
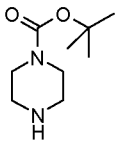
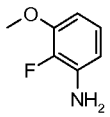
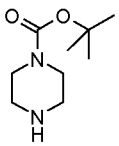
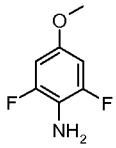
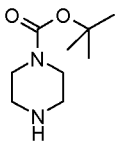
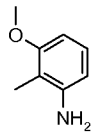
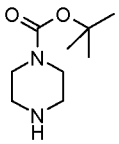
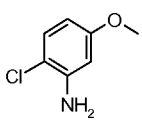
				1H), 2.08 (m, 2H), 1.73 (m, 4H), 1.26 (m, 2H), 1.08 (m, 2H)	yl]-amide
562		--	423.00 (M+H)		1-{4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-cyclopropanol
563			464.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-6-yl-amine
564			464.15 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-5-yl-amine
565			494.10 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridazin-3-yl)-amine

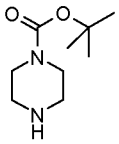
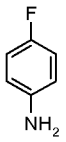
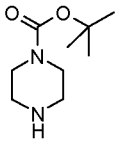
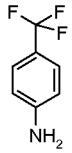
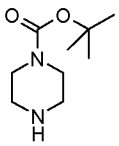
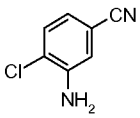
566			490	(dmso-d6) 9.11 (br s, 3H, exch. H's), 9.07 (s, 1H), 8.20 (m, 2H), 7.88 (s, 1H), 7.73 (dd, J = 5.3; 1.4 Hz, 1H), 7.09 (m, 2H), 3.92 (br s, 4H), 3.87 (s, 3H), 3.33 (br s, 4H), 2.69 (m, 1H), 1.26 (m, 2H), 1.09 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-3-methoxy-phenyl)-amine
567			503.9	(dmso-d6) 9.06 (s, 1H), 9.05 (br s, 3H, exch. H's), 8.20 (m, 2H), 7.87 (s, 1H), 7.72 (dd, J = 5.4; 1.3 Hz, 1H), 7.07 (m, 2H), 5.40 (br s, exch. H's), 4.12 (q, J = 7.0 Hz, 2H), 3.93 (br s, 4H), 3.33 (br s, 4H), 2.68 (m, 1H), 1.36 (t, J = 7.0 Hz, 3H), 1.26 (m, 2H), 1.09 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-ethoxy-2,6-difluoro-phenyl)-amine
568			method 5: RT: 3.46 min,MI: 472 [M+H]	1H NMR (DMSO, 500MHz,) 9.06 (1H, s), 8.26 (1H, d), 8.18 (1H, s), 8.05 (1H, s), 7.84 (1H, d), 7.75 (1H, dd), 7.24 (1H, t), 7.11 (1H, s), 3.91 (4H, s), 3.32 (4H, s), 2.68 (1H, m), 2.39 (3H, s), 1.25 (2H, m), 1.08 (2H, m).	(2-Chloro-3-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
569			method 5: RT: 4.22 min,MI: 438.28 [M+H]	1H NMR (DMSO, 500 MHz) 9.59 (1H, br s), 9.05 (1H, s), 8.99 (1H, br s), 8.31 (1H, d), 8.18 (1H, s), 7.97 (1H, s), 7.73-7.69 (2H, m), 7.32 (2H, t), 6.77 (1H, t), 4.96 (4H, br s), 4.32 (1H, br s), 3.37 (2H, br s), 1.34-1.23 (5H, m), 1.07 (2H, br s).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
570			method 5: RT:5.57 min,MI: 476 [M+H]	1H NMR (DMSO, 500MHz,) 9.07 (1H, s), 8.25 (1H, d), 8.19 (1H, s), 8.01 (1H, s), 7.93 (1H, m), 7.76 (1H, d), 7.54(1H, dd), 7.26(1H, m), 3.92 (4H, s), 3.32 (4H, s). 2.68 (1H, m), 1.25 (2H, m), 1.09 (2H, m).	(2-Chloro-4-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

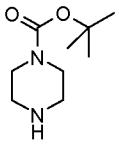
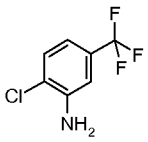
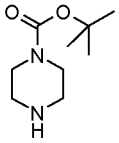
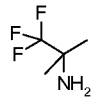
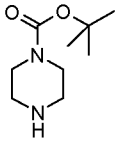
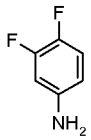
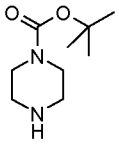
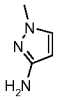
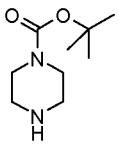
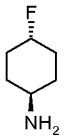
571			method 5: RT:5.27 min,MI: 454 [M+H]	1H NMR (DMSO, 500MHz,) 9.53 (1H, s), 9.06 (1H, s), 8.33 (1H, d), 8.19 (1H, s), 7.98 (1H, s), 7.74 (1H, dd), 7.46 (1H, s), 7.24 (2H, m), 6.56 (1H, d), 3.91 (4H, s), 3.76 (3H, s), 3.33 (4H, s), 2.69 (1H, m),1.25 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-phenyl)-amine
572			method 5: RT: 5.77 min,MI:472 [M+H]	1H NMR (DMSO, 500MHz,) 9.07 (1H, s), 8.22 (1H, d), 8.19 (1H, s), 8.03 (1H, s), 7.76 (1H, dd), 7.46 (1H, s), 7.74 (1H, d), 7.40 (1H, s), 7.20 (1H, d), 3.93 (4H, s), 3.32 (4H, s). 2.66 (1H, m), 2.33 (3H, s), 1.25 (2H, m), 1.08 (2H, m).	(2-Chloro-4-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
573			452.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-dimethyl-phenyl)-amine
574			455.9 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-3-methyl-phenyl)-amine
575			455.9 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-methyl-phenyl)-amine
576			method 5: RT: 4.02	1H NMR (DMSO, 500MHz,) 9.07 (1H, s), 8.87 (1H, s), 8.39 (1H, d), 8.23 (2H, m), 8.19 (1H, s), 7.85 (1H, dd),	(2-Chloro-5-fluoro-phenyl)-[4-(5-cyclopropyl-4-

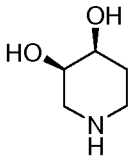
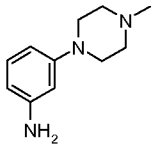
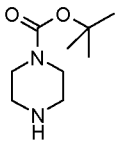
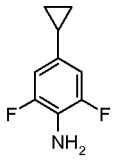
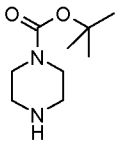
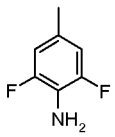
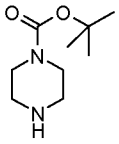
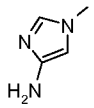
			min,MI: 476 [M+H]	7.51 (1H, m), 6.88 (1H, m), 3.93 (4H, s), 3.33 (4H, s). 2.69 (1H, m), 1.25 (2H, m), 1.08 (2H, m).	piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-Amine
577			method 5: RT: 3.48 min,MI:472 [M+H]	1H NMR (DMSO, 500MHz) 9.07 (1H, s), 8.28 (1H, d), 8.17 (1H, s), 8.05 (1H, s), 7.78 (2H, s), 7.41 (1H, dd), 6.98 (1H, d), 3.92 (4H, s), 3.32 (4H, s). 2.68 (1H, m), 2.32 (3H, s),1.25 (2H, m), 1.08 (2H, m).	(2-Chloro-5-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-Amine
578			method 5: RT: 5.25 min,MI: 476 [M+H]	1H NMR (DMSO, 500MHz) 9.07 (1H, s), 8.33 (1H, d), 8.19 (1H, s), 8.14 (1H, s), 7.97 (1H, d), 7.82 (1H, dd), 7.37-7.32 (1H, m), 7.10-7.06 (1H, m), 3.93 (4H, s), 3.33 (4H, s). 2.69 (1H, m), 1.26 (2H, m), 1.09 (2H, m).	(2-Chloro-3-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-Amine
579			44		5-Cyclopropyl-2-(6,7-dimethoxy-quinolin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
580			471.9	($CDCl_3$) 9.12 (s, 1H), 8.41 (dd, J = 5.3; 0.4 Hz, 1H), 8.05 (s, 1H), 7.98 (dd, J = 7.0; 3.1 Hz, 1H), 7.95 (s, 1H), 7.85 (dd, J = 5.3; 1.3 Hz, 1H), 7.02 (dd, J = 10.8; 8.9 Hz, 1H), 6.89 (m, 1H), 6.45 (m, 1H), 3.82 (s, 3H), 3.78 (br s, 4H), 3.03 (m, 4H), 2.70 (m, 1H), 1.87 (br s, exch. H's), 1.27 (m, 2H), 1.01 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methoxy-phenyl)-amine
581			390.10 (M+H)		N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-

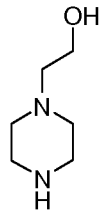
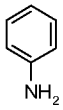
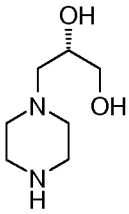
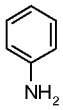
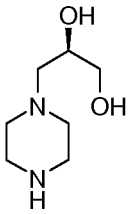
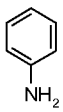
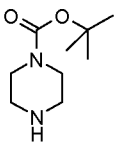
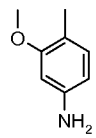
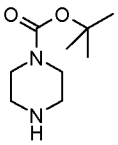
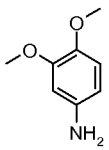
					yl]-acetamide
582			348.05 (M+H)		4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamine
583			418.15 (M+H)		N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-isobutyramide
584			416.10 (M+H)		Cyclopropane-carboxylic acid [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide
585			438		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluorocyclo-butyl)-amine
586			452.0 (M+H)	(dmso-d6) 9.14 (br s, exch. H's), 9.07 (s, 1H), 8.22 (s, 1H), 8.09 (d, J = 6.4 Hz, 1H), 8.02 (br s, 1H), 7.70 (d, J = 6.3 Hz, 1H), 7.47 (m, 2H), 7.40 (m, 2H), 7.30 (m, 1H), 5.10 (m, 1H), 3.90 (br s, 4H), 3.33 (br s, 4H), 2.66 (m, 1H), 1.58 (d, J = 6.7 Hz, 3H), 1.26 (m, 2H), 1.08 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-ethyl)-amine
587			452.0 (M+H)	(dmso-d6) 9.12 (br s, exch. H's), 9.06 (s, 1H), 8.21 (s, 1H), 8.09 (d, J = 6.4 Hz, 1H), 7.98 (br s, 1H), 7.680 (d, J = 6.3 Hz, 1H), 7.47 (m, 2H), 7.39 (m, 2H), 7.29 (m, 1H),	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-

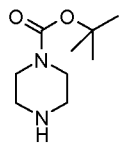
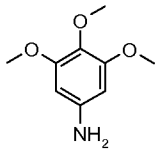
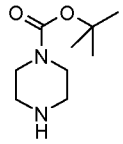
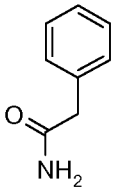
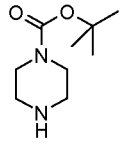
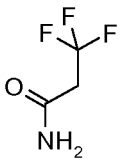
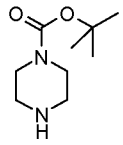
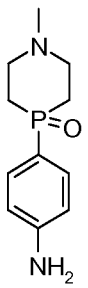
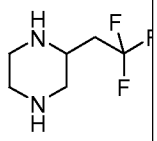
				5.10 (m, 1H), 3.89 (br s, 4H), 3.33 (br s, 4H), 2.65 (m, 1H), 1.57 (d, J = 6.7 Hz, 3H), 1.26 (m, 2H), 1.08 (m, 2H)	yl]-((S)-1-phenyl-ethyl)-amine
588			455.0 (M+H)	(CDCl3) 9.05 (s, 1H), 8.95 (s, 1H), 8.40 (dd, J = 5.2; 0.3 Hz, 1H), 8.05 (s, 1H), 7.89 (dd, J = 5.2; 1.4 Hz, 1H), 7.76 (s, 1H), 7.51 (m, 1H), 6.95 (d, J = 7.8 Hz, 1H), 6.33 (d, J = 7.8 Hz, 1H), 4.10 (s, 3H), 3.75 (br s, 4H), 3.03 (m, 4H), 2.71 (m, 1H), 1.96 (br s, exch. H's), 1.27 (m, 2H), 1.01 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine
589			472.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-3-methoxy-phenyl)-amine
590			489.9 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-4-methoxy-phenyl)-amine
591			468.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-2-methyl-phenyl)-amine
592			method 5: RT: 2.59 min,MI: 488 [M+H]	1H NMR (DMSO, 500MHz) 9.06 (1H, s), 8.32 (1H, d), 8.19 (1H, s), 8.12 (1H, s), 7.80 (1H, dd), 7.76 (1H, d), 7.41 (1H, d), 6.72 (1H, dd), 3.92 (4H, s), 3.77 (3H, s), 3.33 (4H, s), 2.68 (1H, m),	(2-Chloro-5-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-

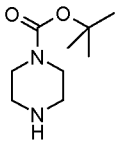
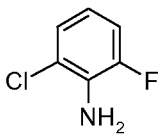
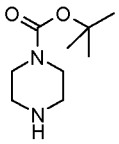
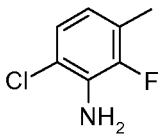
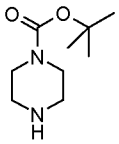
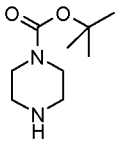
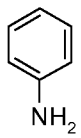
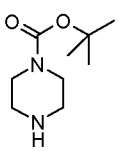
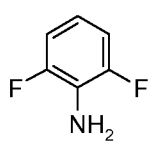
				1.26 (2H, m), 1.08 (2H, m).	yl)-pyridin-2-yl] -amine
594			method 5: RT:2.19 min,MI: 442 [M+H]	1H NMR (DMSO, 500MHz) 9.55 (1H, s), 9.06 (1H, s), 8.31 (1H, d), 8.19 (1H, s), 7.93 (1H, s), 7.76-7.72 (3H, m), 7.16 (2H, t), 3.92 (4H, s), 3.33 (4H, s), 2.69 (1H, m),1.25 (2H, m), 1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine
595			method 5: RT:3.33 min,MI: 492 [M+H]	1H NMR (DMSO, 500MHz) 9.86 (1H, s), 9.07 (1H, s), 8.43(1H, d), 8.19 (1H, s), 8.02 (1H, s), 7.99 (2H, d), 7.83 (1H, dd), 7.64 (2H, d), 3.94 (4H, s), 3.34 (4H, s), 2.69 (1H, m), 1.27 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine
596			method 5: RT: 2.9 min,MI: 483 [M+H]	1H NMR (DMSO, 500MHz) 9.07 (2H, s), 8.71 (1H, d), 8.40 (1H, d), 8.24 (1H, s), 8.19 (1H, s), 7.88 (1H, dd), 7.72 (1H, d), 7.48 (1H, dd), 3.92 (4H, s), 3.34 (4H, s), 2.69 (1H, m), 1.25 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine

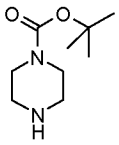
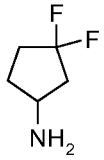
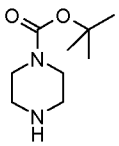
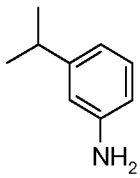
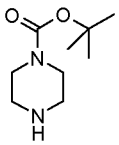
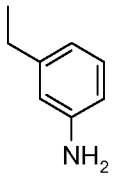
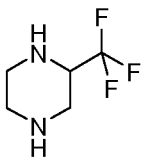
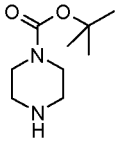
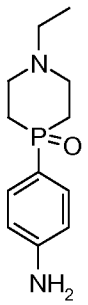
597			method 5: RT: 3.41 min,MI: 526 [M+H]	1H NMR (DMSO, 500MHz) 9.07 (1H, s), 9.02 (1H, s), 8.69 (1H, d), 8.39 (1H, d), 8.25 (1H, s), 8.19 (1H, s), 7.86 (1H, dd), 7.73 (1H, d), 7.36 (1H, dd), 3.94 (4H, s), 3.34 (4H, s), 2.69 (1H, m), 1.26 (2H, m), 1.08 (2H, m).	(2-Chloro-5-trifluoromethyl-phenyl) -[4-(5-cyclopropyl-4-piperazin-1-yl -pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
598			method 5: RT:5.48 min,MI: [M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.13 (1H, d), 8.06 (1H, s), 7.74 (1H, s), 7.51 (1H, d), 6.87 (1H, s), 3.77 (4H, m, br), 2.83 (4H, m, br), 2.62-2.61 (1H, m), 1.66 (6H, s), 1.25-1.23 (2H, m), 1.02-1.01 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-amine
599			method 5: RT: 2.85 min,MI: 460 [M+H]	1H NMR (DMSO, 500MHz) 9.70 (1H, s), 9.06 (1H, s), 8.37 (1H, d), 8.18 (1H, s), 8.12-8.07 (1H, m), 7.94 (1H, s), 7.77 (1H, d), 7.37 (2H, m), 3.94 (4H, s), 3.34 (4H, s), 2.69 (1H, m), 1.27 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4-difluoro-phenyl)-amine
600			428	(dmso-d6) 9.39 (s, 1H), 8.97 (s, 1H), 8.37 (s, 1H), 8.25 (d, J = 5.3 Hz, 1H), 8.09 (s, 1H), 7.63 (dd, J = 5.2; 1.4 Hz, 1H), 7.53 (d, J = 2.2 Hz, 1H), 6.34 (d, J = 2.2 Hz, 1H), 3.77 (s, 3H), 3.70 (br s, 4H), 3.30 - 3.32 (exch. H's), 2.85 (br s, 4H), 2.63 (m, 1H), 1.25 (m, 2H), 1.02 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-pyrazol-3-yl)-amine
601			method 5: RT: 2.29 min,MI: 448.35 [M+H]	1H NMR (500MHZ, DMSO) 9.16 (2H, s, br), 9.06 (1H, s), 8.21 (1H, s), 8.08 (1H, d), 8.05 (1H, s), 4.85 (1H, d), 3.96 (4H, m, br), 3.80 (1H, s, br), 3.37-3.32 (4H, m), 2.66-2.62 (1H, m), 2.02-1.98 (2H, m), 1.87-1.85 (2H, m), 1.73 (1H, t), 1.65-1.61 (3H, m), 1.27-1.23 (2H, m), 1.09-1.06	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluorocyclohexyl)-amine

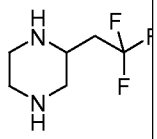
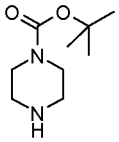
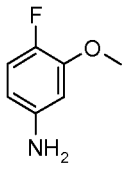
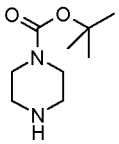
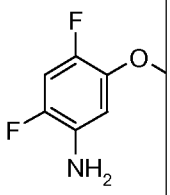
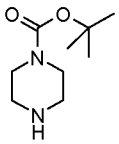
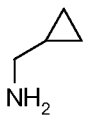
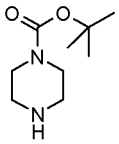
				(2H, m).	
602			553.1 (M+H)	($CDCl_3$) 9.07 (s, 1H), 8.32 (d, J = 5.2 Hz, 1H), 8.08 (br s, 1H), 8.02 (s, 1H), 7.79 (d, J = 5.2 Hz, 1H), 7.24 (dd, J = 8.4 Hz, 1H)), 7.06 (br s, 1H), 6.98 (br s, 1H), 6.82 (br d, J = 7.08 Hz, 1H), 6.69 (dd, J = 8.4; 1.9 Hz, 1H), 3.95 (m, 5H), 3.55 (m, br s, 1H), 3.25 (br s, 5H), 2.60 (m, 5H), 2.34 (s, 3H), 1.91 (m, 1H), 1.7 br s (exch. H's), 1.24 (m, 2H), 0.97 (m, 2H)	(+/-)-(cis)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol
603			500.0 (MH)+		(4-Cyclopropyl-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl -pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
604			473.9 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-4-methyl-phenyl)-amine
605			428.0 (M+H)	($CDCl_3$) 9.13 (s, 1H), 8.37 (d, J = 5.4 Hz, 1H), 8.05 (s, 1H), 7.81 (s, 1H), 7.73 (dd, J = 5.4; 1.3 Hz, 1H), 7.47 (br s, 1H), 7.37 (d, J = 1.5 Hz, 1H), 7.26 (s, 1H, *"shoulder" under solvent's peak), 3.77 (br s, 4H), 3.71 (s, 3H), 3.03 (m, 4H), 2.70 (m, 1H), 2.93 (br s, exch. H's), 1.26 (m, 2H), 1.01 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-imidazol-4-yl)-amine

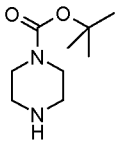
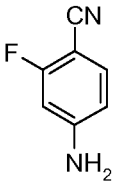
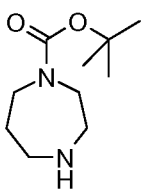
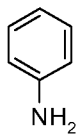
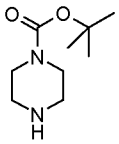
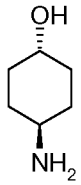
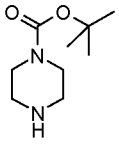
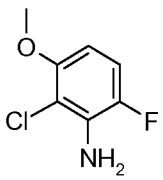
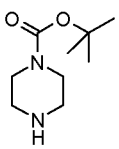
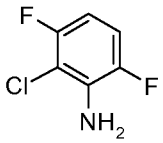
606			468.0 (M+H)	($CDCl_3$) 9.11 (s, 1H), 8.34 (d, J = 5.2 Hz, 1H), 8.04 (s, 1H), 8.01 (s, 1H), 7.78 (dd, J = 5.2; 1.3 Hz, 1H), 7.45 (m, 2H), 7.35 (m, 2H), 7.17 (br s, 1H), 7.06 (m, 1H), 3.79 (br s, 4H), 3.68 (m, 2H), 3.14 (br s, exch. H's), 2.63 (m, 5H), 2.60 (m, 2H), 1.26 (m, 2H), 1.0 (m, 2H)	2-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol
607			498.0 (M+H)	($CDCl_3$) 9.11 (s, 1H), 8.35 (d, J = 5.2 Hz, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.78 (dd, J = 5.3; 1.3 Hz, 1H), 7.45 (m, 2H), 7.35 (m, 2H), 7.06 (m, 1H), 6.98 (br s, 1H), 3.87 (m, 1H), 3.79 (m, 5H), 3.54 (d, J = 11.5; 4.4 Hz, 1H), 3.40-2.10 (br signal, -OH's), 2.78 (m, 2H), 2.64 (m, 2H), 2.58 (m, 2H), 2.40 (dd, J = 12.5 Hz; 3.7 Hz, 1H), 1.25 (m, 2H), 1.00 (m, 2H)	(S)-3-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-propane-1,2-diol
608			498.0 (M+H)	($CDCl_3$) 9.11 (s, 1H), 8.35 (d, J = 5.2 Hz, 1H), 8.04 (s, 1H), 8.00 (s, 1H), 7.78 (dd, J = 5.3; 1.3 Hz, 1H), 7.45 (m, 2H), 7.35 (m, 2H), 7.09 (br s, 1H), 7.06 (m, 1H), 3.87 (m, 1H), 3.79 (m, 5H), 3.54 (d, J = 11.5; 4.4 Hz, 1H), 3.40-2.10 (br signal, -OH's), 2.78 (m, 2H), 2.64 (m, 2H), 2.58 (m, 2H), 2.40 (dd, J = 12.5 Hz; 3.7 Hz, 1H), 1.25 (m, 2H), 1.00 (m, 2H)	(R)-3-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-propane-1,2-diol
609			468.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-4-methyl-phenyl)-amine
610			484.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-

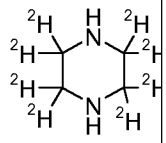
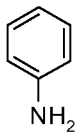
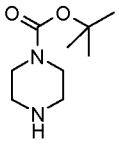
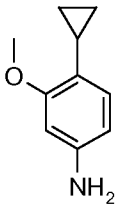
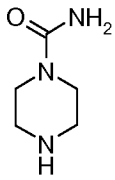
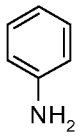
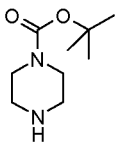
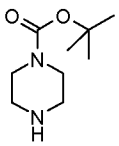
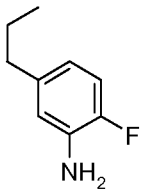
					yl)-pyridin-2-yl]-(3,4-dimethoxy-phenyl)-amine
611			514.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,5-trimethoxy-phenyl)-amine
612			466.15 (M+H)		N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide
613			458.15 (M+H)		N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-3,3,3-trifluoro-propionamide
614			555.25 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(1-methyl-4-oxo-4λ^5-[1,4]azaphos-phinan-4-yl)-phenyl]-amine
615		--	449.10 (M+H)		2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidine

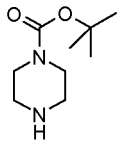
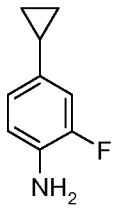
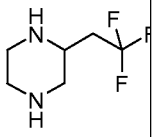
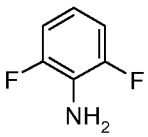
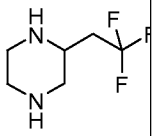
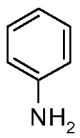
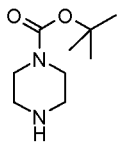
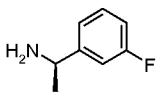
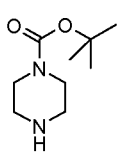
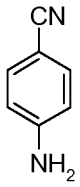
616			method 5: RT: 3.25 min,MI: 476 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (2H, bs), 8.93 (1H, bs), 8.21 (1H, d), 8.17 (1H, s), 7.88 (1H, s), 7.73 (1H, dd), 7.48 (1H, m), 7.25 (1H, m), 4.68 (4H, bs), 3.89 (4H, bs), 2.70 (1H, m), 1.28-1.25 (2H, m), 1.06-1.05 (2H, m).	(2-Chloro-6-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
617			method 5: RT: 3.36 min,MI: 490 [M+H]	1H NMR (DMSO, 500MHz) 9.04 (1H, s), 8.80 (1H, bs), 8.17 (1H, s), 8.15 (1H, d), 7.80 (1H, s), 7.67 (1H, d), 7.30 (1H, dd), 7.19 (1H,m), 3.91 (4H, bs), 3.31 (4H, bs), 2.68 (1H, m), 2.24 (3H, s), 1.23 (2H, m), 1.08-1.07 (2H, m).	(6-Chloro-2-fluoro-3-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
618			method 5: RT: 2.62 min,MI: 494 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 8.86 (1H, bs), 8.20 (1H, d), 8.17 (1H, s), 7.88 (1H, s), 7.73 (1H, dd), 7.47 (1H, m), 7.25 (1H, m), 3.89 (4H, bs), 3.31 (4H, bs), 2.68 (1H, m), 1.28-1.25 (2H, m), 1.08-1.07 (2H, m).	(3-Chloro-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
619			method 5: RT: 3.04 min,MI: 438 [M+H]	(1H, d6-dmso, 500MHz) 9.30 (1H, s), 9.04 (1H, s), 8.69 (1H, s), 8.29 (1H, d), 7.90 (1H, s), 7.74 (2H, d), 7.65 (1H, dd), 7.27 (2H, tr), 6.89 (1H, tr), 4.26-4.20 (1H, m), 3.67 (2H, br s), 3.46 (2H, br s), 2.93 (2H, br s), 2.83 (2H, br s), 2.46-2.43 (2H, m partially hidden by large DMSO peak), 2.21-2.14 (2H, m), 2.10-2.03 (1H, m), 1.92-1.86 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine
620			method 5: RT: 3.39 min,MI: 474 [M+H]	1H NMR (1H, d6-dmso, 500MHz) 9.02 (1H, s), 8.75 (1H, s), 8.68 (1H, s), 8.14 (1H, d), 7.77 (1H, s), 7.63 (1H, dd), 7.29-7.23 (1H, m), 7.15(2H, t), 4.22 (1H, dq), 3.63 (2H, br s), 3.50 (2H, br s), 2.90 (2H, br s), 2.78 (2H, br s), 2.44-2.42 (2H, m,	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine

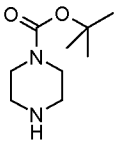
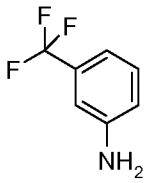
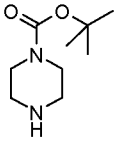
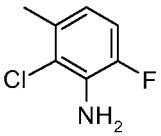
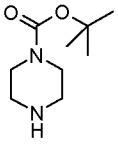
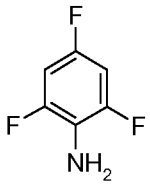
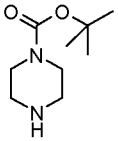
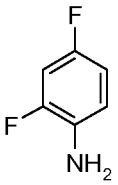
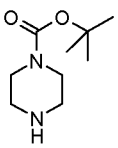
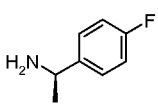
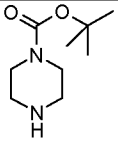
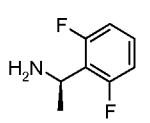
				partially obscured by DMSO peak), 2.20-2.12 (2H, m), 2.10-2.01(1H, m), 1.91-1.86 (1H, m)	
621			method 5: RT:2.24 min,MI: 452.37 [M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.13 (1H, d), 8.06 (1H, s), 7.53 (1H, s), 7.44 (1H, dd), 7.04 (1H, d), 4.42-4.38 (1H, m), 3.75-3.57 (4H, m, br), 2.84 (4H, m), 2.62-2.58 (2H, m), 2.27-1.97 (4H, m), 1.77-1.69 (1H, m),, 1.26-1.22 (2H, m), 1.01-1.00 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclopentyl)-amine
622			466.30 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-isopropyl-phenyl)-amine
623			452.25 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-ethyl-phenyl)-amine
624		--	435.10 (M+H)		2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
625			599.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(1-ethyl-4-oxo-4λ5-[1,4]azaphosphinan-4-yl)-2-methoxy-

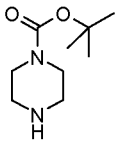
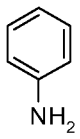
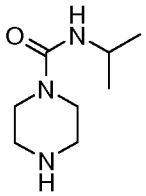
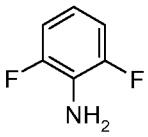
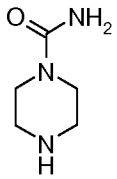
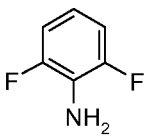
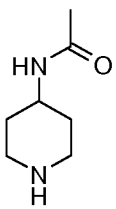
					phenyl]-amine
626			472.00 (M+H)		N-(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-acetamide
627			method 5: RT: 0.48 min,MI:472 [M+H]	1H NMR (DMSO, 500MHz,) 9.62 (1H, s), 9.06(1H, s), 8.32(1H, d), 8.19 (1H, s), 7.96 (1H, s), 7.74 (1H, d), 7.62 (1H, dd), 7.28 (1H, m), 7.17-7.13 (1H, m), 3.85 (7H, m), 3.34 (4H, s), 2.68 (1H, m),1.27 (2H, m), 1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-3-methoxy-phenyl)-amine
628			method 5: RT: 2.37 min,MI:490 [M+H]	1H NMR (DMSO, 500MHz) 9.27 (1H, s), 9.06 (1H, s), 8.30 (1H, d), 8.18 (1H, s), 8.06 (1H, s), 7.96 (1H, t), 7.78 (1H, dd), 7.39 (1H, t), 3.96 (4H, s), 3.84 (3H, s), 3.33 (4H, s), 2.68 (1H, m), 1.27 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-5-methoxy-phenyl)-amine
629			method 5: RT: 2.16 min,MI: 402.22 [M+H]	1H NMR (500MHz, $CDCl_3$) 9.07 (1H, s), 8.21 (1H, s), 8.04 (2H, d), 7.65 (1H, d), 4.10-3.74 (8H, m, br), 3.26 (2H, d), 2.66-2.62 (1H, m), 1.28-1.24 (2H, m), 1.15-1.13 (1H, m), 1.09-1.07 (2H, m), 0.57-0.56 (2H, m), 0.32-0.31 (2H, m).	Cyclopropylmethyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
630			method 5: RT: 1.61 min,MI: 362.19 [M+H]	1H NMR (500MHz, DMSO) 8.94 (1H, s), 8.12 (`1H, d), 8.06 (1H, s), 7.48 (1H, s), 7.41 (1H, dd), 6.72 (1H, d), 3.77-3.55 (4H, m), 2.85 (4H, m, br), 2.82 (3H, d), 2.63-2.59 (1H, m), 1.25-1.22 (2H, m), 1.02-1.00 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-methyl-amine

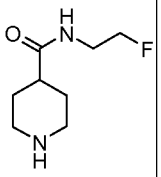
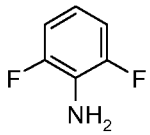
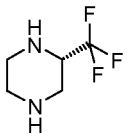
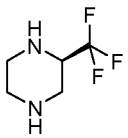
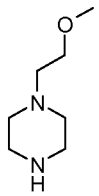
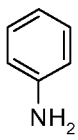
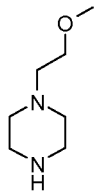
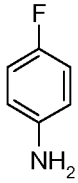
631			method 5: RT: 3.04 min,MI: 467 [M+H]	1H NMR (DMSO, 500MHz,) 10.30 (1H, s), 9.06 (1H, s), 8.50 (1H, d), 8.23 (1H, dd), 8.19 (1H, s), 8.05 (1H, s), 7.92 (1H, dd), 7.75 (1H, t), 7.52 (1H, dd), 3.94 (4H, s), 3.33 (4H, s), 2.68 (1H, m),1.26 (2H, m), 1.09 (2H, m).	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-fluoro-benzonitrile
632			method 5: RT: 1.96 min,MI: 438 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 8.99 (1H, s), 8.31 (1H, dd), 8.18(1H, s), 7.95 (1H, s), 7.72 (1H, dd), 7.70-7.67 (2H, dd), 7.32 (2H, t), 6.97 (1H, t), 4.22 (2H, t), 4.05 (2H, t), 3.50 (2H, t), 3.20 (2H, t), 2.44 (1H, m), 2.11 (2H, quin), 1.27-1.23 (2H, m), 0.97-0.93 (2H, m).	[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine
633			method 5: RT: 2.02 min,MI:446.23 [M+H]	1H NMR (500MHz, DMSO) 8.92 (1H, s), 8.08 (1H, d), 8.06 (1H, s), 7.49 (1H, s), 7.35 (1H, dd), 6.61 (1H, d), 4.53 (1H, d), 3.83-3.67 (5H, m, br), 3.51-3.42 (1H, m), 2.85 (4H, m), 2.61-2.60 (1H, m), 2.53 (2H, m), 1.97-1.95 (2H, m), 1.85-1.83 (2H, m), 1.24-1.20 (6H, m), 1.01-0.95 (6H, m).	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-cyclohexanol
634			method 5: RT: 2.29 min,MI:506 [M+H]	1H NMR (DMSO, 500MHz) 9.06 (1H, s), 8.83 (1H, bs), 8.17 (1H, s), 8.16 (1H, d), 7.81 (1H, s), 7.67 (1H, dd), 7.25 (1H, t), 7.03 (1H, dd), 4.7 (4H, bs), 3.87 (3H, s), 3.31 (4H, m) 2.68 (1H, m), 1.26-1.23 (2H, m), 1.06-1.05 (2H, m).	(2-Chloro-6-fluoro-3-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
635			method 5: RT: 2.53 min,MI: 494 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 9.01 (1H, s), 8.86 (1H, bs), 8.18 (1H, s), 8.17 (1H, d), 7.87 (1H, s), 7.71 (1H, dd), 7.35 (1H, m), 3.89 (4H, bs), 3.31 (4H, m) 2.68 (1H, m), 2.35 (3H, s), 1.25-1.23 (2H, m), 1.08-1.06 (2H, m).	(2-Chloro-3,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

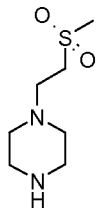
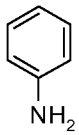
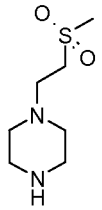
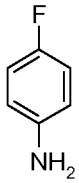
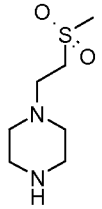
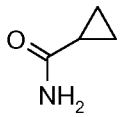
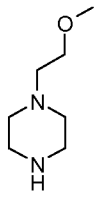
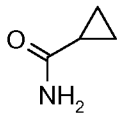
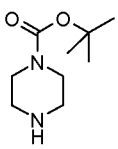
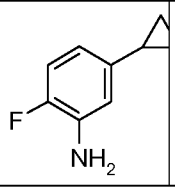
636			method 5: RT: 1.36 min,MI:432 [M+H]	1H NMR (DMSO, 500MHz) 9.05 (1H, s), 9.01 (1H, s), 8.86 (1H, bs), 8.18 (1H, s), 8.17 (1H, d), 7.87 (1H, s), 7.71 (1H, dd), 7.35 (1H, m), 3.89 (4H, bs), 3.31 (4H, m) 2.68 (1H, m), 2.35 (3H, s), 1.25-1.23 (2H, m), 1.08-1.06 (2H, m).	{4-[5-Cyclopropyl-4-(2,2,3,3,5,5,6,6-octadeuterio-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
637			494.0 (MH)+		(4-Cyclopropyl-3-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
638			467.0 (M+H)	(dmso-d6) 9.61 (br s, 1H), 8.95 (s, 1H), 8.21 (d, J = 5.6 Hz, 1H), 8.09 (s, 1H), 7.92 (s, 1H), 7.67 (dd, J = 5.6; 1.1 Hz, 1H), 7.63 (d, J = 7.8 Hz, 2H), 7.29 (dd, J = 7.8; 8.0 Hz, 2H), 6.96 (t, J = 7.2 Hz, 1H), 6.06 (br s, 2H), 3.47-3.95 (br m, 4H), 3.47-3.37 (m, 5H), 2.55 (m, 1H), 1.21 (m, 2H), 0.99 (m, 2H)	4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acidamide
639			502 (M+H)		N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(2,6-difluoro-phenyl)-acetamide
640			484.20 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-propyl-phenyl)-amine

641			482.15 (M+H)		(4-Cyclopropyl-2-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
642			542.10 (M+H)		(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(2,6-difluoro-phenyl)-amine
643			506.20 (M+H)		(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine
644			470 (M+H)	1H NMR (500MHz, DMSO) 8.92 (1H, s), 8.05 (1H, s), 8.04 (1H, d), 7.55 (1H, s), 7.40 (1H, dd), 7.35-7.29 (2H, m), 7.24 (1H, d), 7.21 (1H, d), 6.99 (1H, td), 5.08 (1H, t), 4.09-4.08 (1H, m), 3.78-3.51 (4H, m, br), 2.62-2.58 (1H, m), 1.44 (3H, d), 1.24-1.22 (2H, m), 1.01-1.00 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(3-fluoro-phenyl)-ethyl]-amine
645			method 5: RT: 3.83 min,MI: 449 [M+H]	1H NMR (DMSO, 500MHz,) 9.98 (1H, s), 9.05(1H, s), 8.44(1H, d), 8.18 (1H, s), 8.02 (1H, s), 7.97 (2H, d), 7.85 (1H, dd), 7.72 (2H, d), 3.92 (4H, s), 3.33 (4H, s), 2.68 (1H, m),1.25 (2H, m), 1.07 (2H, m).	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile

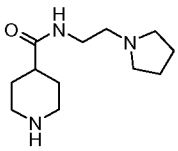
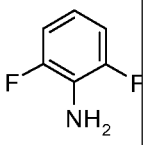
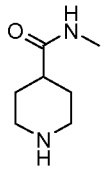
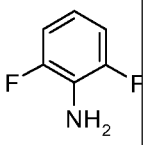
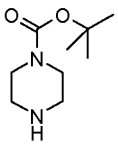
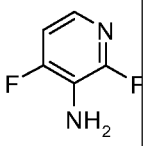
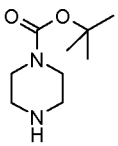
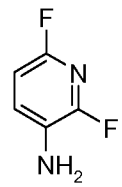
646			method 5: RT: 4.3 min,MI:492 [M+H]	1H NMR (DMSO, 500MHz,) 9.79 (1H, s), 9.06 (1H, s), 8.42 (1H, d), 8.34 (1H, s), 8.18 (1H, s), 7.99 (1H, s), 7.94 (1H, d), 7.80 (1H, dd), 7.52 (1H, t), 7.24 (1H, d), 3.92 (4H, s), 3.34 (4H, s), 2.69 (1H, m), 1.27(2H, m), 1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine
649			method 5: RT: 2.44 min,MI: 490 [M+H]	1H NMR (DMSO, 500MHz) 9.04 (1H, s), 8.79 (1H,bs), 8.17 (1H,s), 8.15 (1H, d), 7.80 (1H, s), 7.66 (1H, dd), 7.27 (1H, dd), 7.20 (1H, t), 3.88 (4H, bs), 3.31 (4H, m) 2.68 (1H, m), 2.35 (3H, s), 1.26-1.23 (2H, m), 1.08-1.06 (2H, m).	(3-Chloro-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
650			method 5: RT: 3.26 min,MI: 478 [M+H]	1H NMR (DMSO, 500MHz,) 9.06 (1H, s), 8.85 (1H, s), 8.18 (2H, s), 7.84 (1H, s), 7.71 (1H, dd), 7.29 (2H, t), 3.90 (4H, s), 3.33 (4H, s), 2.69 (1H, m), 1.25 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine
651			method 5: RT: 3.22 min,MI: 460 [M+H]	1H NMR (DMSO, 500MHz) 9.13 (1H, s), 9.06 (1H, s), 8.28 (1H, d), 8.18 (1H, s), 8.12-8.07 (1H, m), 8.02 (1H, s), 7.75 (1H, dd), 7.35-7.30 (1H, m), 7.11-7.06 (1H, m), 3.92 (4H, s), 3.33 (4H, s), 2.69 (1H, m), 1.26 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-phenyl)-amine
652			method 5: RT:2.71 min,MI:470.37 [M+H]	1H NMR (500MHz, DMSO) 8.92 (1H, s), 8.05 (1H, s), 8.03 (1H, d), 7.63 (1H, s), 7.42 (2H, dd), 7.39 (1H, dd), 7.26 (1H, d), 7.15 (1H, t), 7.10 (2H, t), 5.06 (1H, 03.77-3.52 (4H, m), 2.83 (4H, m), 2.62-2.58 (1H, m), 1.43 (3H, s), 1.30 (1H, d), 1.24-1.22 (2H, m), 1.01-1.00 (2H, m).	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(4-fluoro-phenyl)-ethyl]-amine
653			method 5: RT: 5.46	1H NMR (500MHz, DMSO) 8.92 (1H, s), 8.06 (1H, s), 8.04 (1H, d), 7.61 (1H, d), 7.39 (1H, dd), 7.27 (1H, dt),	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-

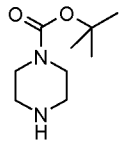
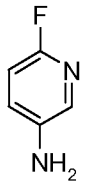
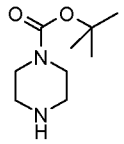
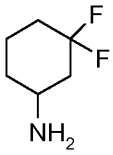
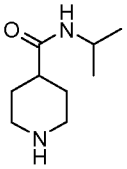
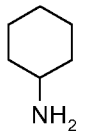
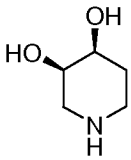
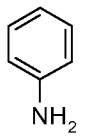
			min,MI: 488.35 [M+H]	7.24 (1H, d), 7.00 (2H, t), 5.47 (1H, t), 3.78-3.54 (4H, m), 2.86 (4H, m), 2.63-2.62 (2H, m), 2.37-2.35 (1H, m), 1.55 (3H, d), 1.24-1.22 (2H, m), 1.01-1.00 (2H, m).	d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2,6-difluoro-phenyl)-ethyl]-amine
654			method 5: RT: 2.31 min,MI: 442.34 [M+H]	1H NMR (500MHz, DMSO) 9.28 (1H, s), 8.93 (1H, s), 8.24 (1H, d), 8.11 (1H, s), 7.66 (1H, d), 7.62 (2H, d), 7.26 (2H, t), 6.89 (1H, t), 3.68 (4H, s, br), 3.15 (1H, d), 2.82 (4H, s, br), 2.59-2.57 (1H, m), 1.26-1.24 (2H, m), 1.03-1.02 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-phenyl-amine
655			544 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid isopropylamide
656			502 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid amide
657			516 (M+H)		N-(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-acetamide

658			548 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-fluoro-ethyl)-amide
659			458		N-{4-[5-Cyclopropyl-4-((S)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide
660		--	435		2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
661			482		(4-{5-Cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine
662			500		(4-{5-Cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(4-fluoro-phenyl)-amine

663			530		(4-{5-Cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine
664			548		(4-{5-Cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(4-fluoro-phenyl)-amine
665			522		Cyclopropane-carboxylic acid (4-{5-cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-amide
666			474		Cyclopropane-carboxylic acid (4-{5-cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-amide
667			482		(5-Cyclopropyl-2-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-

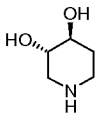
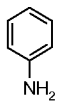
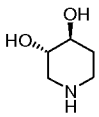
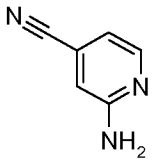
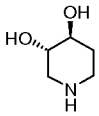
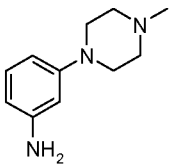
					pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

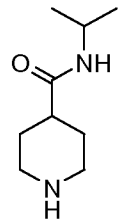
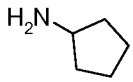
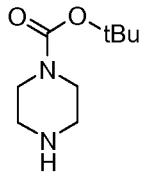
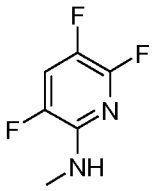
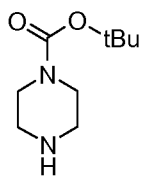
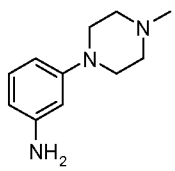
668			599 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide
669			516 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid methylamide
670			461.2 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-pyridin-3-yl)-amine
671			461.0 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-pyridin-3-yl)-amine

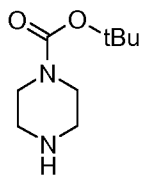
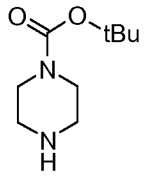
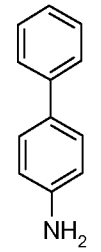
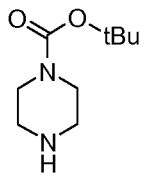
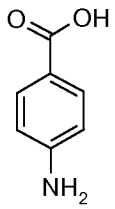
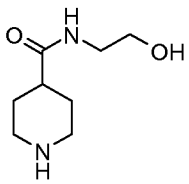
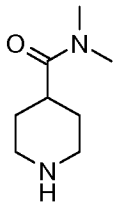
672			443.1 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-3-yl)-amine
673			method 5: RT: 2.41 min,MI: 466.32 [M+H]	1H NMR (500MHz, DMSO) 9.05 (1H, s), 8.19 (1H, s), 8.10 (1H, d), 7.91 (1H, s, br), 7.64 (1H, d, br), 3.98-3.80 (5H, m), 3.31 (4H, m, br), 2.67-2.62 (1H, m), 2.03-2.01 (2H, m), 1.94-1.79 (3H, m), 1.54-1.51 (1H, m), 1.35-1.32 (1H, m), 1.26-1.24 (2H, m), 1.07-1.06 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclohexyl)-amine
674			514 (M+H)		1-[2-(2-Cyclohexylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carboxylicacid isopropylamide
675			455.1	(dmso-d6) 9.84 (br s, 1H), 8.98 (s, 1H), 8.26 (d, J = 5.7 Hz, 1H), 8.12 (s, 1H), 7.99 (s, 1H), 7.74 (dd, J = 5.7; 1.2 Hz, 1H), 7.67 (d, J = 7.8 Hz, 2H), 7.38 (app t, J = 8.00 Hz, 2H), 7.07 (app t, 6.8 Hz, 1H), 4.19 (large br s, exch. H's), 3.77 (br s, 4H), 3.70-3.47 (m, 2H), 3.47-3.25 (m, 1H), 3.13-1.78 (m, 1H), 1.68 (br s, 1H), 1.47-1.13 (m, 2H), 1.13-0.87 (m, 2H)	(+/-)-(cis)-1-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

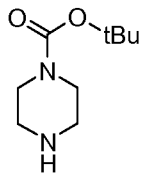
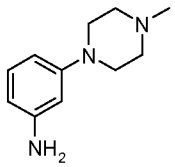
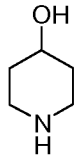
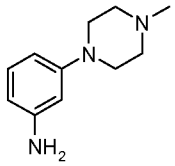
The following compounds were synthesised according to the general synthesis shown in scheme [B4]

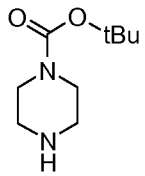
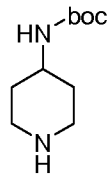
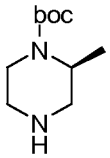
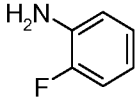
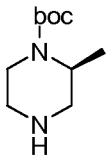
Ex	Amine 1	Amine 2	Analysis	Name

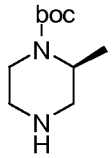
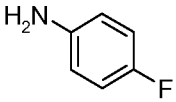
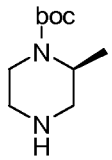
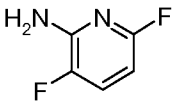
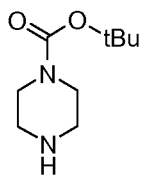
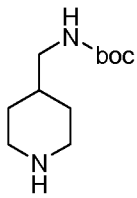
			LCMS	NMR	
676			455.1 (M+H)	NMR (dmso-d6) 9.74 (br s, 1H), 8.98 (s, 1H), 8.27 (d, J = 5.6 Hz, 1H), 8.13 (s, 1H), 7.98 (s, 1H), 7.73 (d, J = 6.4 Hz, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.36 (app t, J = 8.0 Hz, 2H), 7.04 (app t, J = 7.2 Hz, 1H), 3.80 (large br s, exch. H's - overlapping other signals), 3.52 (br s, 2H), 3.40-3.35 (m, 2H), 2.23-1.83 (m, 2H), 1.55 (br s, 1H), 1.49 (br s, 1H), 1.35 (br s, 1H), 1.12-0.92 (m, 2H)	(+/-)-(trans)-1-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol
677			481.1 (M +H)	($CDCl_3$) 10.39 (br s, 1H), 8.97 (br s, 1H), 8.65 (s, 1H), 8.50 (d, J = 4.8 Hz, 1H), 8.46 (d, J = 5.2 Hz, 1H), 8.35 (s, 1H), 8.10 (s, 1H), 7.89 (d, J = 4.9 Hz, 1H), 7.30 (d, J = 4.9 Hz, 1H), 5.25-4.65 (m, 2H), 4.40-3.70 (m, 4H), 3.52 (br s, 1H), 2.25-1.85 (m, 1H), 1.65-1.50 (m, 1H), 1.50-1.15 (m, 3H), 1.10-0.90 (m, 2H)	(+/-)-2-{4-[5-Cyclopropyl-4-((trans)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile
678			553.26 (M+H)	($CDCl_3$) 9.16 (s, 1H), 8.94 (s, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.08 (s, 1H), 7.91 (s, 1H), 7.66 (dd, J = 5.2; 1.0 Hz, 1H), 7.34 (app t, J = 2.0 Hz, 1H), 7.22 (dd, J = 8.0; 1.1 Hz, 1H), 7.11 (app t, J = 8.1 Hz, 1H), 6.52 (dd, J = 8.2; 1.8 Hz, 1H), 5.28-4.67 (m,	(+/-)- (trans)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4d]pyrimidin-4-yl)-piperidine-3,4-diol

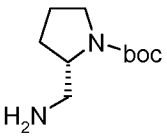
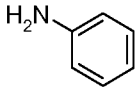
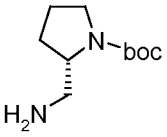
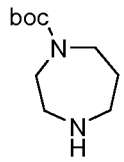
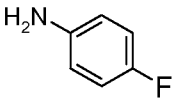
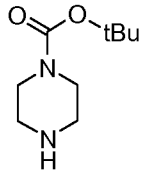
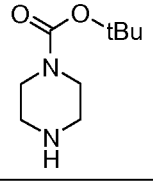
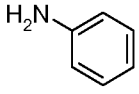
				2H), 4.28-3.71 (m, 2H), 3.50 (br s, 1H), 3.15-3.11 (m, 4H), 2.61-2.53 (m, 1H), 2.49-2.45 (m, 4H), 2.23 (s, 3H), 2.18-1.73 (m, 2H), 1.44-1.11 (m, 3H), 1.10-0.90 (m, 2H)	
679			500 (M+H)		1-[2-(2-Cyclopentylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carboxylicacid isopropylamide
680			479.1 (M+H)+	^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.69 (s, 1 H) 8.98 (s, 1 H) 8.81 (s, 1 H) 8.40 (dd, *J*=5.3, 0.8 Hz, 1 H) 8.21 - 8.30 (m, 1 H) 8.10 (s, 1 H) 7.92 (dd, *J*=5.1, 1.4 Hz, 1 H) 3.77 (d, *J*=11.3 Hz, 4 H) 2.85 (br. s., 4 H) 2.59 - 2.65 (m, 1 H) 1.21 - 1.31 (m, 3 H) 1.00 - 1.07 (m, 2 H)	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine
681			522.19 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.55 (1 H, s), 9.07 (1 H, s), 8.73 - 9.00 (2 H, m), 8.38 (1 H, d, J=5.5 Hz), 8.19 (1 H, s), 7.99 (1 H, s), 7.87 (2 H, d, J=8.5 Hz), 7.75 (1 H, dd, J=5.3, 1.3 Hz), 7.60 - 7.69 (4 H, m), 7.45 (2 H, t, J=7.7 Hz), 7.25 - 7.36 (1 H, m), 3.94 (4 H, br. s.), 3.34 (4 H, br. s.), 2.70 (1 H, br. s.), 1.21 - 1.31 (2	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine

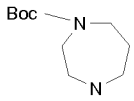
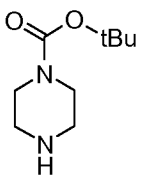
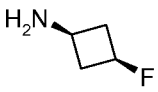
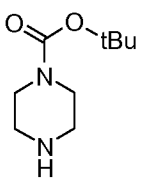
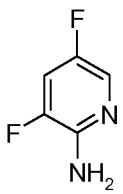
				H, m), 1.09 (2 H, d, J=3.5 Hz)	
682			479.1 (M+H)+	1H NMR (400 MHz, DMSO-d6) 9.82 (1 H, s), 9.07 (1 H, s), 8.69 - 8.99 (2 H, m), 8.43 (1 H, d, J=5.3 Hz), 8.19 (1 H, s), 8.03 (1 H, s), 7.88 (4 H, s), 7.82 (1 H, dd, J=5.3, 1.3 Hz), 3.94 (4 H, br. s.), 3.34 (4 H, br. s.), 2.67 - 2.75 (1 H, m), 1.26 (2 H, d, J=8.5 Hz), 1.09 (2 H, d, J=5.5 Hz)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-pyridin-4-yl)-amine
683			500 (M+H)		Biphenyl-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
684			468 (M+H)		4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzoic acid
685			546 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-hydroxy-ethyl)-amide
686			530 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-

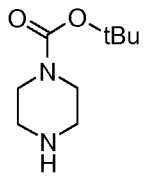
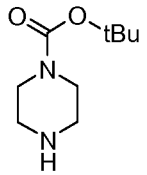
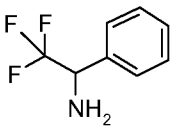
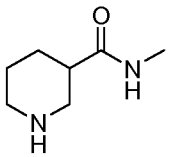
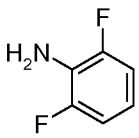
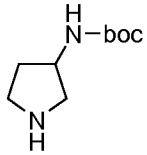
					yl}-piperidine-4-carboxylic acid dimethylamide
687			565.18 (M+H)	(dmso-d6) 9.99 (br s, 1H), 9.87 (s, 1H), 9.02 (s, 1H), 8.26 (d, J = 5.8 Hz, 1H), 8.16 (s, 1H), 8.02 (s, 1H), 7.76 (dd, J = 5.8; 1.4 Hz, 1H), 7.37 (s, 1H), 7.27 (app t, J = 8.1 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 6.75 (dd, J = 8.2; 1.6 Hz, 1H), 6.13 (br s, 1H), 4.56 (br s, exchangeable H's), 3.87-3.81 (m, 4H), 3.67 (br s, 2H), 3.60-3.50 (m, 7H), 3.19 (br s, 2H), 3.01 (app t, J = 12.2 Hz, 2H), 2.89 (s, 3H), 2.65-2.60 (m, 1H), 1.31-1.26 (m, 2H), 1.09-1.04 (m, 2H)	4-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid amide
688			537.3 (M+H)	(dmso-d6) 9.17 (s, 1H), 8.96 (s, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.09 (s, 1H), 7.92 (s, 1H), 7.66 (dd, J = 5.3; 1.4 Hz, 1H), 7.34 (app t, J = 2.0 Hz, 1H), 7.22 (dd, J = 8.0; 1.2 Hz, 1H), 7.11 (app t, J = 8.0 Hz, 1H), 6.52 (dd, J = 8.2 Hz; 1.8 Hz, 1H), 4.82 (br s, 1H), 4.1-4.06 (m, 2H), 3.79 (br s, 1H), 3.51 (br s, 2H), 3.15-3.11 (m, 4H), 2.50 (br s, 1H), 2.50-2.45 (m, 4H), 2.23 (s, 3H), 1.91-1.87 (m, 2H), 1.54 (br s, 2H), 1.27-1.24 (m, 2H), 1.04 - 1.02 (m, 2H)	1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-ol

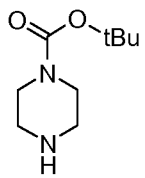
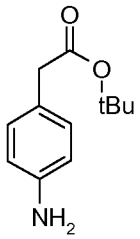
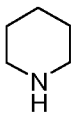
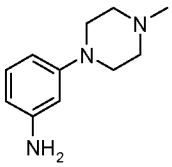
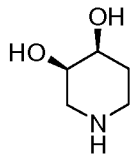
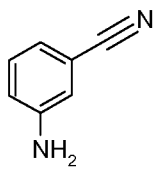
689		--	method 5: RT: 2.86 min,MI: 351.25 [M+H]	1H NMR (500MHz, DMSO) 8.98 (1H, s), 8.41 (1H, d), 8.26 (1H, d), 8.11 (1H, s), 7.95 (1H, d), 3.79-3.61 (4H, m), 2.83 (4H, m), 2.65-2.57 (1H, m), 1.26-1.24 (2H, m), 1.03-1.01 (2H, m).	5-Cyclopropyl-2-(2-fluoro-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
690			474 (M+H)		{4-[4-(4-Amino-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
691			method 5: RT: 2.43 min,MI:456 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 9.06 (1H, s), 8.32 (1H, dd), 8.22 (1H, s), 8.10 - 8.05 (1H, td), 7.98 (1H, s), 7.75 (1H, dd), 7.25 - 7.15 (2H, m), 7.09 - 7.03 (1H, m), 4.30 (2H, m), 3.55 (2H, m), 3.42 (1H, m), 3.36 - 3.23 (2H, m), 2.66 (1H, m), 1.32 (3H, d), 1.26 (2H, m), 1.05 (2H, m).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-phenyl)-amine
692			method 5: RT: 2.42 min,MI: 474 [M+H]	1H NMR (DMSO, 500MHz) 9.06 (1H, s), 8.22 (2H, m), 7.76 (1H, s), 7.71(1H, dd), 7.32 - 7.25 (1H, m), 7.16 (2H, m), 2.67 (1H, m), 1.31 (3H, d), 1.26 (2H, m), 1.05 (2H, m). [methyl piperazine side chain peaks not integrated).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine

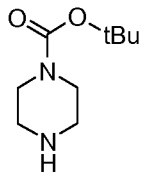
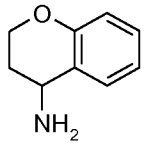
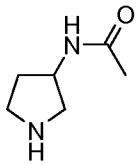
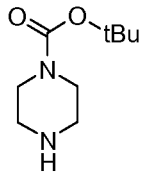
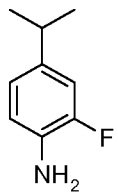
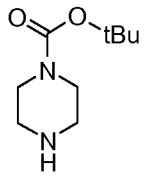
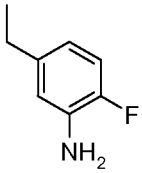
693			method 5: RT: 2.27 min,MI:456 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 9.07 (1H, s), 8.32 (1H, dd), 8.22 (1H, s), 7.90 (1H, s), 7.70 (3H, m), 7.11 (2H, m), 4.34 (2H, m), 3.55 (2H, m), 3.43 (1H, m), 3.30 (2H, m), 2.67 (1H, m), 1.32 (3H, d), 1.24 (2H, m), 1.04 (2H, m).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine
694			method 5: RT:2.65 min,MI: 475 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 9.08 (1H, s), 8.94 (1H, m), 8.46 (1H, dd), 8.23 (1H, s), 8.00 (1H, dd), 7.83 - 7.77 (1H, m), 6.69 - 6.65 (1H, m), 4.36 (2H, m), 3.58 (2H, m), 3.46 - 3.27 (3H, m), 2.67 (1H, m), 1.31 (3H, d), 1.27 (2H, m), 1.05 (2H, m).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine
695			442 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.07 (1 H, s), 8.93 (2 H, br. s.), 8.22 (1 H, s), 8.07 (1 H, d, J=6.3 Hz), 7.80 - 8.03 (1 H, m), 7.65 (1 H, br. s.), 3.91 - 4.00 (2 H, m), 3.61 - 3.65 (4 H, m), 3.27 - 3.34 (4 H, m), 2.62 - 2.67 (1 H, m), 2.30 (1 H, br. s.), 1.85 (1 H, br. s.), 1.41 - 1.64 (4 H, m), 1.12 - 1.38 (6 H, m), 1.01 - 1.12 (2 H, m)	(+/-)-(1RS,2RS,4SR)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
696			488 (M+H)		{4-[4-(4-Aminomethyl-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-

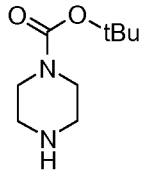
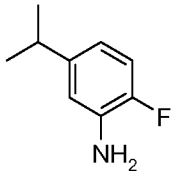
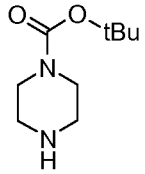
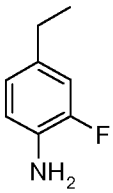
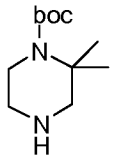
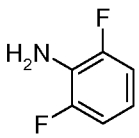
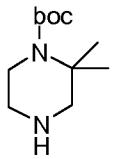
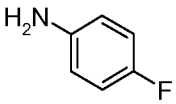
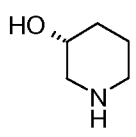
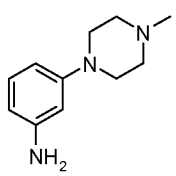
					difluoro-phenyl)-amine
697			438.1 (MH)+		[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine
698			474.3 (MH)+		{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(S)-1-pyrrolidin-2-ylmethyl-amine
699			method 5: RT: 2.19 min,MI:456 [M+H]	1H NMR (DMSO, 500MHz) 9.49 (1H, s), 8.96 (1H, s), 8.30 (1H, d), 8.14 (1H, s), 7.91(1H, s), 7.76 (2H, m), 7.71 (1H, dd), 7.17 (2H, m), 4.17 (2H, m), 4.01 (2H, m), 3.49 (2H, m), 3.16 (2H, m), 2.35 (1H, m), 2.06 (2H, m), 1.24 (2H, m), 0.97 (2H, m).	[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine
700			method 5: RT: 2.59 min,MI: 414.29 [M+H]	1H NMR (500MHz, DMSO) 8.94 (1H, s), 8.18 (1H, d), 8.06 (1H, s), 7.58 (1H, s), 7.46 (1H, dd), 7.39 (1H, s), 3.74-3.63 (4H, m), 2.88 (4H, m), 2.62-2.60 (2H, m), 2.09 (6H, s), 1.24-1.22 (2H, m), 1.01-0.99 (4H, m).	Bicyclo[1.1.1]pent-1-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
701			method 5: RT:3.76 min,M	1H NMR (500MHz, DMSO) 8.98 (1H, d), 8.94 (1H, s), 8.11 (1H, s), 8.06 (1H, d), 7.81 (2H, d), 7.42	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-

			I:442.33 [M+H]	(1H, t), 7.28 (2H, t), 6.95 (1H, t), 3.73 (4H, s, br), 2.82 (4H, s, br), 2.63-2.57 (1H, m), 1.27-1.25 (2H, m), 1.03-1.02 (2H, m).	yl)-3-fluoro-pyridin-2-yl]-phenyl-amine
702			method 5: RT: 2.35 min,MI: 474 [M+H]	1H NMR (DMSO, 500MHz) 9.04 (1H, s), 8.98 (1H, s), 8.18 (1H, d), 8.15(1H, s), 7.84 (1H, s), 7.71 (1H, dd), 7.31 (1H, m), 7.19 (2H, t), 4.18 (2H, m), 4.01 (2H, m), 3.47 (2H, m), 3.16 (2H, m), 2.35(1H, m), 2.06 (2H, m), 1.26 (2H, m), 0.98 (2H, m).	[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine
703			method 5: RT: 2.19 min,MI: 420.29 [M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.11 (1H, d), 9.06 (1H, s), 7.48 (1H, s), 7.44 (1H, dd), 7.14 (1H, d), 5.34-5.20 (1H, m), 4.85 (1H, m,br), 3.77-3.56 (5H, m, br), 2.84 (4H, s), 2.62-2.59 (2H, m), 2.36-2.27 (2H, m), 1.26-1.23 (2H, m), 1.03-1.00 (2H, m).	(+/-)cis-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-cyclobutyl)-amine
704			461.54	^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.39 (s, 1 H) 8.98 (s, 1 H) 8.67 (s, 1 H) 8.35 (d, *J*=5.3 Hz, 1 H) 8.22 (d, *J*=2.5 Hz, 1 H) 8.10 (s, 1 H) 7.94 (ddd, *J*=10.7, 8.3, 2.6 Hz, 1 H) 7.84 (dd, *J*=5.1, 1.4 Hz, 1 H) 3.58 - 3.86 (m, 4 H) 2.85 (br. s., 4 H) 2.73-52 (m, 1 H) 1.22 - 1.31 (m, 2 H) 0.99 - 1.07 (m, 2 H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine

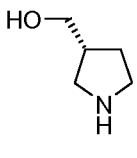
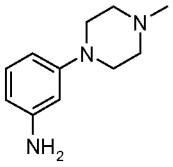
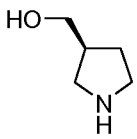
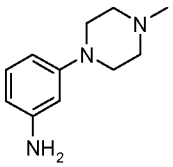
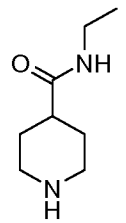
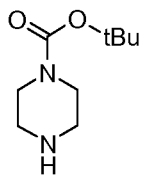
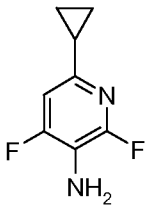
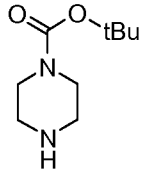
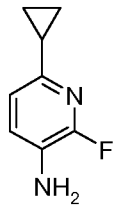
705			461.63		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-4-yl)-amine
706			506.53 (M+H)	(dmso-d6) 9.05 (s, 1H), 8.99 (br s, 1H), 8.22-8.16 (m, 2H), 8.13 (d, J = 10.0 Hz, 1H), 7.89 (s, 1H), 7.65 (app d, J = 7.2 Hz, 2H), 7.61 (dd, J = 5.4; 1.4 Hz, 1H), 7.48-7.35 (m, 3H), 6.23 (quint, J = 9.2 Hz, 1H), 4.51 (br s, exch. H's), 3.91 (br s, 6H), 2.74-2.64 (m, 1H), 1.30-1.22 (m, 2H), 1.12-1.04 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-1-phenyl-ethyl)-amine
707			516 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-3-carboxylic acid methylamide
708			460 (M+H)		{4-[4-(3-Amino-pyrrolidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine

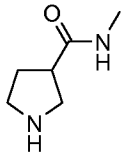
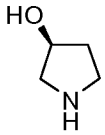
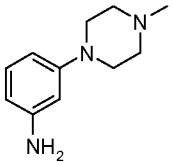
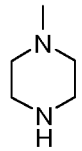
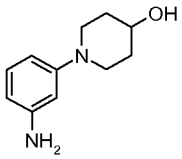
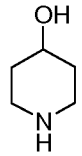
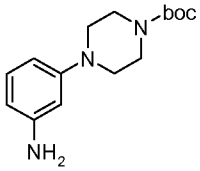
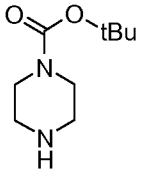
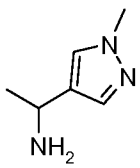
709			482 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.52 (1 H, br. s.), 9.06 (1 H, s), 8.76 - 9.04 (2 H, m), 8.31 (1 H, d, J=5.3 Hz), 8.19 (1 H, s), 7.97 (1 H, s), 7.72 (1 H, dd, J=5.5, 1.3 Hz), 7.65 (2 H, d, J=8.5 Hz), 7.21 (2 H, d, J=8.5 Hz), 3.78 - 3.99 (4 H, m), 3.52 (2 H, s), 3.33 (4 H, br. s.), 2.65 - 2.78 (1 H, m), 1.19 - 1.34 (2 H, m), 0.99 - 1.14 (2 H, m)	{4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-phenyl}-acetic acid
710			521.78	($CDCl_3$) 9.06 (s, 1H), 8.35 (d, J = 5.2 Hz, 1H), 8.07 (s, 1H), 8.01 (s, 1H), 7.79 (dd, J = 5.2; 1.3 Hz, 1H), 7.23 (app t, J = 8.0 Hz, 1H), 7.05-7.02 (m, 1H), 7.00- 6.98 (m, 1H), 6.93 (dd, J = 8.0; 1.6 Hz, 1H), 6.65 (dd, J = 8.0; 2.0 Hz, 1H), 3.70 (br s, 4H), 3.28-3.24 (m, 4H), 2.66-2.62 (m, 1H), 2.61-2.56 (m, 4H), 2.35 (s, 3H), 1.69 br s, 6H), 1.26-1.18 (m, 2H), 1.00-0.95 (m, 2H)	[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine
711			480.59		3-{4-[5-Cyclopropyl-4-((3R,4S)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzonitrile

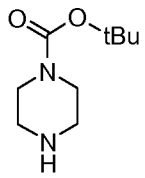
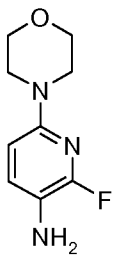
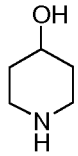
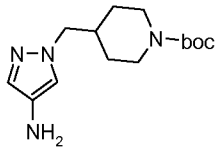
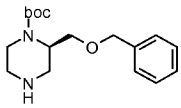
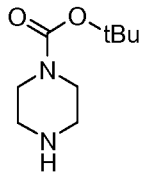
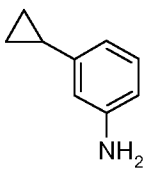
712			480 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.06 (1 H, s), 8.88 (2 H, br. s.), 8.13 - 8.25 (2 H, m), 7.89 (1 H, br. s.), 7.63 (1 H, br. s.), 7.33 (1 H, d, J=7.3 Hz), 7.23 (1 H, t, J=7.5 Hz), 6.92 (1 H, t, J=7.3 Hz), 6.86 (1 H, d, J=8.3 Hz), 5.21 (1 H, br. s.), 4.18 - 4.31 (3 H, m), 3.83 - 3.94 (4 H, m), 3.31 (4 H, br. s.), 2.64 - 2.72 (1 H, m), 2.13 - 2.26 (1 H, m), 2.00 - 2.13 (1 H, m), 1.20 - 1.33 (2 H, m), 1.01 - 1.12 (2 H, m)	Chroman-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
713			502 (M+H)		N-(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-acetamide
714			484.25		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-isopropyl-phenyl)-amine
715			470		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-ethyl-2-fluoro-phenyl)-amine

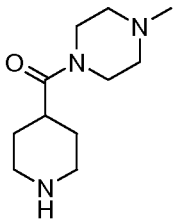
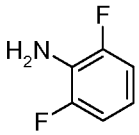
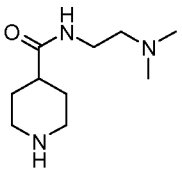
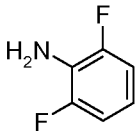
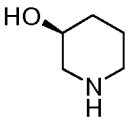
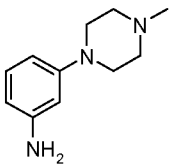
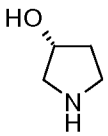
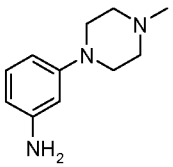
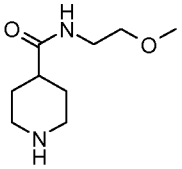
716			484.2		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-isopropyl-phenyl)-amine
717			470.2		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-ethyl-2-fluoro-phenyl)-amine
718			488 (M+H)	1H NMR (500MHz, DMSO) 8.92 (1H, s), 8.75 (1H, s), 8.15 (1H, d), 8.08 (1H, s), 7.74 (1H, s), 7.64 (1H, dd), 7.34-7.24 (1H, m), 7.16 (2H, t), 3.91-3.52 (4H, m, br), 2.85 (2H, s), 2.50-2.45 (1H, m), 1.23-1.22 (2H, m), 1.08-0.98 (6H, m), 0.78 (2H, s, br).	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
719			470 (M+H)	1H NMR (500MHz, DMSO) 9.32 (1H, s), 8.93 (1H, s), 8.28 (1H, d), 8.08 (1H, s), 7.85 (1H, s), 7.76-7.73 (2H, m), 7.66 (1H, d), 7.11 (2H, t), 3.95-3.55 (4H, m), 2.87 (2H, m, br), 2.53 (1H, m), 1.24-1.22 (2H, m), 1.06-0.78 (9H, m).	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine
720			537.67		(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-

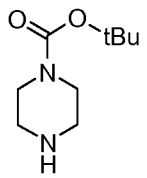
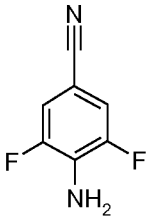
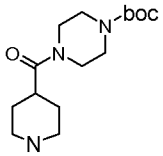
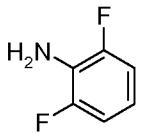
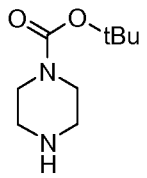
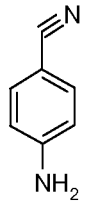
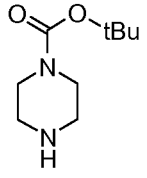
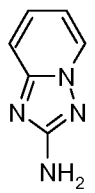
					d]pyrimidin-4-yl)-piperidin-3-ol

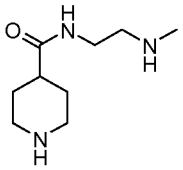
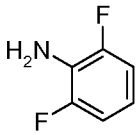
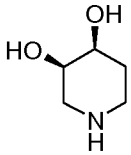
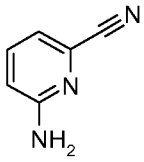
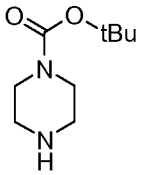
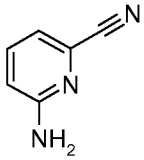
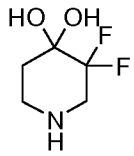
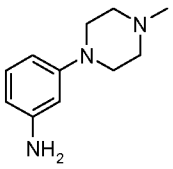
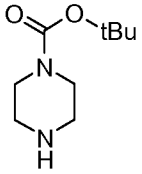
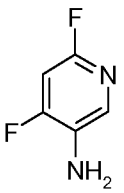
721			537.71		[(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-methanol
722			537.7		[(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-methanol
723			530 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid ethylamide
724			501.57 (MH)+		(6-Cyclopropyl-2,4-difluoro-pyridin-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine; bis-trifluoroacetic salt
725			483.61 (MH)+		(6-Cyclopropyl-2-fluoro-pyridin-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-

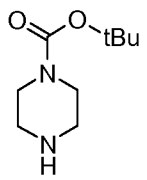
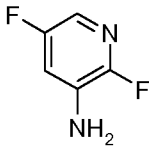
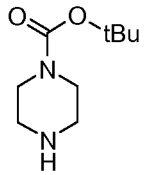
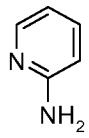
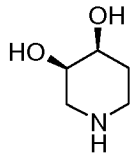
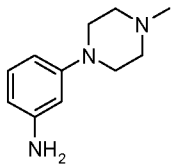
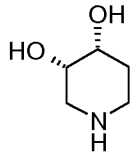
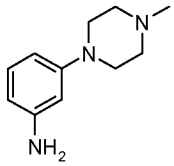
					amine; bis-trifluoroacetic acid salt
726			502 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidine-3-carboxylic acid methylamide
727			523.66 (M+H)+		(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-ol
728			537.73 (M+H)+		1-(3-{4-[5-Cyclopropyl-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-piperidin-4-ol
729			523.70 (M+H)+		1-{5-Cyclopropyl-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
730			456 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.08 (4 H, s), 8.22 (1 H, s), 8.08 (1 H, d, J=6.5 Hz), 8.04 (1 H, br. s.), 7.75 (1 H, s), 7.70 (1 H, dd, J=6.5,	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(1-methyl-

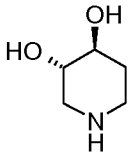
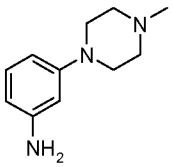
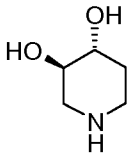
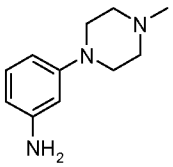
				1.3 Hz), 7.49 (1 H, s), 5.06 (1 H, br. s.), 3.6-3.9 (8 H, m), 3.32 (4 H, br. s.), 2.62 - 2.68 (1 H, m), 1.55 (3 H, d, J=6.8 Hz), 1.21 - 1.31 (2 H, m), 1.05 - 1.12 (2 H, m)	1H-pyrazol-4-yl)-ethyl]-amine
731			528.63 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-6-morpholin-4-yl-pyridin-3-yl)-amine
732			526		1-{5-Cyclopropyl-2-[2-(1-piperidin-4-ylmethyl-1H-pyrazol-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
733		--	487.15		4-((R)-3-Benzyloxymethyl-piperazin-1-yl)-2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidine
734			464.2		(3-Cyclopropyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

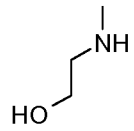
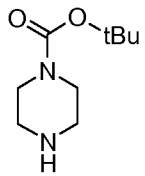
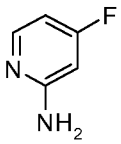
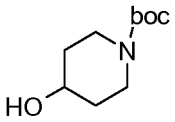
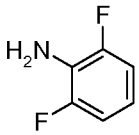
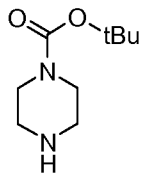
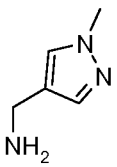
735			585 (M+H)		(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-(4-methyl-piperazin-1-yl)-methanone
736			573 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-dimethylamino-ethyl)-amide
737			537.72 (M+H)		(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-ol
738			523.68 (M+H)+		(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-ol
739			560 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-

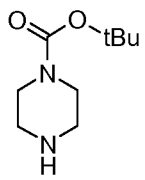
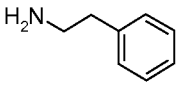
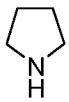
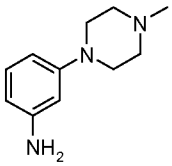
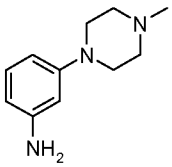
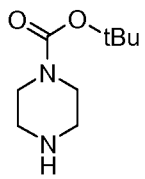
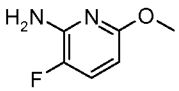
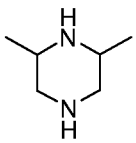
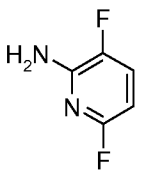
					yl}-piperidine-4-carboxylic acid (2-methoxy-ethyl)-amide
740			485 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.13 (1 H, s), 9.02 - 9.09 (1 H, m), 8.75 - 8.98 (2 H, m), 8.39 (1 H, br. s.), 8.17 - 8.31 (2 H, m), 7.74 - 8.06 (2 H, m), 3.84 - 4.04 (4 H, m), 3.36 (4 H, br. s.), 2.71 (1 H, br. s.), 1.19 - 1.33 (2 H, m), 1.04 - 1.16 (2 H, m)	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-3,5-difluoro-benzonitrile
741			571 (M+H)		(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-piperazin-1-yl-methanone
742			467 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.72 (1 H, s), 9.07 (1 H, s), 8.78 - 9.03 (2 H, m), 8.41 (1 H, d, J=5.3 Hz), 8.19 (1 H, s), 8.01 (1 H, s), 7.69 - 7.89 (6 H, m), 7.14 (1 H, br. s.), 3.94 (4 H, br. s.), 3.34 (4 H, br. s.), 2.64 - 2.77 (1 H, m), 1.20 - 1.32 (2 H, m), 1.01 - 1.13 (2 H, m)	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzamide
743			465.56 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl-amine

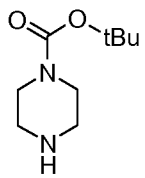
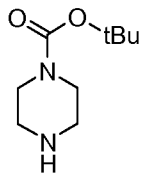
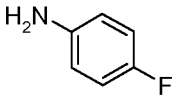
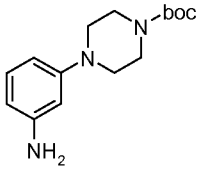
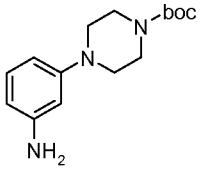
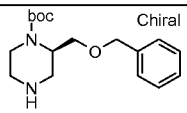
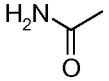
744			559 (M+H)		1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-methylamino-ethyl)-amide
745			481.53		6-{4-[5-Cyclopropyl-4-((cis)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-pyridine-2-carbonitrile
746			450.55 (M+H)+		6-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile
747			589.70 (M+H)+		1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-3,3-difluoro-piperidine-4,4-diol
748			461.51 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-3-yl)-

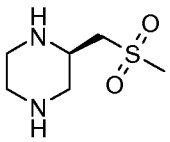
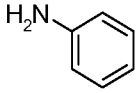
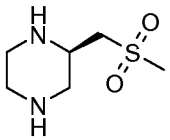
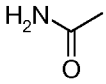
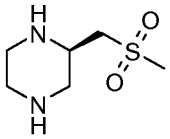
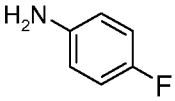
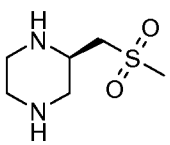
					amine
749			461.50 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-difluoro-pyridin-3-yl)-amine
750			425.54 (M+H)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine
751	 Or enantiomer		553.28	($CDCl_3$) 9.07 (s, 1H), 8.32 (d, J = 5.2 Hz, 1H), 8.08 (br s, 1H), 8.02 (s, 1H), 7.79 (d, J = 5.2 Hz, 1H), 7.24 (dd, J = 8.4 Hz, 1H)), 7.06 (br s, 1H), 6.98 (br s, 1H), 6.82 (br d, J = 7.08 Hz, 1H), 6.69 (dd, J = 8.4; 1.9 Hz, 1H), 3.95 (m, 5H), 3.55 (m, br s, 1H), 3.25 (br s, 5H), 2.60 (m, 5H), 2.34 (s, 3H), 1.91 (m, 1H), 1.7 br s (exch. H's), 1.24 (m, 2H), 0.97 (m, 2H)	(3R,4S or 3R,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol Single enantiomer, unassigned
752	 Or enantiomer		553.29	($CDCl_3$) 9.07 (s, 1H), 8.32 (d, J = 5.2 Hz, 1H), 8.08 (br s, 1H), 8.02 (s, 1H), 7.79 (d, J = 5.2 Hz, 1H), 7.24 (dd, J = 8.4 Hz, 1H)), 7.06 (br s, 1H), 6.98 (br s, 1H), 6.82 (br d, J = 7.08 Hz, 1H), 6.69 (dd, J = 8.4; 1.9 Hz, 1H), 3.95 (m, 5H),	(3R,4S or 3R,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol Single

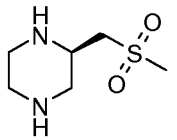
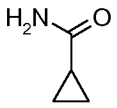
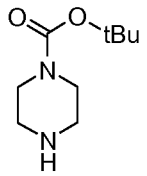
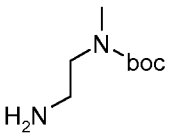
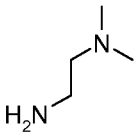
				3.55 (m, br s, 1H), 3.25 (br s, 5H), 2.60 (m, 5H), 2.34 (s, 3H), 1.91 (m, 1H), 1.7 br s (exch. H's), 1.24 (m, 2H), 0.97 (m, 2H)	enantiomer, unassigned
753	 Or enantiomer		553.3	($CDCl_3$) 9.16 (s, 1H), 8.94 (s, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.08 (s, 1H), 7.91 (s, 1H), 7.66 (dd, J = 5.2; 1.0 Hz, 1H), 7.34 (app t, J = 2.0 Hz, 1H), 7.22 (dd, J = 8.0; 1.1 Hz, 1H), 7.11 (app t, J = 8.1 Hz, 1H), 6.52 (dd, J = 8.2; 1.8 Hz, 1H), 5.28-4.67 (m, 2H), 4.28-3.71 (m, 2H), 3.50 (br s, 1H), 3.15-3.11 (m, 4H), 2.61-2.53 (m, 1H), 2.49-2.45 (m, 4H), 2.23 (s, 3H), 2.18-1.73 (m, 2H), 1.44-1.11 (m, 3H), 1.10-0.90 (m, 2H)	(3S,4S or 3R,4R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol Single enantiomer, unassigned
754	 Or enantiomer		553.3	($CDCl_3$) 9.16 (s, 1H), 8.94 (s, 1H), 8.30 (d, J = 5.3 Hz, 1H), 8.08 (s, 1H), 7.91 (s, 1H), 7.66 (dd, J = 5.2; 1.0 Hz, 1H), 7.34 (app t, J = 2.0 Hz, 1H), 7.22 (dd, J = 8.0; 1.1 Hz, 1H), 7.11 (app t, J = 8.1 Hz, 1H), 6.52 (dd, J = 8.2; 1.8 Hz, 1H), 5.28-4.67 (m, 2H), 4.28-3.71 (m, 2H), 3.50 (br s, 1H), 3.15-3.11 (m, 4H), 2.61-2.53 (m, 1H), 2.49-2.45 (m, 4H), 2.23 (s, 3H), 2.18-1.73 (m, 2H), 1.44-1.11 (m, 3H), 1.10-	(3S,4S or 3R,4R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol Single enantiomer, unassigned

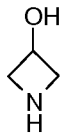
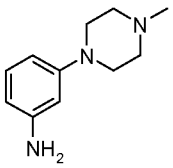
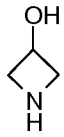
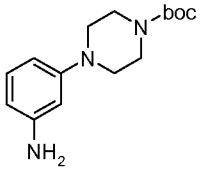
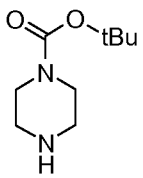
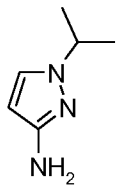
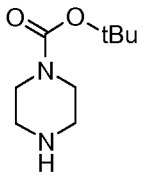
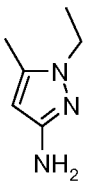
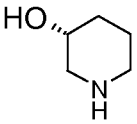
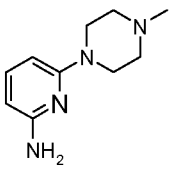
				0.90 (m, 2H)	
755			449 (M+H)		{4-[5-Cyclopropyl-4-(2-methylamino-ethoxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
756			443 (M+H)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-pyridin-2-yl)-amine
757			475 (M+H)		{4-[5-Cyclopropyl-4-(piperidin-4-yloxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
758			442 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.08 (1 H, s), 8.78 - 9.01 (2 H, m), 8.22 (1 H, s), 8.11 (1 H, d, J=6.3 Hz), 7.90 - 8.05 (1 H, m), 7.76 (1 H, s), 7.68 (1 H, d, J=6.8 Hz), 7.50 (1 H, s), 4.45 (2 H, br. s.), 3.88 (4 H, br. s.), 3.83 (3 H, s), 3.31 (4 H, br. s.), 2.63 - 2.70 (1 H, m), 1.19 - 1.34 (2 H, m), 1.02 - 1.15 (2 H, m)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-pyrazol-4-ylmethyl)-amine

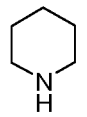
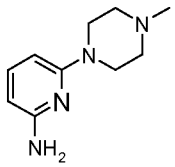
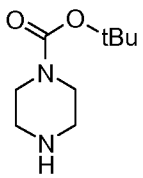
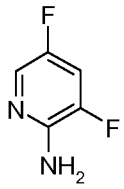
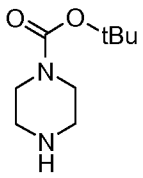
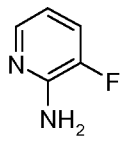
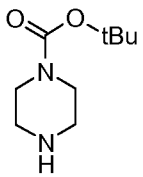
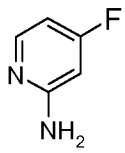
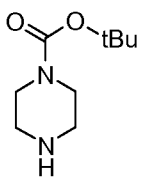
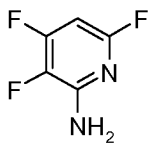
759			method 5: RT: 2.56 min,MI: 452 [M+H]	1H NMR (DMSO, 500MHz) 8.99 (1H, s), 8.17 (4H, m), 7.55 (1H, m), 7.44 (1H, m), 7.28 (4H, m), 7.20 (1H, m), 6.89 (1H, m), 3.75 (4H, s), 3.56 (6H, m), 2.88 (2H, m), 2.66 (1H, m), 1.25(2H, m), 1.03(2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenethyl-amine
760			507.35 (M+H)		[4-(5-Cyclopropyl-4-pyrrolidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine
761			493.39 (M+H)		[4-(4-Azetidin-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine
762			method 5: RT: 3.12 min,MI: 473 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 9.14 (1H, s), 9.00 (1H, s), 8.44 (1H, dd), 8.22 (1H, s), 7.96 (1H, dd), 7.62 (1H, m), 6.41 (1H, dd), 4.06 (3H, s), 3.97 (4H, t), 3.35 (4H, t), 2.68 (1H, m), 1.28 (2H, m), 1.03 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-6-methoxy-pyridin-2-yl)-amine
763			method 5: RT: 3.03 min,MI:489 [M+H]	1H NMR (DMSO, 500MHz) 9.72 (1H, s), 9.08 (1H, s), 8.64 (1H, m), 8.48 (1H, m), 8.21 (1H, s), 8.01 (1H, s), 7.88 (1H, m), 6.94 (1H, s), 6.73 (1H, m), 2.94 (2H, m), 2.78	{4-[5-Cyclopropyl-4-(3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-

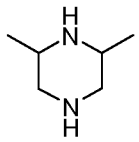
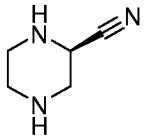
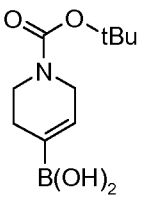
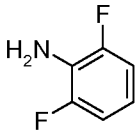
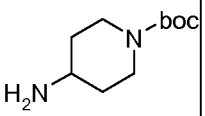
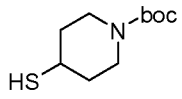
				(2H, m), 1.95 (1H, m). [Much of the piperazine side chain peaks had poor signalling therefore not integrated).	2-yl)-amine
764			method 5: RT:4.20 min,MI:478.39 [M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.75 (1H, s), 8.11 (1H, d), 8.10 (1H, s), 7.50 (1H, d), 7.26-7.23 (1H, m), 7.15 (2H, t), 4.09-4.08 (2H, m), 3.67 (4H, s, br), 2.80 (4H, s, br), 2.58-2.54 (1H, m), 1.26-1.24 (2H, m), 1.03-1.01 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine
765			method 5: RT: 4.58 min,MI:460.40 [M+H]	1H NMR (500MHz, DMSO) 9.31 (1H, s), 8.94 (1H, s), 8.23 (1H, d), 8.18 (1H, s), 8.12 (1H, s), 7.67 (2H, dd), 7.58 (1H, 7.11 (2H, t), 3.69 (4H, s, br), 2.88 (4H, s, br), 2.60-2.56 (1H, m), 1.26-1.24 (2H, m), 1.03-1.02 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-(4-fluoro-phenyl)-amine
766			493.39 (M+H)		[4-(5-Cyclopropyl-4-pyrrolidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine
767			479.29 (M+H)		[4-(4-Azetidin-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine
768			510.25		N-{4-[4-((R)-3-Benzyloxymethyl-piperazin-1-yl)-

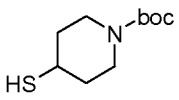
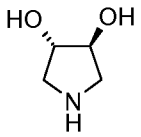
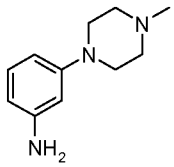
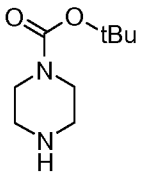
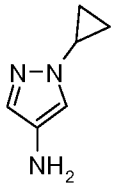
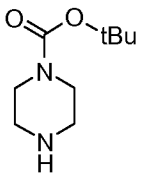
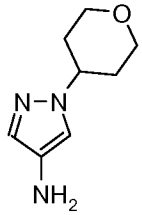
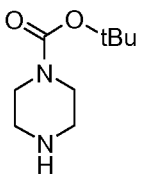
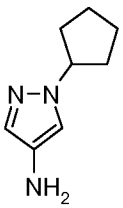
					5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide
769			516		{4-[5-Cyclopropyl-4-((R)-3-methanesulfonyl-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
770			482		N-{4-[5-Cyclopropyl-4-((R)-3-methanesulfonyl-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide
771			534.2		{4-[5-Cyclopropyl-4-((R)-3-methanesulfonyl-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine
772			552.2		{4-[5-Cyclopropyl-4-((R)-3-methanesulfonyl-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine

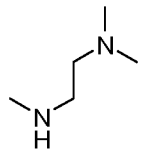
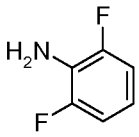
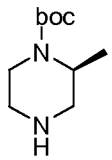
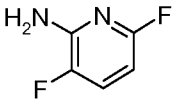
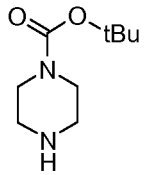
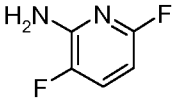
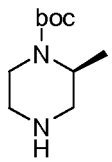
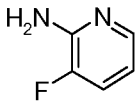
773			508.2		Cyclopropanecar-boxylic acid {4-[5-cyclopropyl-4-((R)-3-methanesulfonyl-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide
774			479 (M+H)+	^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.08 (s, 1 H) 8.96 - 9.02 (m, 1 H) 8.89 - 9.13 (m, 3 H) 8.43 - 8.53 (m, 1 H) 8.19 (s, 1 H) 8.00 (dd, *J*=5.1, 1.4 Hz, 1 H) 7.01 (dt, *J*=9.3, 3.0 Hz, 1 H) 3.77 - 4.13 (m, 4 H) 3.28 - 3.41 (m, 4 H) 2.63 - 2.74 (m, 1 H) 1.20 - 1.33 (m, 2 H) 1.04 - 1.13 (m, 2 H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,6-trifluoro-pyridin-2-yl)-amine
775			448 (M+H)		N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N'-methyl-ethane-1,2-diamine
776			462 (M+H)		N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N',N'-dimethyl-ethane-1,2-diamine

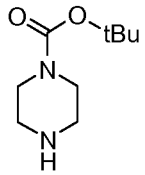
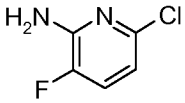
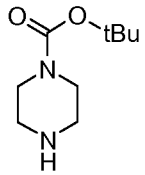
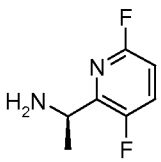
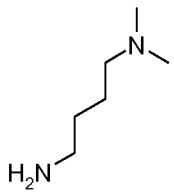
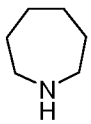
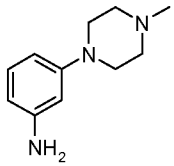
777			509.26 (M+H)		1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-azetidin-3-ol
778			495.29 (M+H)		1-{5-Cyclopropyl-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-azetidin-3-ol
779			456.22 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-isopropyl-1H-pyrazol-3-yl)-amine
780			456.24 (M+H)		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-ethyl-5-methyl-1H-pyrazol-3-yl)-amine
781			538.36 (M+H)		(R)-1-(5-Cyclopropyl-2-{2-[6-(4-methyl-piperazin-1-yl)-pyridin-2-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-ol

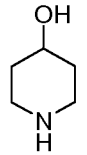
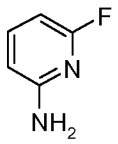
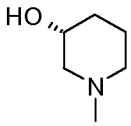
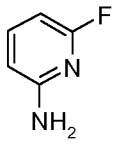
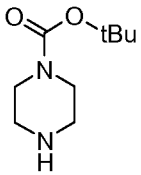
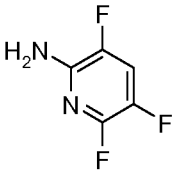
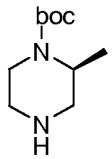
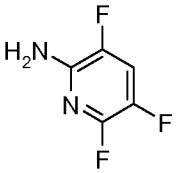
782			523.66 (M+H)		[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine
783			475.19 (MH)+		[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine
784			457.25 (MH)+		[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-pyridin-2-yl)-amine
785			457.29 (M+H)+		[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-pyridin-2-yl)-amine
786			593.28 (M+H)+	^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.09 (s, 1 H) 9.15 (s, 1 H) 8.79 - 8.96 (m, 3 H) 8.48 (d, *J*=5.3 Hz, 1 H) 8.00 (dd, *J*=5.1, 1.4 Hz, 1 H) 7.02 (dt, *J*=9.5, 3.0 Hz, 1 H) 4.17 - 4.32 (m, 1 H) 3.81 - 3.92 (m, 4 H) 3.19 - 3.39 (m, 4 H) 1.86 - 2.44 (m, 6 H)	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,6-trifluoro-pyridin-2-yl)-amine

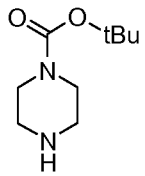
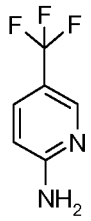
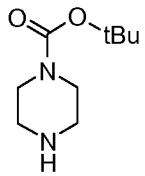
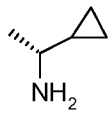
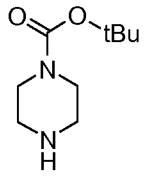
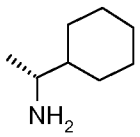
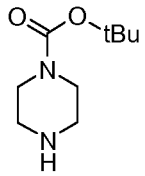
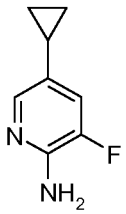
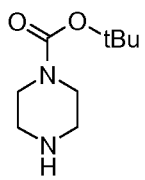
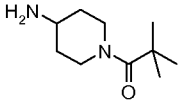
787			method 5: RT: 3.09 min,MI: 488 [M+H]	1H NMR (DMSO, 500MHz) 9.06 (1H, s), 8.90 (1H, s), 8.71 (1H, s), 8.20(1H, s), 7.80 (1H, s), 7.72 (1H, dd), 7.30 (1H, m), 7.19 (2H, t), 4.33 (2H, m), 3.74 (1H, m), 3.35 (2H, m), 2.87 (1H, m), 1.23 (7H, m), 1.15 (2H, m), 1.09 (2H, m).	{4-[5-Cyclopropyl-4-(3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
788			method 5: RT: 4.07 min,MI: 485 [M+H]		(R)-4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-2-carbonitrile
789			457 (M+H)		{4-[5-Cyclopropyl-4-(1,2,3,6-tetrahydro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
790			474 (M+H)		{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine
791			491 (M+H)		{4-[5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-

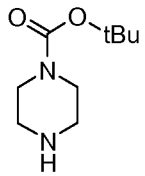
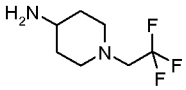
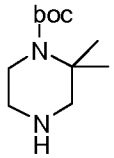
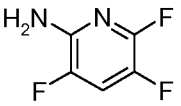
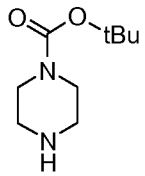
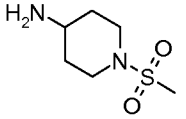
					difluoro-phenyl)-amine
792			491 (M+H)		{4-[5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
793			539.5 (M+H)		(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3,4-diol
794			454.25		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-cyclopropyl-1H-pyrazol-4-yl)-amine
795			498.25		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine
796			482.2		(1-Cyclopentyl-1H-pyrazol-4-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

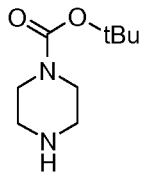
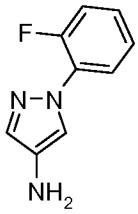
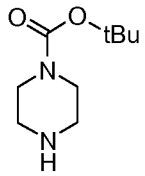
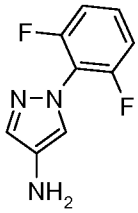
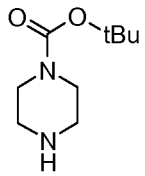
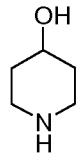
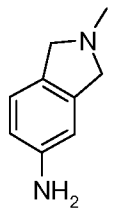
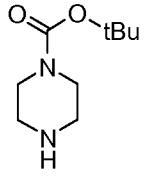
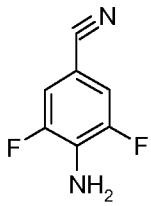
797			476 (M+H)		N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N,N',N'-trimethyl-ethane-1,2-diamine
798			method: 5, RT: 2.78min, MI: 489 [M+H]	1H NMR (DMSO, 500MHz) 9.70(1H, s), 9.17 (1H,s,br), 9.11 (1H, s), 8.69 (1H, s), 8.46 (1H, m), 7.98 (1H, m), 7.85 (1H, m), 6.71 (1H, m), 4.28 (1H, m), 4.26 (1H, m), 4.06 (1H, m), 3.91 (1H, m), 3.79 (1H, m) , 3.65 (1H, m), 3.23 (1H, m), 3.06 (1H, m), 2.52 (3H, s), 2.16 (2H, m), 2.21 (2H, m), 2.09 (1H, m), 1.91 (1H, m).	{4-[5-Cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine
799			method 5: RT: 2.72min, MI: 475 [M+H]	1H NMR (DMSO, 500MHz) 9.70(1H, s), 9.14 (1H, s,br), 9.02 (1H, s), 8.80 (1H, d), 8.46 (1H, m), 7.97 (1H, m), 7.86 (1H, m), 6.71 (1H, m), 4.25 (1H, m), 3.86 (4H, m), 3.58 (4H, m), 2.80 (2H, m), 2.21 (2H, m), 2.08 (1H, m), 1.93 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,6-difluoro-pyridin-2-yl)-amine
800			method 5: RT: 1.62min, MI: 457 [M+H]	1H NMR (DMSO, 500MHz) 9.10 (2H, s), 8.88 (1H, s), 8.51 (1H, d), 8.27 (1H, dd), 8.24 (1H, s), 8.16 (1H, dd), 7.92 (1H, m), 7.27 (1H, m), 4.35 (2H, s), 3.51 (5H, m), 2.54	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3-fluoro-pyridin-2-yl)-

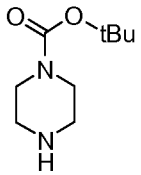
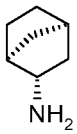
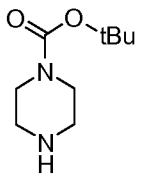
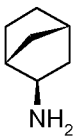
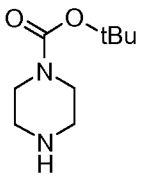
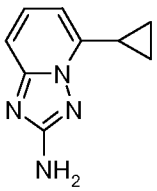
				(1H, m), 1.29 (3H, m), 1.25 (2H, m), 1.09 (2H, m).	amine
801			method 5: RT: 2.59min, MI: 477 [M+H]	1H NMR (DMSO, 500MHz) 9.76 (1H, s), 9.06 (1H, s), 8.99 (1H, s), 8.47 (1H, s), 8.18 (1H, s), 8.01 (1H, s), 7.74 (1H, m), 7.11 (1H, m), 3.93 (4H, s), 3.34 (4H, s), 2.70 (1H, m), 1.26 (2H, m), 1.09 (2H, m).	(6-Chloro-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
802		Chiral 	method 5: RT: 2.57 min, MI: 489.49 [M+H]	1H NMR (500MHz, DMSO) 8.93 (1H, s), 8.06 (1H, s), 8.01 (1H, d), 7.92-7.84 (1H, m), 7.66 (1H, s), 7.39 (1H, d), , 7.33 (1H, d), 7.12-7.07 (1H, m), 5.42 (1H, t, br), 3.83-3.57 (4H, m, br), 3.16 (1H, s, br), 2.84 (4H, s, br), 2.61 (1H, m, br), 1.45 (3H, d), 1.25-1.22 (2H, m), 1.03-1.01 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(3,6-difluoro-pyridin-2-yl)-ethyl]-amine
803			490 (M+H)		N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N',N'-dimethyl-butane-1,4-diamine
804			535.50 (M+H)		[4-(4-Azepan-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine

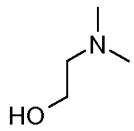
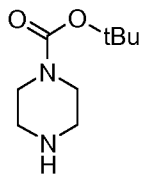
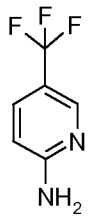
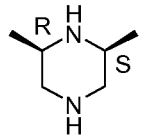
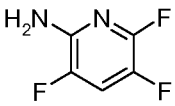
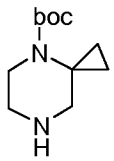
805			458.36 (M+H)		1-{5-Cyclopropyl-2-[2-(6-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
806			458.20 (M+H)		(R)-1-{5-Cyclopropyl-2-[2-(6-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ol
807			method 5: RT: 2.88min, MI: 493 [M+H]	1H NMR (DMSO, 500MHz) 9.74 (1H, s), 9.13 (1H, s br), 8.80 (2H, dd), 8.42 (1H, d), 8.26 (1H, m), 7.94 (1H, d), 4.23 (1H, m), 3.84 (4H, m), 3.25 (4H, m), 2.38 (2H, m), 2.21(2H, m), 2.10 (1H, m), 1.89 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine
808			method 5: RT: 2.90min, MI: 506 [M+H]	1H NMR (DMSO, 500MHz) 9.76 (1H, s), 9.17 (1H, s br), 9.11 (1H, s), 8.70 (1H, s), 8.44 (1H, m), 8.28 (1H,m), 7.95 (1H, m), 4.27 (1H, m), 4.26 (1H, m), 4.06 (1H, m), 3.91 (1H, m), 3.79 (1H, m), 3.65 (1H, m), 3.23 (1H, m), 3.06 (1H, m), 2.53 (3H, s), 2.16 (2H, m), 2.16 (2H, m), 2.07 (1H, m), 1.89 (1H, m).	{4-[5-Cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine

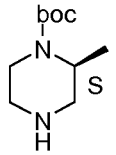
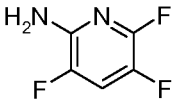
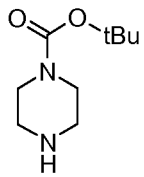
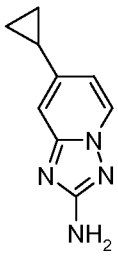
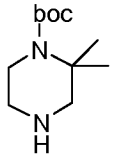
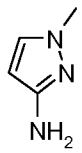
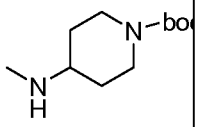
809			507.19 (MH)+		[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine
810			416.26 (M+H)		((R)-1-Cyclopropyl-ethyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
811			458.29 (M+H)		((R)-1-Cyclohexyl-ethyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
812			483.21 (MH)+		(5-Cyclopropyl-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
813			method 5: RT: 2.60 min, MI: 515.51 [M+H]	1H NMR (500MHz, DMSO, 90°C) 9.07 (1H, s), 8.23 (1H, s), 8.13 (1H, d), 7.76 (1H, s), 7.57 (1H, dd), 4.22-4.19 (2H, m), 4.11-4.06 (1H, m), 3.97 (4H, t, br), 3.35 (4H, t, br), 3.15-3.08 (2H, m), 2.70-2.66 (1H, m), 2.05-2.03 (2H, m), 1.52-1.42 (2H, m),	1-{4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-piperidin-1-yl}-2,2-dimethyl-propan-1-one

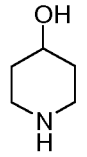
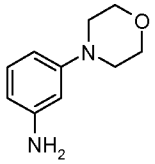
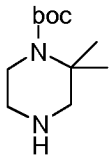
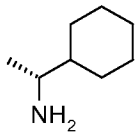
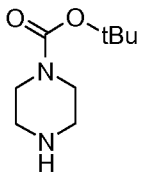
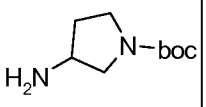
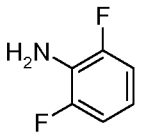
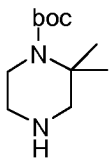
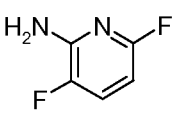
				1.29-1.27 (2H, m), 1.26 (9H, s), 1.05-1.03 (2H, m).	
814			method 5: RT: 2.43 min, MI: 513.41 [M+H]	1H NMR (500MHz, DMSO, 90°C) 9.07 (1H, s), 8.23 (1H, s), 8.10 (1H, d), 7.81 (1H, s), 7.58 (1H, dd), 3.97 (4H, t, br), 3.86-3.81 (1H, m), 3.34 (4H, t, br), 3.20 (2H, q), 3.01-2.98 (2H, m), 2.70-2.67 (1H, m), 2.61 (2H, t), 2.00-1.97 (2H, m), 1.66-1.57 (2H, m), 1.30-1.25 (2H, m), 1.05-1.03 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine
815			method 5: RT: 3.71 min, MI: 507.41 [M+H]	1H NMR (500MHz, DMSO, 90°C) 9.07 (1H, s), 8.71 (1H, s), 8.43 (1H, d), 8.26 (1H, s), 8.12 (1H, q), 7.98 (1H, dd), 4.02 (2H, t, br), 3.95 (2H, s), 3.38 (2H, t), 2.56-2.54 (1H, m), 1.31 (6H, s), 1.30-1.27 (2H, m), 1.02 (2H, dd).	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine
816			method 5: RT: 2.06 min, MI: 509.44 [M+H]	1H NMR (500MHz, DMSO, 90°C) 9.07 (1H, s), 8.22 (1H, s), 8.14 (1H, d), 7.74 (1H, s), 7.57 (1H, dd), 3.97 (4H, t, br), 3.65-3.60 (2H, m), 3.35 (4H, t, br), 3.04-2.97 (2H, m), 2.90 (3H, s), 2.71-2.65 (1H, m), 2.12-2.07 (2H, m), 1.68-1.59 (2H, m), 1.29-1.26 (2H, m), 1.05-1.03 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methanesulfonyl-piperidin-4-yl)-amine

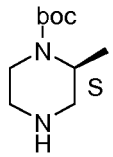
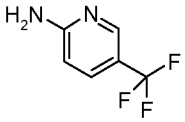
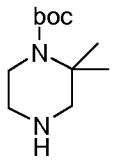
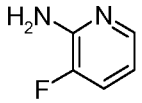
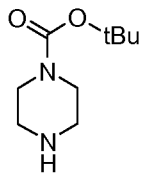
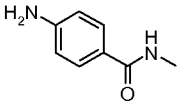
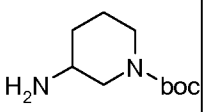
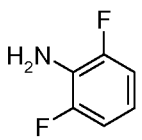
817			508.05		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2-fluoro-phenyl)-1H-pyrazol-4-yl]-amine
818			526.2		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,6-difluoro-phenyl)-1H-pyrazol-4-yl]-amine
820			544.2		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,4,6-trifluoro-phenyl)-1H-pyrazol-4-yl]-amine
821			494.25 (M+H)		1-{5-Cyclopropyl-2-[2-(2-methyl-2,3-dihydro-1H-isoindol-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
822			486 (M+H-NH3)	1H NMR (400 MHz, DMSO-d6) 9.10 (1 H, s), 8.93 (3 H, d, J=7.8 Hz), 8.45 - 8.51 (1 H, m), 8.22 (1 H, s), 8.03 (1 H, dd, J=7.7, 1.9 Hz), 7.97 (1 H, ddd,	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-3,5-difluoro-

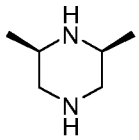
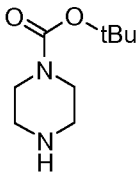
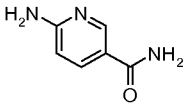
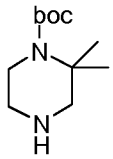
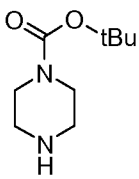
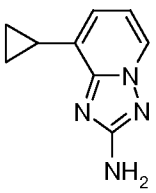
				J=10.6, 8.8, 2.9 Hz), 7.86 (1 H, dt, J=8.5, 1.5 Hz), 4.00 (4 H, br. s.), 3.40 (4 H, br. s.), 2.65 - 2.78 (1 H, m), 1.26 - 1.36 (2 H, m), 1.07 - 1.16 (2 H, m)	benzamide
823			442 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.10 (1 H, s), 8.97 (2 H, br. s.), 8.25 (1 H, s), 8.08 (2 H, d, J=6.3 Hz), 7.70 (1 H, d, J=5.8 Hz), 4.19 - 4.47 (4 H, m), 3.66 (2 H, br. s.), 3.34 (4 H, br. s.), 2.65 - 2.76 (1 H, m), 2.32 - 2.39 (2 H, m), 1.85 - 1.96 (1 H, m), 1.43 - 1.69 (4 H, m), 1.05 - 1.41 (8 H, m)	(1S,2S,4R)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
824			442 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.09 (1 H, s), 8.82 - 9.05 (2 H, m), 8.24 (1 H, s), 8.08 (2 H, d, J=6.8 Hz), 7.63 - 7.74 (1 H, m), 4.02 - 4.30 (4 H, m), 3.63 - 3.67 (2 H, m), 3.34 (4 H, br. s.), 2.66 - 2.71 (1 H, m), 2.26 - 2.41 (2 H, m), 1.90 (1 H, m), 1.54 (4 H, br. s.), 1.06 - 1.42 (8 H, m)	(1R,2R,4S)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
825			505.24 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine

826			463 (M+H)		{4-[5-Cyclopropyl-4-(2-dimethylamino-ethoxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
827			493.19 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine
828			method 5: RT: 2.69min, MI: 507 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 9.08 (1H, s), 8.67 (1H, s), 8.43(1H, dd), 8.23(1H, s), 8.12 (1H, m), 7.97 (1H, m), 4.39 (2H, m), 3.23 (2H, m), 2.67 (1H, m), 1.34 (6H, m),1.26 (2H, m), 1.15 (2H, m), 1.06 (2H, m).	{4-[5-Cyclopropyl-4-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine
829			method 5; RT: 3.32 min, MI: 486.42 [M+H]	1H NMR (500MHz, DMSO, 90°C) 9.05 (1H, s), 8.23 (1H, s), 8.20 (1H, d), 7.76 (1H, s), 7.69 (1H, dd), 7.32-7.27 (2H, m), 7.14 (2H, t), 4.04 (2H, t), 3.96 (2H, s), 3.67-3.60 (1H, m), 3.42 (2H, t), 2.64-2.60 (1H, m), 1.28-1.24 (2H, m), 1.03-1.00 (4H, m), 0.82 (2H, t).	{4-[5-Cyclopropyl-4-(4,7-diaza-spiro[2.5]oct-7-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine

830			method 5: RT: 2.66min, MI: 493 [M+H]	1H NMR (DMSO, 500MHz) 9.81 (1H, s), 9.07 (1H, s), 8.43 (1H, d), 8.28 (1H, m), 8.20 (1H, s), 7.97 (1H, m), 4.25 (2H, m), 2.54 (1H, m), 1.23 (3H, m), 1.16 (2H, m), 1.09 (3H, m). (Piperazine aliphatic protons under the water peak at 3.33ppm, therefore not integrated).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine
831			505.27 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(7-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine
832			456.27 (M+H)		{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-methyl-1H-pyrazol-3-yl)-amine
833			488 (M+H)		{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

834			524.26		1-{5-Cyclopropyl-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
835			486.33		((R)-1-Cyclohexyl-ethyl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine
836			461.18 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-2-yl)-amine
837			460 (M+H)		{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl -amine
838			metho d 5: RT: 3.52 min, MI: 489.41 [M+H]	1H NMR (500MHz, DMSO, 90°C) 8.97 (1H, s), 8.90 (1H, s), 8.42 (1H, d), 8.14 (1H, s), 7.97 (1H, dd), 7.81-7.75 (1H, m), 6.67-6.63 (1H, m), 3.81 (2H, s, br), 3.68 (2H, s), 2.95 (2H, s), 1.25 (2H,	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine

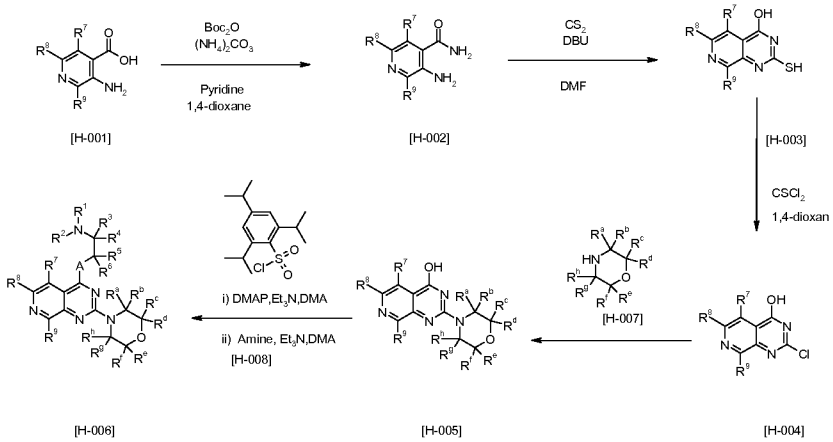
				dd), 0.99-0.96 (8H, m).	
839			method 5: RT: 2.39min, MI: 507 [M+H]	1H NMR (DMSO, 500MHz) 10.91 (1H, s), 9.09 (1H, s), 9.03 (1H, s), 8.78 (1H, s), 8.65 (1H, s), 8.49 (1H, d), 8.20 (1H, s), 8.09 (1H, dd), 7.99 (1H, dd), 7.92 (1H, m), 4.34 (2H, m), 3.71 (1H, m), 3.42 (4H, m), 3.06 (1H, m), 1.30 (5H, m), 1.08 (2H, m).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(5-trifluoromethyl-pyridin-2-yl)-amine
840			method 5: RT: 2.50 min, MI: 471.42 [M+H]	1H NMR (500MHz, DMSO, 90°C) 8.97 (2H, s), 8.64 (1H, s, br), 8.39 (1H, dd), 8.15 (1H, dd), 8.13 (1H, s), 7.89 (1H, dd), 7.65-7.60 (1H, m), 7.07-7.02 (1H, m), 3.79 (2H, t, br), 3.67 (2H, s), 2.95 (2H, s), 1.25 (2H, dd), 0.99-0.96 (8H, m).	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3-fluoro-pyridin-2-yl)-amine
841			method 5: RT: 3.13 min, MI: 481.47 [M+H]	1H NMR (500MHz, DMSO, 90°C) 9.08 (1H, s), 8.40 (1H, dd), 8.23 (1H, s), 8.01 (1H, s), 7.85 (1H, s, br), 7.79-7.78 (5H, m), 3.99-3.97 (4H, m), 3.37-3.35 (4H, m), 2.82 (3H, s), 2.72-2.68 (1H, m), 1.29-1.27 (2H, m), 1.06-1.04 (2H, m).	-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-N-methyl-benzamide
842			474 (M+H)		{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl-

					amine
843			method 5: RT: 2.36min, MI: 488 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 9.06 (1H, s), 8.22 (2H, m), 7.74 (1H, s), 7.71 (1H, dd), 7.29 (1H, m), 7.13 (2H, t), 4.30 (2H, m), 3.53 (2H, m), 3.21 (2H, m), 2.66 (1H, m), 1.33 (6H, d), 1.93 (2H, m), 1.04 (2H, m).	{4-[5-Cyclopropyl-4-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
844				1H NMR (500MHz, DMSO) 9.09 (1H, s), 8.83 (1H, d), 8.64 (1H, s), 8.51 (1H, d), 8.29 (1H, dd), 8.21 (1H, s), 8.12 (1H, s), 8.07 (1H, d), 7.63 (1H, d), 7.54 (1H, s), 3.96 (4H, s, br), 3.34 (4H, s), 2.72-2.67 (1H, m), 1.27-1.24 (2H, m), 1.09-1.08 (2H, m).	6-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide
845			method 5: RT: 3.87 min, MI: 507.41 [M+H]	1H NMR (500MH, DMSO) 10.07 (1H, s), 9.05 (1H, s), 8.85 (1H, s), 8.47 (1H, d), 8.20 (1H, s), 8.02 (1H, d), 7.01 (1H, dd), 3.91 (4H, s, br), 3.35 (2H, s, br), 2.55 (2H, s, br), 1.32-1.02 (13H, m).	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine
846			505.25 (MH)+		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine

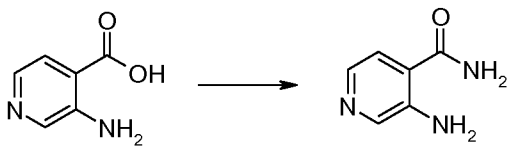
General synthesis of substituted substituted 2-morpholin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [H-006] Scheme C1

Amino-isonicotinamide derivatives of general formula [H-002] were prepared by reaction of a substituted amino-isonicotinamide derivative of general formula [H-001] with di-tert-butyl dicarbonate and ammonium carbonate in a polar aprotic solvent such as DMA, DMF, NMP with a base pyridine. Substituted 2-mercapto-3H-pyrido[3,4-d]pyrimidin-4-one derivatives of general formula [H-003] were prepared by cyclisation of a Amino-isonicotinamide derivatives of general formula [H-002] with carbon disulfide in a polar aprotic solvent such as DMA, DMF, NMP with a hindered base such as DBU. 2-Chloro-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [H-004] were prepared by reaction of a Substituted 2-mercapto-3H-pyrido[3,4-d]pyrimidin-4-one derivatives of general formula [H-003] with thiophosgene in a polar aprotic solvent such as 1,4-dioxane. The 2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-ol derivatives of general formula [H-005] were prepared by the reaction of a 2-Chloro-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [H-004] with a sunstituted morpholine derivative of general formula [H-007] in a polar aprotic solvent such as DMA, DMF, NMP at high temperature either by heating thermally or using a microwave reactor. 2-morpholin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [H-006] were prepared by the reaction of a 2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-ol derivatives of general formula [H-005] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-morphol-4-yl- pyrido[3,4-d]pyrimidin -4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [H-008], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme C1



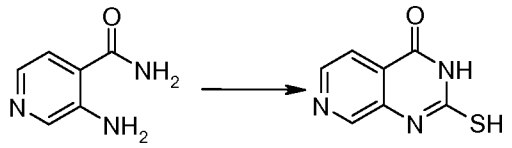
Synthesis of 4-((S)-3-Benzyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine [1000]



[C001]

3-Amino-isonicotinamide [C001]

A slurry of 3-aminoisonicotinic acid (1.00 g, 7.24 mmol) and CDI (1.76 g, 10.85 mmol) in DMF (15 mL) was heated to 40 °C for 0.5 h then cooled. Concentrated aqueous ammonia (50 mL) was added and the mixture was stirred for 15 min then extracted with ethyl acetate. Removal of the solvent gave a solid which was dissolved in EtOAc. The organic phase was washed with water and brine, dried over $MgSO_4$, filtered and then concentrated under reduced pressure to give the title compound [C001] (780 mg, 79%) LCMS method: 5, RT: 0.54 min, MI 138 [M+H].

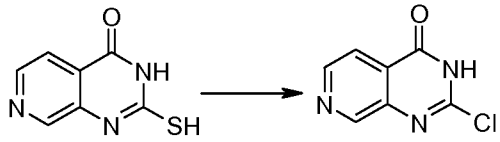


[C001] [C002]

2-Mercapto-3H-pyrido[3,4-d]pyrimidin-4-one hydrochloride [C002]

3-Amino-isonicotinamide [C001] (5g, 36.46 mmol) was dissolved in DMF (40 mL). Carbon disulfide (11 mL, 183 mmol) and DBU (10.9 mL, 73 mmol) were added and the reaction heated to 60oC for 2 hours. 2M HCl (40 mL) was added and the precipitate was collected, washed with water and dried under vacuum, to yield the title compound [C002]

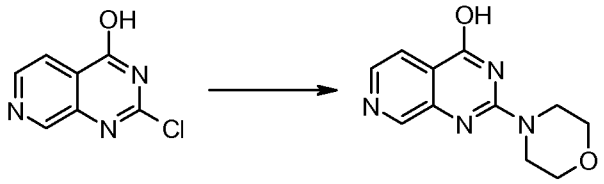
as a white solid which was was used without further purification: LCMS method: 5, RT:1.55 min, MI 180 [M+H].



[C002] [C003]

2-Chloro-3H-pyrido[3,4-d]pyrimidin-4-one hydrochloride [C003]

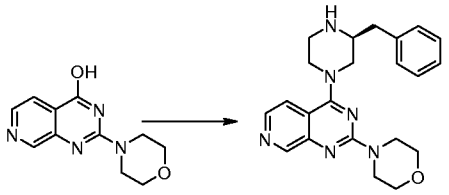
To a mixture of 2-Mercapto-pyrido[3,4-d]pyrimidin-4-ol [C002] (5.45 g, 30.41 mmol) in dioxine (100 mL) was added thiophosgene (3.5 mL, 45.6 mmol) dropwise and the mixture was heated at 100°C for 3h. The mixture was allowed to cool to room temperature and the resulting solid was diluted with Et_2O (100 mL) and the precipitate was collected by fitration and the solid was washed with Et_2O to yield the title compound which was used without further purification: LCMS method: 5, RT: 2.61 min, MI 182 [M+H].



[C003] [C004]

2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [C004]

In a microwave vial, a solution of 2-Chloro-pyrido[3,4-d]pyrimidin-4-ol hydrochloride (300 mg, 1.38 mmol) and morpholine (0.22 mL, 2.48 mmol) in DMA (4 mL) was heated under microwave irradiation to 150 °C for 20 min. The solvent was removed under reduced pressure and the resulting solid was washed with ether and collected to give the title compound [C004] which was used without further purification. LCMS method: 5, RT: 2.20 min, MI 232 [M+H].

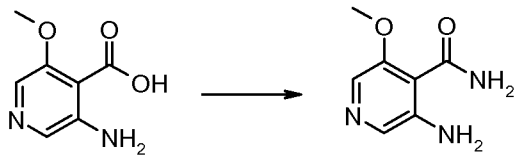


[C004] [1000]

4-((S)-3-Benzyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine [1000]

To a solution of 2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [C004] (100 mg, 0.43 mmol) in DMA (3 mL), 2,4,6-Triisopropylbenzenesulfonyl chloride (143 mg, 0.47 mmol), NEt_3 (0.12 mL, 0.86 mmol) and DMAP (10 mg) were added successively. The mixture was stirred at rt for 1 h and (S)-1-Boc-2-benzylpiperazine (154 mg, 0.56 mmol) was added. The reaction was stirred overnight and the solvent was removed under reduced pressure. The mixture was purified by column chromatography on silica gel eluting with CH_2Cl_2 containing 0 – 10% MeOH. The appropriate fractions were combined and the solvent removed by rotary evaporation. The residue was dissolved in CH_2Cl_2 (2 mL) and TFA (0.5 mL) was added. The solution was stirred for 3 h and then loaded onto a SCX-2 cartridge, washing with MeOH (6 mL)and eluting with 2 M ammonia in MeOH. The solvent was removed from the ammonia fraction to give the title compound [1000]: LCMS method: 5, RT:2.33 min, MI 391 [M+H]; NMR: (1H, 300MHz, $CDCl_3$); 8.88 (1H, s), 8.10 (1H, d), 7.35 – 7.21 (7H, m), 4.31 – 4.21 (2H, m), 3.78 – 3.71 (8H, m), 3.39 – 3.30 (1H, m), 3.18 – 3.08 (2H, m), 2.98 – 2.90 (2H, m), 2.76 (2H, d).

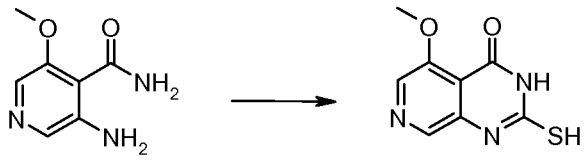
Synthesis of 2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol hydrochloride [C-005]



[C-006]

3-amino-5-methoxy-isonicotinamide [C-006]

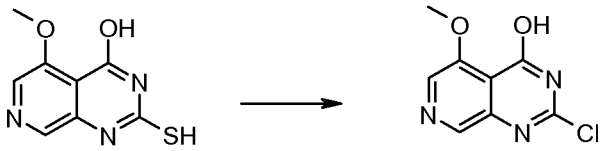
A stirred suspension of 3-Amino-5-methoxy-isonicotinic acid (1.00 g, 5.947 mmol) in anhydrous dioxane (10 mL) was prepared under nitrogen at room temperature. Pyridine (0.53 mL, 6.542 mmol) was added followed by di-*tert*-butyl dicarbonate (1.43 g, 6.542 mmol) and ammonium carbonate (1.26 g, 13.083 mmol). The reaction mixture was stirred at room temperature for 5 hours then diluted with diethyl ether (50 mL) and the suspension stirred at room temperature for 18 hours. The suspension was filtered and the solid washed with diethyl ether (50 mL) then dissolved in methanol and filtered to remove the inorganic salts. The filtrate was concentrated by rotary evaporation to give the title compound [C-006] (690 mg, 70%) as a cream coloured solid. LCMS method: 5, RT 1.27 min, MI 168 [M+H]; NMR: (1H, 300MHz, d6-dmso) 7.77 (s, 1H), 7.65 (br. S, 1H), 7.58 (br. S, 1H), 7.57 (s, 1H), 6.30 (s, 2H), 3.85 (s, 3H).



[C-006] [C-007]

2-Mercapto-5-methoxy-3H-pyrido[3,4-d]pyrimidin-4-one [C-007]

A suspension of 3-Amino-5-methoxy-isonicotinamide [C-006] (1.10 g, 6.58 mmol) in anhydrous DMF (10 mL) was prepared under nitrogen. Carbon disulfide (1.97 mL, 32.90 mmol) was added followed by drop-wise addition of DBU (1.96 mL, 13.16 mmol) and the reaction mixture heated to 60 °C for 2.5 hours. The reaction mixture was cooled to room temperature and diluted with 2M HCl, the precipitate was filtered and washed with water. The precipitate was suspended in toluene (40 mL), the toluene was decanted and this was repeated once more. The precipitate was then suspended in toluene (30 mL) and concentrated by rotary evaporation to yield the title compound [C-007] (1.05 g, 65%) as a yellow solid. LCMS method: 5, RT 2.33 min, MI 210 [M+H]; NMR: (1H, 500MHz, d6-dmso) 12.71 (1H, s), 12.38 (1H, s), 8.30 (1H, s), 8.22 (1H, s), 3.95 (3H, s).

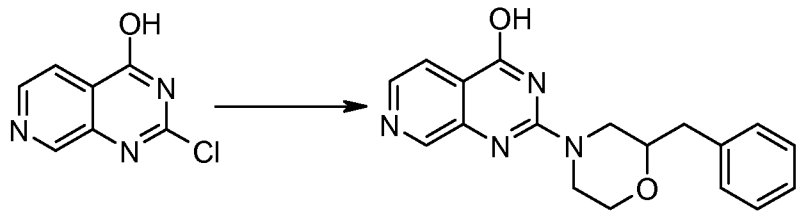


[C-007] [C-005]

2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol hydrochloride [C-005]

A suspension of 2-Mercapto-5-methoxy-3H-pyrido[3,4-d]pyrimidin-4-one hydrochloride [C-007] (1.145 g, 4.660 mmol) in anhydrous dioxane (20 mL) was prepared under nitrogen. Thiophosgene (0.54 mL, 6.990 mmol) was added drop-wise. The reaction mixture was stirred at room temperature for 10 min and then heated to 95 °C for 4 hours. A further portion of thiophosgene (0.09 mL, 1.165 mmol) was added and heating continued for a further 1.5 hours before stirring at room temperature overnight. The reaction mixture was diluted with diethyl ether and the precipitate was filtered, washed with diethyl ether and dried under vacuum to give the title compound [C-003] (1.16 g, 100%) as a pale yellow solid. LCMS method: 5, RT 2.71 min, MI 212 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.53 (1H, s), 8.40 (1H, s), 3.98 (3H, s).

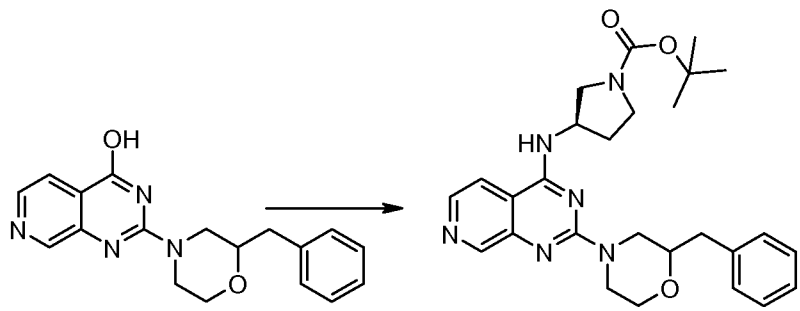
Synthesis of [2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine [1001]



[C003] [C008]

2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [C008]

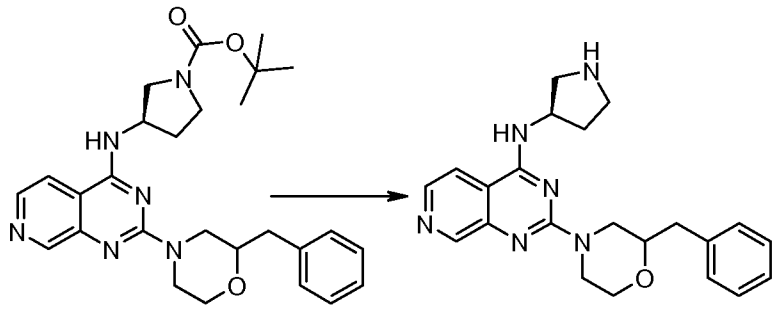
Following the procedure described in Scheme C1, 2-Chloro-pyrido[3,4-d]pyrimidin-4-ol hydrochloride (100 mg, 0.459 mmol) was reacted with 2-Benzyl-morpholine (146 mg, 0.825 mmol) to give the title compound [C008] (114 mg, 64%) following column chromatography on silica, eluting with CH_2Cl_2 containing 0 – 10% MeOH. LCMS method: 5, RT 2.37 min, MI 323.24 [M+H].



[C008] [C009]

(R)-3-[2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester [C009]

To a stirred solution of 2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [C008] (70 mg, 0.21 mmol), NEt_3 (90 mL, 0.63 mmol) and DMAP (3 mg, 0.02 mmol) in DMA (1 mL) was added 2,4,6-triisopropylbenzenesulfonyl chloride (77 mg, 0.25 mmol). After 4 h (R)-(+)-1-Boc-3-aminopyrrolidine (43 mL, 0.25 mmol) was added and stirred overnight at RT. The reaction mixture was partitioned between CH_2Cl_2 and H_2O and the organic phase separated and evaporated. The residue was purified by column chromatography on silica, eluting with CH2Cl2 containing 0 – 5% MeOH. The appropriate fractions were combined and evaporated to give the title compound [C009] (43 mg, 33%) as an off-white solid. LCMS method: 5, RT 3.59 min, MI 491.33 [M+H].



[C009] [1001]

[2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine [1001]

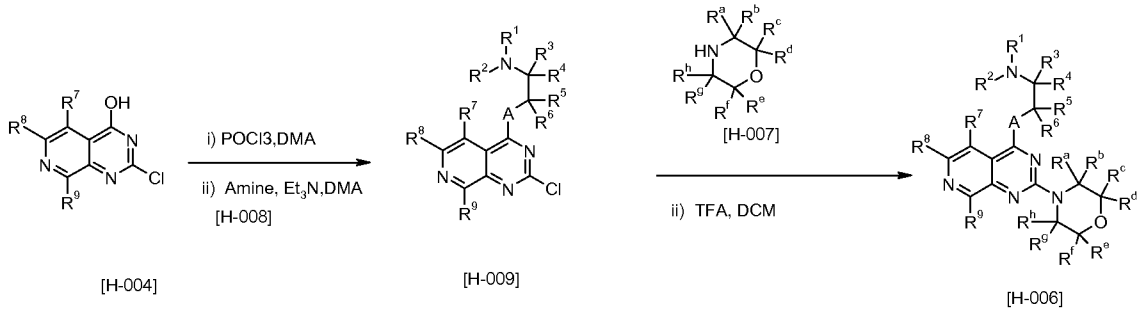
(R)-3-[2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester [C009] (34 mg, 0.069 mmol) was stirred in 4N HCl in dioxane (2 mL) for 1 h. The reaction mixture was diluted with MeOH and loaded onto a SCX- cartridge, washing with MeOH and eluting with ammonia in methanol. The ammonia phase was evaporated to give the title compound [1001] (21 mg, 78%). LCMS method: 5, RT 1.97 min, MI 391.21 [M+H]; NMR: (1H, 300MHz, d4-MeOD) 8.66 (1H, s), 8.14 (1H, dd), 7.83 (1H, ddd), 7.35-7.22 (5H, m), 4.66-4.59 (2H, m), 4.50-4.48 (1H, m), 3.98 (1H, dd), 3.71-3.55 (2H, m), 3.44-3.41 (1H, m), 3.16-3.07 (2H, m), 2.99-2.91 (1H, m), 2.85-2.74 (3H, m), 2.34-2.13 (3H, m).

General synthesis of substituted substituted 2-morpholin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [H-006] Scheme C2

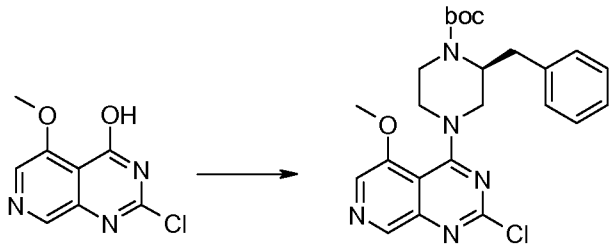
The 2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl derivatives of general formula [H-009] were prepared by the reaction of a 2-Chloro-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [H-004] with a chlorinatation agent such as phosphorous oxychloride and then reacted with primary or secondary amino derivative of general formula [H-008], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the 2-morpholin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [H-009] were reacted with a substituted morpholine derivative of general formula [H-007] in a polar aprotic solvent such as DMA, DMF, NMP at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA,

methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme C2



Synthesis of (S)-N^1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine [1002]

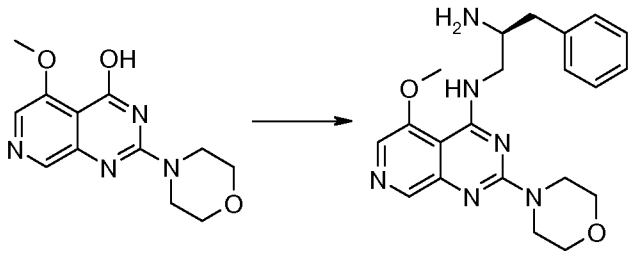


[C-005] [C-010]

(S)-2-Benzyl-4-(2-chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C010]

A solution of 2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [C005] (1.04 g, 4.911 mmol) in DCE (50 mL) was prepared under nitrogen. DIPEA (1.72 mL 9.822 mmol) and $POCl_3$ (0.46 mL, 4.911 mmol) were added and the reaction mixture stirred at room temperature for 2 hours. The reaction mixture was evapourated under reduced pressure and the residue used directly in the next step. A solution of 2,4-Dichloro-5-methoxy-pyrido[3,4-d]pyrimidine (280 mg of crude residue, 1.228 mmol assuming complete conversion) in DCM (15 mL) was prepared under nitrogen. Triethylamine (0.34 mL, 2.456 mmol) was added followed by (S)-2-Benzyl-piperazine-1-carboxylicacidtert-butylester (170 mg, 0.614 mmol). The reaction mixture was stirred at room temperature over night. The reaction mixture was evapourated under reduced pressure and the residue purified by chromatography on silica, eluting with DCM containing 0 - 10% MeOH to yield the title compound [C-010] (110 mg, 19%): LCMS method: 5, RT 2.55 min, MI 263

[M+H]; NMR: (1H, 500MHz, d6-dmso) 8.69 (1H, d, J = 3.7 Hz), 8.39 (1H, d, J = 3.7 Hz), 4.10 (3H, s), 3.63 (4H, broad s), 3.54 (4H, broad s), 1.47 (9H, s).

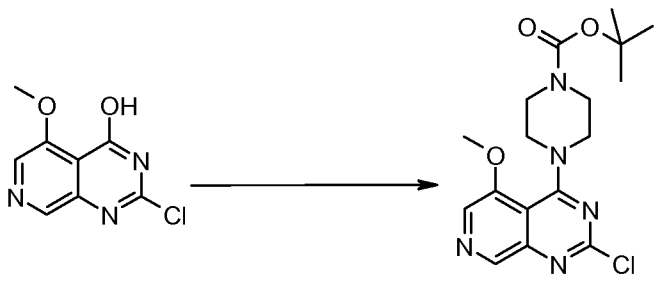


[C010] [1002]

(S)-N^1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine [1002]

A solution of (S)-2-Benzyl-4-(2-chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C010] (100 mg, 0.213 mmol) in anhydrous DMA (2 mL) was prepared. Morpholine (19 mg, 0.213 mmol) and DIPEA (0.04 mL, 0.213 mmol) were added and the mixture heated to 150 °C for 20 min in the microwave. The reaction mixture was evapourated under reduced pressure and the crude residue was purified by chromatography on silica eluting with DCM containing 0 - 10% MeOH. The product was stirred in 4M HCl in dioxane at room temperature for 1 hour and the reaction mixture was evapourated under reduced pressure and loaded onto an SCX cartridge, washing with methanol and eluting with 7N ammonia in methanol. The ammonia eluent was evapourated under reduced pressure to the title compound [1001] (46 mg, 51%) as a yellow solid: LCMS method: 5, RT 2.51 min, MI 421 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.34 (1H, s), 7.82 (1H, s), 7.35 - 7.32 (2H, m), 7.28 - 7.25 (3H, m), 4.0 - 3.97 (1H, m), 3.80 (4H, broad s), 3.62 - 3.61 (8H, broad m), 3.08 - 3.03 (1H, m), 2.98 - 2.91 (1H, m), 2.76 - 2.57 (6H, m).

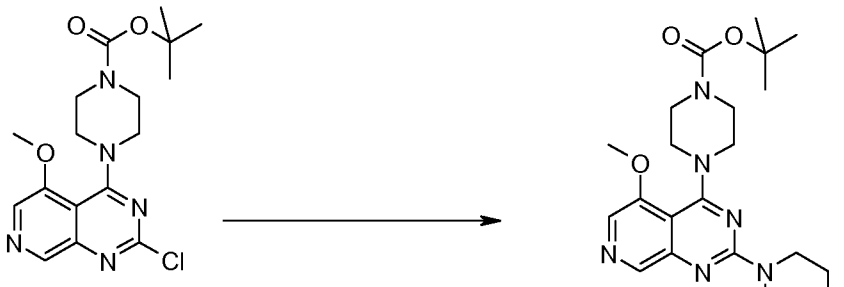
Synthesis of 5-Methoxy-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine [1003]



[C005] [C011]

4-(2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C011]

A stirred suspension of 2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol hydrochloride [C005] (200 mg, 0.806 mmol) in DCE (10 mL) was prepared under nitrogen. DIPEA (0.31 mL, 1.773 mmol) was added followed by drop-wise addition of $POCl_3$ (0.08 mL, 0.887 mmol). The reaction mixture was stirred at room temperature for 2 hours. A further portion of DIPEA (0.31 mL, 1.773 mmol) and POCL3 (0.08 mL, 0.887 mmol) were added and stirring continued at room temperature for 3 hours. The reaction mixture was evapourated under reduced pressure and the residue partitioned between CH_2Cl_2 (30 mL) and sat. $NaHCO_3$ (aq) (30 mL). The organic phase was separated and the aqueous extracted with CH_2Cl_2 (2 x 10 mL). The combined organic portions were dried (phase separator) and evapourated under reduced pressure to give a crude residue containing 2,4-Dichloro-5-methoxy-pyrido[3,4-d]pyrimidine (assumed 185mg, 100%) which was used without further purification. A solution containing crude 2,4-Dichloro-5-methoxy-pyrido[3,4-d]pyrimidine (assumed 185 mg, 0.806 mmol) in CH_2Cl_2 (10 mL) was prepared under nitrogen. Triethylamine (0.17 mL, 1.209 mmol) was added followed by piperazine-1-carboxylic acid *tert*-butyl ester (120 mg, 0.645 mmol) and the reaction mixture stirred at room temperature overnight. The reaction mixture was evapourated under reduced pressure and the residue purified by chromatography on silica eluting with CH_2Cl_2 containing 0 - 10% MeOH. The appropriate fractions were combined and concentrated to yield the title compound [1003] (177 mg, 58%) as a yellow solid. LCMS method: 5, RT 5.44 min, MI 380 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.65 (s, 1H), 8.34 (s, 1H), 4.06 (s, 3H), 3.59 (br. m, 4H), 3.49 (br. m, 4H), 1.42 (s, 9H).

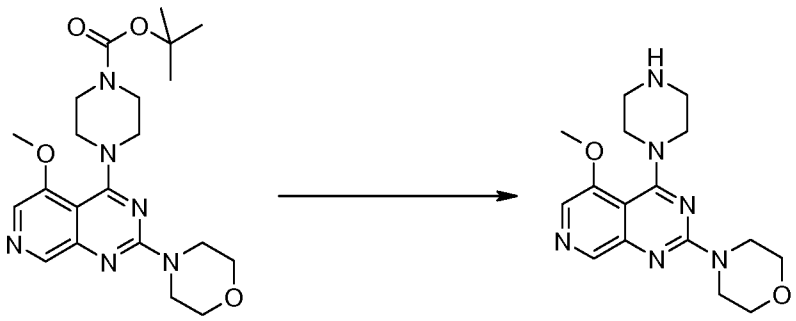


[C011] [C012]

5-Methoxy-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine [C012]

To a solution of 2,4-Dichloro-5-methoxy-pyrido[3,4-d]pyrimidine [C011] (70 mg, 0.19 mmol) in DMA (2 mL) was added morpholine (20 mg, 0.228 mmol) and DIPEA (0.04

mL, 0.228 mmol). The reaction mixture was heated to 150 ºC for 20 min in a microwave. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by chromatography on silica (eluting with CH2Cl2 containing 0 - 10% MeOH) to give the title compound [C012] LCMS method: 5, RT 4.01 min, MI 431 [M+H].

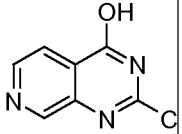
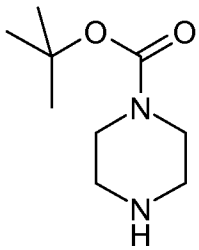


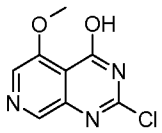
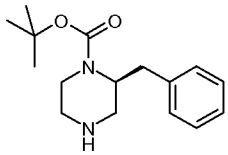
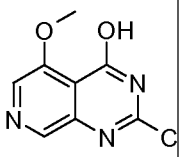
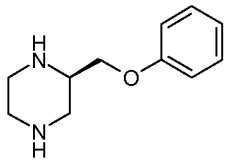
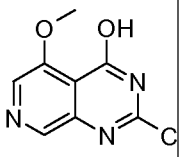
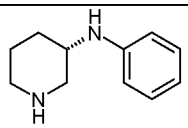
[C012] [1003]

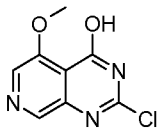
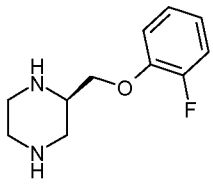
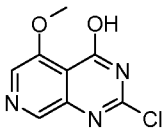
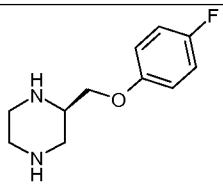
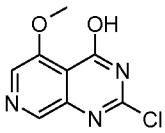
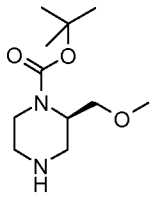
5-Methoxy-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine [1003]

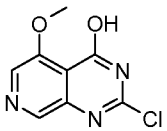
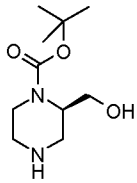
5-Methoxy-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine [C012] was stirred in 4M HCl in dioxane (2 mL) at room temperature for 2 hours. The reaction mixture was diluted with methanol (to dissolved precipitate) and loaded onto a SCX cartridge, washing with methanol and eluting with 7M ammonia in methanol. The ammonia fraction was evapourated under reduced pressure and dried under vacuum to give the title compound [1003] (48 mg, 83%): LCMS method: 5, RT 3.54 min, MI 331 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.33 (1H, broad d, J = 0.9 Hz), 7.88 (1H, s), 3.95 (3H, s), 3.73 - 3.71 (4H, m), 3.64 - 3.62 (4H, m), 3.38 (4H, broad m), 2.82 - 2.80 (4H, broad t, J = 4.5 Hz).

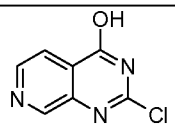
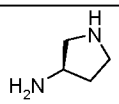
The following intermediate compounds were synthesised according to the general synthesis shown in scheme [C2]

Int	SM	Amine	Analysis		Name
			LCMS	NMR	
[C013]	 [C003]		Method 5: RT: 5.22 min, MI: 350 [M+H]		4-(2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester

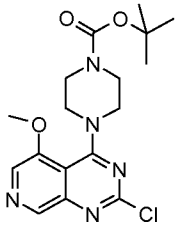
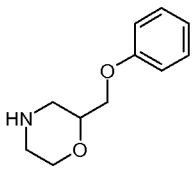
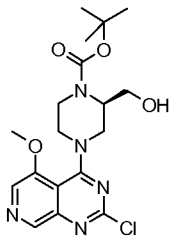
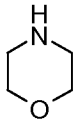
[C014]	 [C005]		Method 5: RT: 6.18 min, MI: 470 [M+H]		(S)-2-Benzyl-4-(2-chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester
[C015]	 [C005]		Method 5: RT: 2.99 min, MI: 386 [M+H]	(1H, 500MHz, $CDCl_3$) 8.82 (1H, s), 8.18 (1H, s), 7.31 - 7.28 (2H, m), 6.98 (1H, t, J = 7.4), 6.90 (2H, d, J = 7.9 Hz), 4.27 - 4.24 (1H, br. d, J = 12.1 Hz), 4.15 - 4.10 (1H, m), 4.06 (3H, s), 4.03 - 4.00 (1H, m), 3.98 - 3.94 (1H, m), 3.39 - 3.34 (1H, br. s), 3.27 - 3.18 (2H, m), 3.11 - 3.02 (2H, m).	2-Chloro-5-methoxy-4-((R)-3-phenoxymethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
[C016]	 [C005]		Method 5: RT: 5.40 min, MI: 370 [M+H]	(1H, 500MHz, d6-dmso) 8.61 (1H, s), 8.29 (1H, s), 7.06 (2H, t, J = 7.6 Hz), 6.77 (1H, br. d, J = 7.3 Hz), 6.51 (1H, t, J = 7.3 Hz), 5.61 (1H, d, J = 7.2 Hz), 4.48 (1H, br. s), 4.03 (3H, s), 3.85 (1H, br, d, J = 12.7 Hz), 3.46 - 3.40 (1H, br. m), 3.55 - 3.30 (1H, br. m), 2.83 (1H, t, J = 10.7 Hz), 1.99 (1H, br. s), 1.79 - 1.78 (1H, br. m), 1.57 - 1.49 (2H,	[(S)-1-(2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-yl]-phenyl-amine

				br. m).	
[C017]	 [C005]		Method 5: RT: 3.00 min, MI: 404 [M+H]	(1H, 500MHz, d6-dmso) 8.62 (1H, s), 8.32 (1H, s), 7.21 - 7.16 (2H, m), 7.11(1H, t, J = 7.9 Hz), 6.96 - 6.93 (1H, m), 4.15 - 4.13 (1H, br. m), 4.05 - 3.97 (3H, m), 4.02 (3H, s), 3.19- 3.18 (1H, br. m), 3.12 - 3.03 (2H, m), 2.99 - 2.95 (1H, m), 2.84 - 2.79 (1H, br. m).	2-Chloro-4-[(R)-3-(2-fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-pyrido[3,4-d]pyrimidine
[C018]	 [C005]		Method 5: RT: 3.13 min, MI: 404 [M+H]	(1H, 500MHz, d6-dmso) 8.63 (1H, s), 8.34 (1H, s), 7.14 – 7.10 (2H, m), 6.98 – 6.95 (2H, m), 4.16 – 4.12 (1H, br m), 4.04 (3H, s), 4.04 – 3.99 (1H, br m), 3.93 (2H, d), 3.16 – 3.09 (3H, m), 2.98 – 2.94 (1H, m), 2.84 – 2.79 (1H, m).	2-Chloro-4-[(R)-3-(4-fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-pyrido[3,4-d]pyrimidine
[C019]	 [C005]		Method 5: RT: 5.45 min, MI: 423 [M+H]	(1H, 500MHz, d6-dmso) 8.64 (1H, s), 8.34 (1H, s), 4.26 (1H, br. s), 4.20 (1H, br. d, J = 13.2 Hz), 4.06 (3H, s), 3.92 (1H, br. d, J = 8 Hz), 3.82 - 3.80 (1H, br. m), 3.39 - 3.35 (1H, br. m), 3.31 - 3.24 (2H, m), 3.21 - 3.19 (2H, m), 3.10 (3H, br. s),	(R)-4-(2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-2-methoxymethyl -piperazine-1-carboxylic acid tert-butyl ester

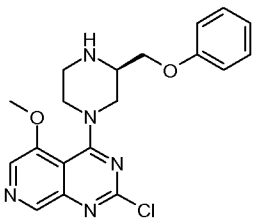
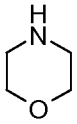
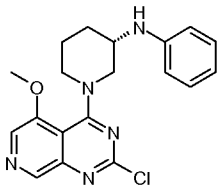
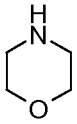
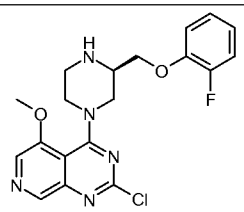
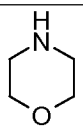
				1.40 (9H, s).	
[C020]	 [C005]		Method 5: RT: 4.89 min, MI: 410 [M+H]	(1H, 500MHz, d6-dmso) 1.40 (s, 9H), 3.17 (t, 1H), 3.22-3.33 (m, 1H), 3.33-3.39 (m, 2H), 3.72-3.82 (m, 1H), 3.87-3.92 (m, 1H), 4.05n (s, 3H), 4.02-4.10 (m, 1H), 4.18-4.24 (m, 1H), 4.76-4.78 (m, 1H), 8.33 (s, 1H), 8.63 (s, 1H).	(R)-4-(2-Chloro-5-methoxy-pyrido[3, 4-d]pyrimidin-4-yl)-2-hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester

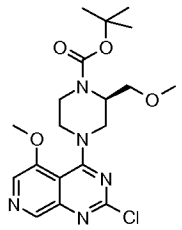
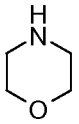
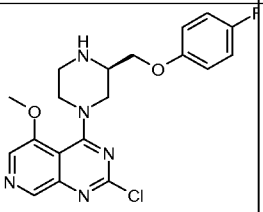
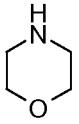
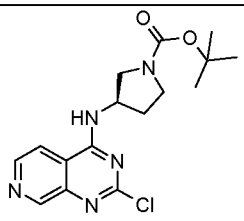
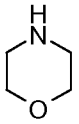
[C021]	 [C003]		Method 5: RT: 4.10 min, MI: 350 [M+H]		(2-Chloro-5-methoxy-pyrido[3,4-d]py rimidin-4-yl)-(R)-pyrrolidin-3-yl-amine

The following compounds were synthesised according to the general synthesis shown in scheme [C2]

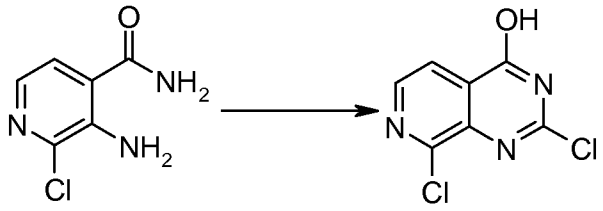
Ex	Precursor	Amine	Analysis		Name
			LCMS	NMR	
1004	 [C011]		Method 5: RT: 2.74 min, MI: 437 [M+H]	(1H, 500MHz, d6-dmso) 8.39 (1H, s), 7.94 (1H, s), 7.36 - 7.32 (2H, m), 7.03 - 6.97 (3H, m), 4.70 (1H, broad d, J = 12.8 Hz), 4.53 (1H, broad d, J = 13.1 Hz), 4.16 - 4.10 (2H, m), 4.04 - 4.00 (1H, m), 4.00 (3H, s), 3.86 - 3.81 (1H, m), 3.63 - 3.57 (1H, m), 3.44 - 3.43 (4H, broad m), 3.20 (1H, d, J = 6 Hz), 3.11 - 3.06+ (1H, m), 2.99 - 2.94 (1H, m), 2.86 (4H, broad t, J = 4.7 Hz)	5-Methoxy-2-(2-phenoxymethyl-morpholin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1005	 [C020]		Method 5: RT: 3.49 min, MI: 361 [M+H]	(1H, 500MHz, d6-dmso) 8.34 (1H, s), 7.90 (1H, s), 4.66 (1H, br t, J = 5.1Hz), 3.98 - 3.94 (1H, m), 3.95 (3H, s), 3.86 (1H, br d, J = 11.8 Hz), 3.74 - 3.73 (4H, m), 3.66 - 3.44 (4H, m), 3.40 - 3.33 (2H, m), 2.97 - 2.88 (2H, m), 2.81 - 2.75 (2H, m), 2.62 -	[(R)-4-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-methanol

				2.57 (1H, m).	

1006	 [C015]		Method 5: RT: 5.02 min, MI: 437 [M+H]	(1H, 500MHz, d6-dmso) 8.34 (1H, s), 7.90 (1H, s), 7.30 - 7.27 (2H, m), 6.94 - 6.93 (3H, m), 4.90 (1H, br. d, J = 11.9 Hz), 3.96 - 3.90 (2H, m), 3.94 (3H, s), 3.84 (1H, br. d, J = 11.8 Hz), 3.72 - 3.70 (4H, m), 3.63 - 3.61 (4H, m), 3.19 (1H, br. s), 3.02 - 2.98 (2H, br. m), 2.81 - 2.74 (2H, br. m).	5-Methoxy-2-morpholin-4-yl-4-((R)-3-phenoxymethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
1007	 [C016]		Method 5: RT: 3.12 min, MI: 421 [M+H]	(1H, 500MHz, $CDCl_3$) 8.54 (1H, s), 7.83 (1H, s), 7.17 - 7.14 (2H, m), 6.69 (1H, br. t, J = 7.3 Hz), 6.62 (2H, br. d, J = 7.5 Hz), 4.02 - 3.97 (1H, br. m), 4.00 (3H, s), 3.87 - 3.86 (4H, m), 3.77 - 3.75 (4H, m), 3.69 (1H, br. s), 3.59 - 3.55 (1H, br. m), 3.36 - 3.27 (2H, br. m), 2.04 - 1.97 (1H, br. m), 1.89 - 1.84 (1H, br. m), 1.71 - 1.65 (2H, br. m).	[(S)-1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-yl]-phenyl-amine
1008	 [C017]		Method 5: RT: 2.54 min, MI: 455 [M+H]	(1H, 500MHz, d6-dmso): 8.33 (1H, s), 7.89 (1H, s), 7.22 - 7.16 (2H, m), 7.11 (1H, br. t, J = 7.5 Hz), 6.96 - 6.92 (1H, m), 4.14 (1H, br. d, J = 12.3 Hz), 4.05 - 4.02 (1H, m), 3.97 - 3.93 (1H, m), 3.93 (3H, s), 3.83 - 3.80 (1H, m), 3.72 - 3.70 (4H, m), 3.63 - 3.61 (4H, m), 3.20	4-[(R)-3-(2-Fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine

				(1H, br. s), 3.03 - 2.96 (2H, m), 2.78 - 2.73 (2H, m).	
1009	 [C019]		Method 5: RT: 1.26 min, MI: 375 [M+H]	(1H, 500MHz, d6-dmso): 8.34 (1H, s), 7.90 (1H, s), 3.95 (3H, s), 3.91 (1H, br. d., J = 12.4 Hz), 3.84 (1H, br. d., J = 12.5 Hz), 3.74 - 3.72 (4H, m), 3.66 - 3.64 (4H, m), 3.28 (2H, d, J = 5.9 Hz), 3.26 (3H, s), 2.98 - 2.93 (3H, m), 2.78 - 2.74 (1H, m), 2.66 - 2.61 (1H, m).	5-Methoxy-4-((R)-3-methoxymethyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine
1010	 [C018]		Method 5: RT: 2.62 min, MI: 455 [M+H]	(1H, 500MHz, d6-dmso): 8.35 (1H, s), 7.91 (1H, s), 7.14 - 7.10 (2H, m), 6.97 - 6.95 (2H, m), 4.07 (1H, br. d, J = 12.2 Hz), 3.95 (3H, s), 3.92 - 3.90 (2H, m), 3.84 (1H, br. d, J = 12.2 Hz), 3.73 - 3.71 (4H, m), 3.64 - 3.62 (4H, m), 3.17 - 3.16 (1H, br. m), 3.01 - 2.97 (2H, br. m), 2.80 - 2.73 (2H, br. m).	4-[(R)-3-(4-Fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine
1011	 [C021]		Method 5: RT: 0.54 min, MI: 301 [M+H]	1H NMR ($CDCl_3$, 500MHz) 8.83 (s, 1H), 8.19 (d, 1H), 7.49 (d, 1H), 6.74 (d, 1H), 4.85-4.75 (m, 1H), 3.92-3.87 (m, 4H), 3.80-3.75 (m, 4H), 3.31-3.06 (m, 4H), 2.38-2.22 (m, 2H).	(2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine

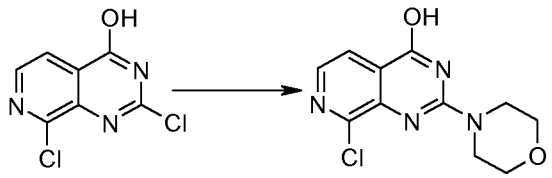
Synthesis of [2-Morpholin-4-yl-8-(2H-pyrazol-3-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine [1012]



[C022]

2,8-Dichloro-pyrido[3,4-d]pyrimidin-4-ol [C022]

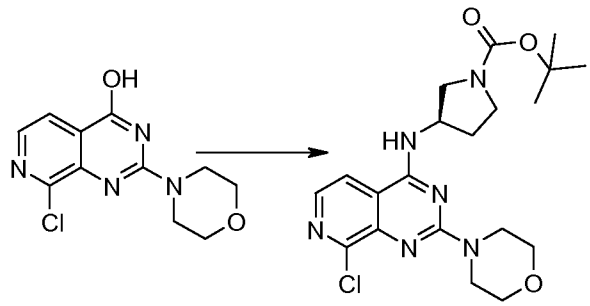
To a suspension of 3-Amino-2-chloro-isonicotinamide (2.00 g, 11.65 mmol) in dioxane (30 mL), thiophosgene (2.25 mL, 29.13 mmol) was added dropwise and the suspension was stirred 15min. The reaction was then heated at 100 °C for 3 h then cooled down to room temperature and diluted with Et_2O. The resulting solid was collected and dried to give the title compound [C022] (2.41 g, 96%) which was used without further purification. LCMS method: 5, RT 3.51 min, MI 216 [M+H].



[C022] [C023]

8-Chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [C023]

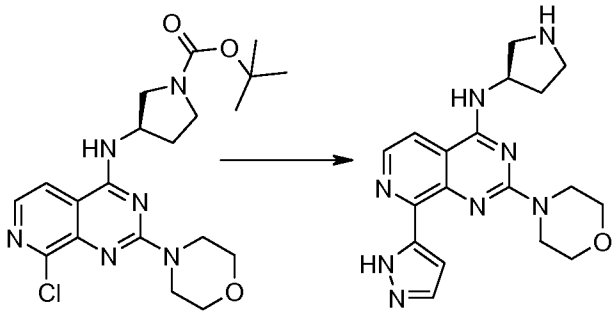
To a solution of 2,8-Dichloro-pyrido[3,4-d]pyrimidin-4-ol [C022] (200 mg, 0.926 mmol) in DMA (2 mL), morpholine (0.1 mL, 1.20 mmol) was added. The solution was stirred at room temperature for 30 min then heated to 40 °C for 3 h. The solvent was removed under reduced pressure, a minimum amount of CH_2Cl_2 was added to dissolve the crude residue and Et_2O was added. The resulting solid was collected and dried to give the title compound [C022] (200 mg, 80%) which was used without further purification. LCMS method: 5, RT 3.95 min, MI 267 [M+H].



[C023] [C024]

(R)-3-(8-Chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-pyrrolidine-1-carboxylic acid tert-butyl ester [C024]

To a solution of 8-Chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [C022] (500 mg, 1.87 mmol) in DMA (1o mL), 2,4,6-Triisopropylbenzenesulfonyl chloride (690 mg, 2.25 mmol), NEt_3 (0.52 mL, 3.75 mmol) and DMAP (50 mg, 0.41 mmol) were added successively. The mixture was stirred at 40 °C for 1 h and then (R)-3-Amino-pyrrolidine-1-carboxylic acid tert-butyl ester (460 mg, 2.44 mmol). The reaction was stirred overnight at room temperature then the solvent was removed under reduced pressure. The mixture was purified by column chromatography on silica eluting with CH_2Cl_2 containing 0 – 10% MeOH. The appropriate fractions were combined and evapourated under reduced pressure to give the title compound [C023] (310 mg, 38%). LCMS method: 5, RT 5.77 min, MI 435 [M+H].



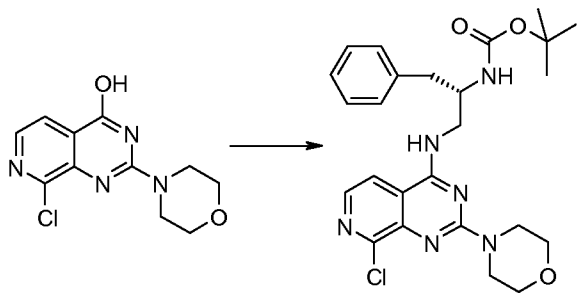
[C024] [1012]

[2-Morpholin-4-yl-8-(2H-pyrazol-3-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine [1012]

A microwave vial was charged with (R)-3-(8-Chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-pyrrolidine-1-carboxylic acid tert-butyl ester [C024] (100 mg, 0.23 mmol), 1H-Pyrazole-5-boronic acid (38 mg, 0.35 mmol), $Pd(Ph_3P)_4$ (27 mg, 0.023 mmol), a solution of K_3PO_4 (0.92 mL of a 0.5M in H_2O, 0.46 mmol) and DMA (3.5 mL). The mixture was heated under microwave irradiation to 150 °C for 10 min. The solvent was removed under reduced pressure and the residue purified by chromatography on silica, eluting with CH_2Cl_2 contaiing 0 – 10% MeOH. The appropriate fractions were combined and the solvent evaporated under reduced pressure to give the Boc-protected intermediate which was dissolved in CH_2Cl_2 (2 mL) and TFA (0.5 mL) was added. The solution was stirred for 3 h and then loaded onto a SCX-2 cartridge, washing with MeOH and eluting with 2N ammonia in MeOH solution. The solvent was removed from the

ammonia fraction under reduced pressure to yield the title compound [1012]: LCMS method: 5, RT 4.39 min, MI 367 [M+H]; NMR: (1H, 300MHz, d6-dmso) 8.28 (d, 1H), 7.96 (d, 1H), 7.60 (d, 1H), 7.33 (d, 1H), 4.61-4.68 (m, 1H), 3.78-3.81 (m, 4H), 3.68-3.74 (m, 4H), 3.33-3.40 (m, 2H), 3.18-3.23 (m, 1H), 3.02-3.07 (m, 1H), 2.15-2.24 (m, 1H), 1.98-2.04 (m, 1H).

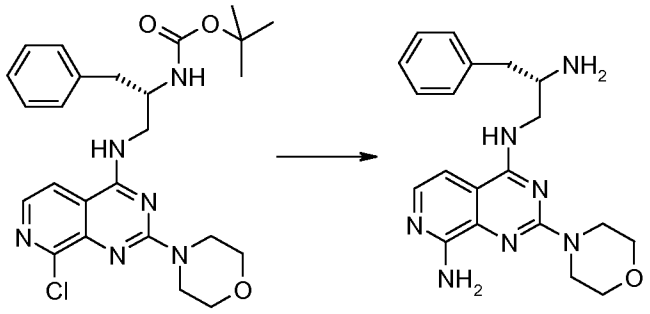
Synthesis of N^4-((S)-2-Amino-3-phenyl-propyl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine [1013]



[C023] [C025]

[(S)-1-Benzyl-2-(8-chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [C025]

Following the procedure described above, 8-Chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-o [C023]l (500 mg, 1.87 mmol) was reacted with ((S)-1-Aminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester (600 mg, 2.44 mmol) to give the title conmpound [C024] (350 mg, 38%). LCMS method: 5, RT 5.90 min, MI 499 [M+H].



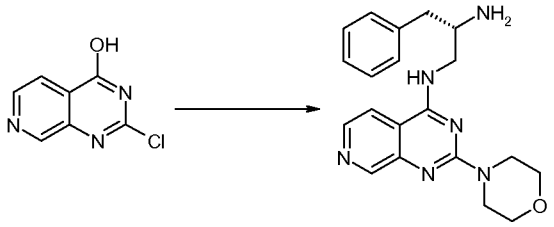
[C025] [1013]

N^4-((S)-2-Amino-3-phenyl-propyl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine [1013]

A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [C025] (100 mg, 0.20 mmol), EtOH (2 mL) and NH_4OH (2 mL). The reaction mixture was heated under

microwave irradiation to 150 °C for 1 h. This was repeated until reasonable conversion to the desired product was identified by LCMS analysis. The solvent was then removed under reduced pressure and the BOC protected compounds were diluted in CH_2Cl_2 (2mL) and TFA (0.5 mL) was added. The solution was stirred for 3 h and then loaded onto a SCX-2 cartridge, washing with MeOH and eluting with 2M ammonia in MeOH solution. The solvent was removed from the ammonia fraction and the residue was purified by preparative HPLC (method A) to yield the title compound [1013] LCMS method: 5, RT 2.11 min, MI 380 [M+H]; NMR: (1H, 300MHz, d6-dmso) 8.30-8.35 (m, 1H), 8.27 (br s, 1H), 7.49 (d, 1H), 7.22-7.33 (m, 4H), 6.97 (d, 1H), 6.34 (br s, 2H), 3.68-3.78 (m, 1H), 3.61-3.65 (m, 1H), 3.37-3.54 (m, 8H), 3.25-3.35 (m, 2H), 2.91 (dd, 1H), 2.73 (dd, 1H).

Synthesis of (S)-N^1-(2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine [1014]



[C003] [1014]

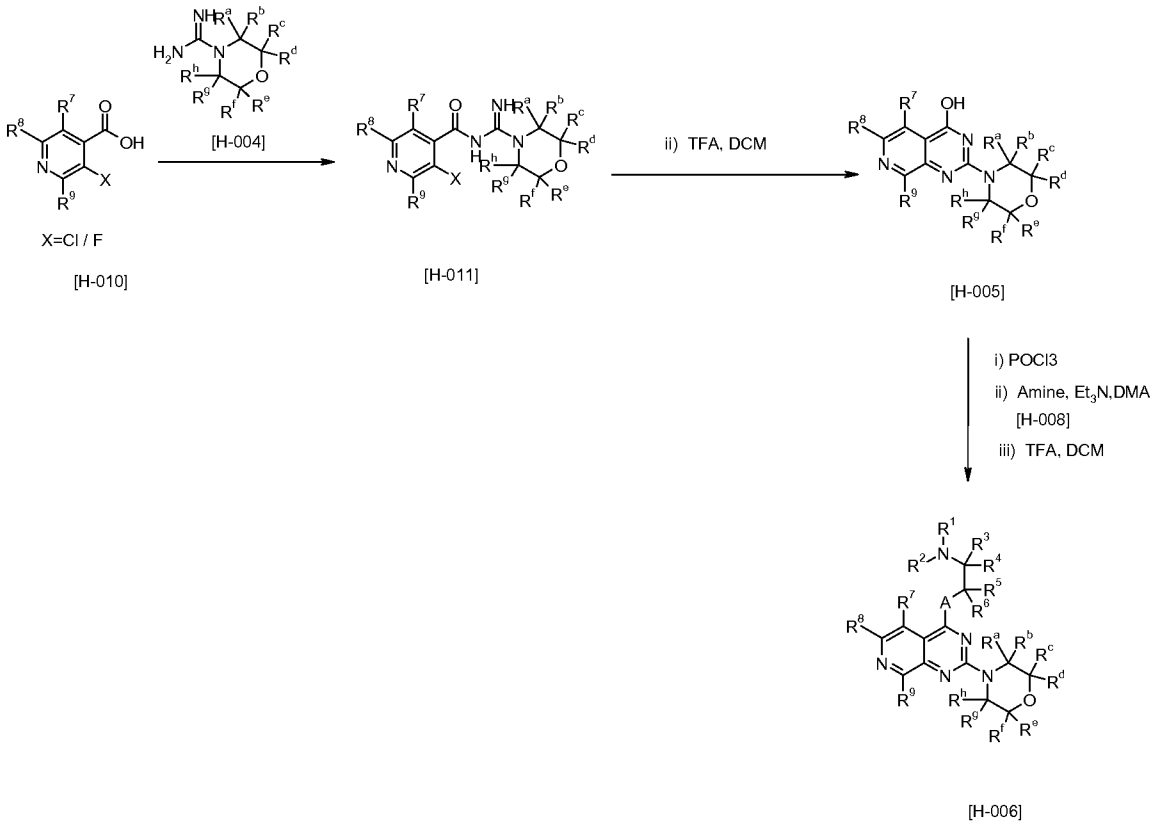
2-Chloro-pyrido[3,4-d]pyrimidin-4-ol [C003] (1.50 g, 8.26 mmol) was suspended in DMA (30 mL). Triethylamine (2.3 mL, 16.52 mmol) was added and the reaction mixture stirred at room temperature. 2,4,6-Triisopropylbenzenesulfonyl chloride (2.75 g, 9.09 mmol) and DMAP (50 mg, 0.41 mmol) were both added and the mixture was stirred at room temperature for 6 hours. ((S)-1-Aminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester (3.10 g, 12.39 mmol) was added to the reaction mixture and stirring continued at room temperature for 18hours. To the crude solution was added morpholine (1 mL) and the mixture sealed and heated under microwave irradiation to 150 °C for 20 min. The mixture was taken up in DCM and washed with water and brine. The layers were separated and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude mixture purified by flash column chromatography; eluting with a 5% methanol in CH_2Cl_2. The appropriate fractions were combined and concentrated and the residue stirred in 4M HCl in dioxane for 18 hours. The mixture was concentrated under reduced pressure and the residue loaded onto a SCX cartridge, washing with MeOH and eluting with 2M ammonia in methanol. The solvent was removed from the ammonia fraction under reduced pressure to give the title compound [1014] (150 mg,

22%). LCMS method: 5, RT 1.79 min, MI 365 [M+H]; NMR: (1H, 300MHz, d6-dmso) 8.73 (1H, br s), 8.64 (1H, s), 8.29 (2H, br s), 8.20 (1H, d), 8.00 (1H, d), 7.38 – 7.28 (5H, m), 3.90 – 3.83 (1H, m), 3.62 – 3.34 (10H overlapping br m), 3.13 – 3.07 (1H, m), 2.88 – 2.81 (1H, m).

General synthesis of substituted substituted 2-morpholin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [H-006] Scheme C3

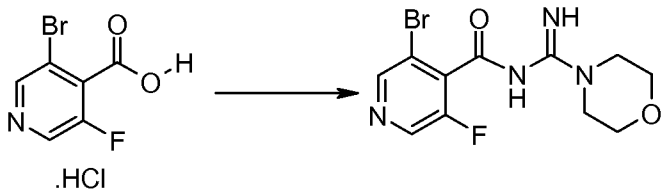
3-halo-N-(imino-morpholin-4-yl-methyl)-isonicotinamide derivatives of general formula [H-011] were prepared by coupling of a ortho-halo-isonicotinic acid derivative of general formula [H-010] with an appropriately substituted 4-carbamimidoyl-morpholine of general formula [H-004] with a suitable coupling agent such as O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) in a polar aprotic solvent such as DMA or DMF. The isonicotinoyl-amidine derivative of general formula [H-011] were cyclised to displace the relevant halogen group to yield the desired morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [H-005]. The 2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl derivatives of general formula [H-006] were prepared by the reaction of a morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [H-005] with a chlorinatation agent such as phosphorous oxychloride or a triflating agent such as N-Phenyl-bis(trifluoromethanesulfonimide and then reacted with primary or secondary amino derivative of general formula [H-008], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme C3



Synthesis of 5-Bromo-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

[1015]

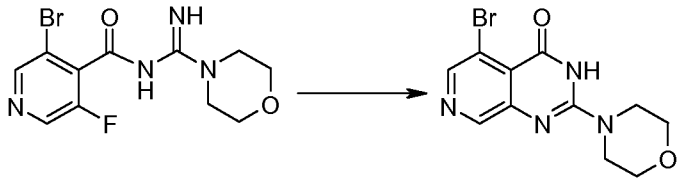


[C026]

3-Bromo-5-fluoro-N-(imino-morpholin-4-yl-methyl)-isonicotinamide [C026]

A stirred solution of 3-Bromo-5-fluoro-isonicotinic acid hydrochloride (800 mg, 3.119 mmol) and DIPEA (1.91 mL, 10.917 mmol) in DMF (11 mL) was prepared. HATU (1.186 g, 3.119 mmol) was added and the reaction mixture stirred at room temperature for 1 hour, during which time reaction mixture turned slowly brown. 4-Morpholinylformamidine hydrobromide (655 mg, 3.119 mmol) was added and stirring continued at room temperature for 2 hours. The reactionmixture was diluted with water (30 mL) and stirred at room temperature for 10 mins. The reaction mixture was extracted with EtOAc (3 x 20 mL) and the combined organics dried and evapoutrated under reduced

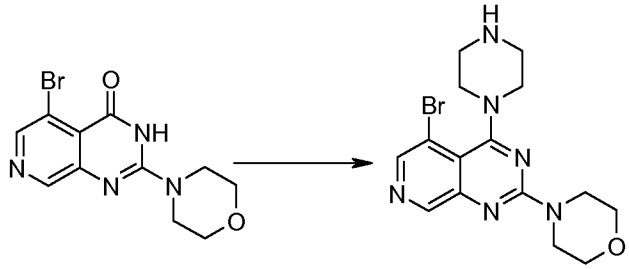
pressure to give the title compound [C026] a brown gum (1.15 g, 87%) which was used without purification in the next step: LCMS method: 5, RT 2.86 min, MI 331 [M+H].



[C026] [C027]

5-Bromo-2-morpholin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [C027]

A solution of 3-Bromo-5-fluoro-N-(imino-morpholin-4-yl-methyl)-isonicotinamide [C025] (crude product containing 1.03 g, 3.119 mmol starting material assuming 100% conversion) in anhydrous DMA (10 mL) was prepared and potassium carbonate (453 mg, 3.275 mmol) was added. The reaction mixture was heated to 150 °C for 1 hour in the microwave. The reaction mixture was poured into water (20 mL) and acidified with acetic acid. The resulting beige precipitate was filtered, washed with water and dried in the vac. oven over night to give the title compound [C027] (400 mg, 41%): LCMS method: 5, RT 1.42 min, MI 313 [M+H].



[C027] [1015]

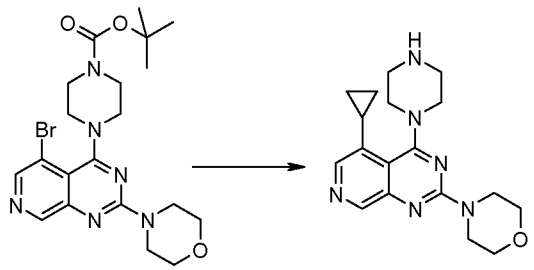
5-Bromo-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine [1015]

A solution of 5-Bromo-2-morpholin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one (50 mg, 0.161 mmol) in anhydrous DMF (2 mL) was prepared under nitrogen. N-Phenyl-bis(trifluoromethanesulfonimide) (60 mg, 0.169 mmol) was added followed by DIPEA (0.06 mL, 0.354 mmol) and the reaction mixture stirred at room overnight. Piperazine-1-carboxylic acid tert-butyl ester (60 mg, 0.322 mmol) was added and stirring continued at room temperature overnight. The reaction mixture was concentrated under reduced pressure and the residue diluted with EtOAc (10 mL) and washed with water (3 x 5 mL). The organic phase was dried, filtered and concentrated by rotary evaporation. The residue was purified by chromatography on silica, eluting with cyclohexane containing 5 – 50% EtOAc. The appropriate fractions were combined and concentrated to give 4-(5-Bromo-2-

morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C027] (35 mg, 45%) as a yellow solid. LCMS method: 5, RT 5.92 min, MI 479 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.67 (1H, s), 8.29 (1H, s), 3.78 - 3.76 (4H, m), 3.66 - 3.62 (4H, m), 3.62 (2H, very broad s), 3.52 - 3.47 (4H, very broad m), 3.24 (2H, very broad s), 1.40 (9H, s).

The Boc protected intermediate [C026] was taken up in 4M HCl in dioxane (2 mL) and stirred at room temperature 2 hours. The reaction mixture was concentrated by rotary evaporation and the residue loaded onto a SCX-2 cartridge, washing with MeOH and eluting with 7N ammonia in MeOH. The ammonia fraction was concentrated under reduced pressure to give the title compound [1015] (24 mg, 86%) as a yellow solid. LCMS method: 5, RT 2.24 min, MI 379 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.76 (1H, s), 8.28 (s, 1H), 3.89 - 3.87 (4H, m), 3.78 - 3.76 (4H, m), 3.70 (2H, br. s), 3.33 (2H, br. s), 3.09 (2H, br. s), 3.00 (2H, br. s).

Synthesis of 5-Cyclopropyl-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine [1016]



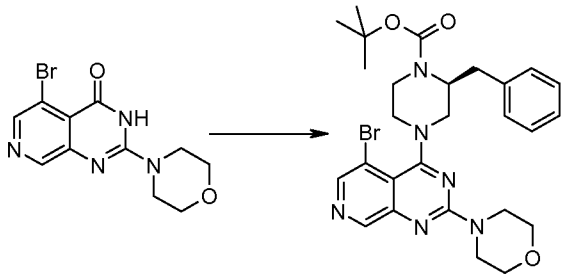
[C028] [1016]

A solution of 4-(5-Bromo-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C028] (110 mg, 0.229 mmol) in anhydrous dioxane (2.5 mL) was prepared in a microwave vial. potassium phosphate (tribasic) (ground, 145 mg, 0.687 mmol) and cyclopropyl boronic acid (30 mg, 0.344 mmol) were added. The reaction mixture was purged with argon (vacuum/argon balloon) 3 times and then Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (9 mg, 0.011 mmol) was added and the vial sealed and heated to 95 °C for 5 hours. The reaction mixture was cooled to room temperature and allowed to stand overnight. The reaction mixture was evaporated onto silica and purified by chromatography on silica, eluting with CH_2Cl_2 containing 0 - 8% MeOH. The product was not purified with this solvent system and so the appropriate fractions were concentrated and purification repeated, eluting with cyclo-hexane containing 50 - 100% EtOAc. The appropriate

fractions were combined and concentrated to give 4-(5-Cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (53 mg, 52%) as a yellow glassy solid. LCMS method: 5, RT 4.09 min, MI 441 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.50 (1H, s), 7.68 (1H, s), 3.79 - 3.19 (8H, very broad set of signals), 3.79 - 3.74 (4H, m), 3.66 - 3.64 (4H, m), 2.62 - 2.59 (1H, m), 1.40 (9H, s), 1.18 - 1.14 (2H, m), 0.93 - 0.90 (2H, m).

The Boc-protected intermediate was stirred in 4M HCl in dioxane (2 mL) at room temperature for 2 hours. The reaction mixture was concentrated by rotary evaporation and loaded onto a SCX cartridge, washing with MeOH and eluting with 7N ammonia in MeOH. The ammonia fraction was concentrated by rotary evaporation to give the title compound [1016] (37 mg, 90%) as a pale yellow solid. LCMS method: 5, RT 4.41 min, MI 341 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.48 (1H, s), 7.65 (1H, s), 3.75 - 3.73 (4H, m), 3.66 - 3.62 (overlapping 4H m and 2H very broad s), 3.19 (2H, very broad s), 2.80 (4H, br. m), 2.63 - 2.58 (1H, m), 1.17 - 1.14 (2H, m), 0.93 - 0.90 (2H, m).

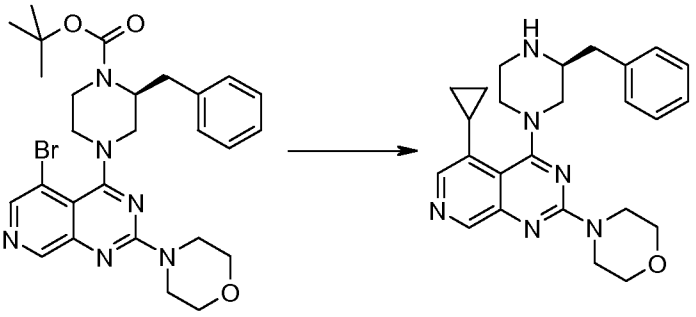
Synthesis of 4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine [1017]



[C027] [C029]

(S)-2-Benzyl-4-(5-bromo-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C029]

Following the procedure described in Sceme C3, 5-Bromo-2-morpholin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [C027] (200 mg, 0.64 mmol) was reacted with (S)-2-Benzyl-piperazine-1-carboxylicacidtert-butylester (355 mg, 1.28 mmol) to give (S)-2-Benzyl-4-(5-bromo-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C028] (139 mg, 38%). LCMS method: 5, RT: 5.64 min, MI: 569/571 [M+1].

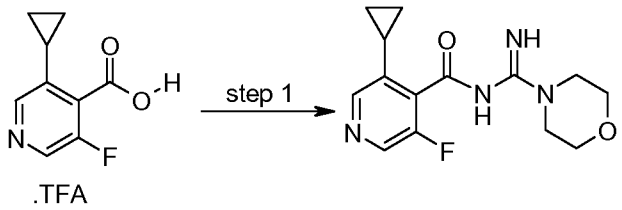


[C029] [1017]

4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine

Following the procedure described in Scheme C3, (S)-2-Benzyl-4-(5-bromo-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C029] (135 mg, 0.24 mmol) was reacted with cyclopropyl boronic acid (31 mg, 0.36 mmol) to give 4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine [1017] (62 mg, 61%)s a yellow solid. LCMS method: 5, RT 2.74 min, MI 431 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.66 (1H, s), 7.65 (1H, s), 7.33 - 7.19 (5H, m), 4.35 - 2.42 (18H, very broad overlapping multiplets), 1.16 - 1.08 (2H, br m), 0.90 - 0.82 (2H, br m).

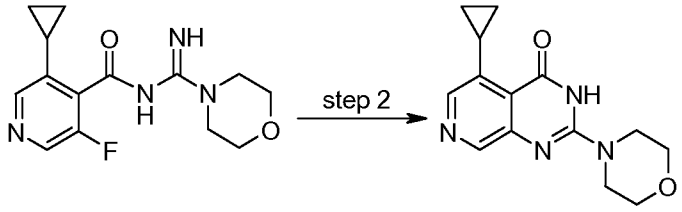
Synthesis of [(S)-4-(5-Cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-acetonitrile [1018]



[C030]

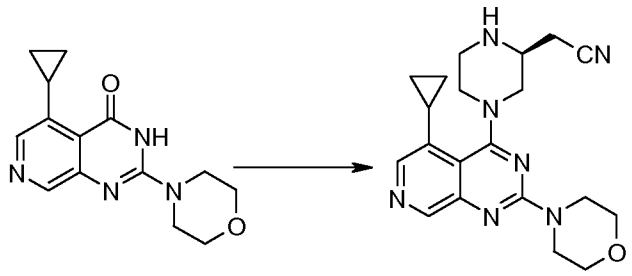
3-Cyclopropyl-5-fluoro-N-(imino-morpholin-4-yl-methyl)-isonicotinamide [C030]

Following the procedure described in Scheme C3, trifluoro-acetate 4-carboxy-3-cyclopropyl-5-fluoro-pyridinium (1.51 g, 5.10 mmol) was reacted with 4-Morpholinylformamidine hydrobromide (1.56 g, 5.10 mmol) to give 3-Cyclopropyl-5-fluoro-N-(imino-morpholin-4-yl-methyl)-isonicotinamide [C029] (1.23 g, 84%) which was used without purification in the next step. LCMS method: 5, RT 2.35 min, MI 293 [M+H].



[C030] [C031]

Step 2: 5-Cyclopropyl-2-morpholin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [C031] Following the procedure described in Scheme C3, 3-Cyclopropyl-5-fluoro-N-(imino-morpholin-4-yl-methyl)-isonicotinamide (1.26 g, 4.30 mmol) was treated with K_2CO_3 under microwave irradiation to 5-Cyclopropyl-2-morpholin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [C030] (402 mg, 34%). LCMS method: 5, RT 3.41 min, MI 273 [M+H].

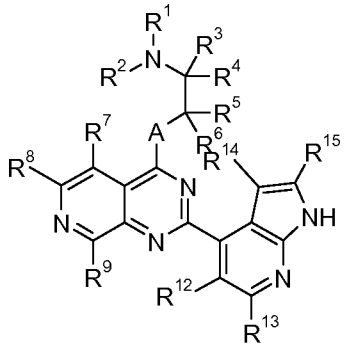


[C031] [1018]

[(S)-4-(5-Cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-acetonitrile [1018] A stirred solution of 5-Cyclopropyl-2-morpholin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [C031] (50 mg, 0.184 mmol) in DMF (5 mL) was prepared at room temperature under nitrogen. Triethylamine (0.03 mL, 0.193 mmol) was added followed by 2,4,6-triisopropylbenzenesulfonyl chloride (56 mg, 0.186 mmol). The reaction mixture was stirred at room temperature for 2 hours then (S)-Piperazin-2-yl-acetonitrile (23 mg, 0.184 mmol) was added. The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure and the residue purified by chromatography on silica, eluting with CH_2Cl_2 containing 0 - 10% MeOH. The appropriate fractions were combined and concentrated to give the title compound [1018] (30 mg, 43%) as a yellow solid. LCMS method: 5, RT 5.76 min, MI 380 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.69 (1H, s), 7.70 (1H, s), 4.46 - 4.29 (1H, br s), 3.95 - 3.93 (1H, br m), 3.88 (4H, t), 3.78 (4H, t), 3.32 - 3.27 (1H, m), 3.20 - 2.66 (5H, br m), 2.50 (2H, br s), 1.80 (1H, br s), 1.16 (2H, br s), 0.95 (2H, br s).

4PPAZ compounds

Several methods for the chemical synthesis of 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline compounds (for convenience, collectively referred to herein as "4PPAZ compounds") of the present invention are described herein, of general formula [I-001]. These and/or other well known methods may be modified and/or adapted in known ways in order to facilitate the synthesis of additional compounds within the scope of the present invention.



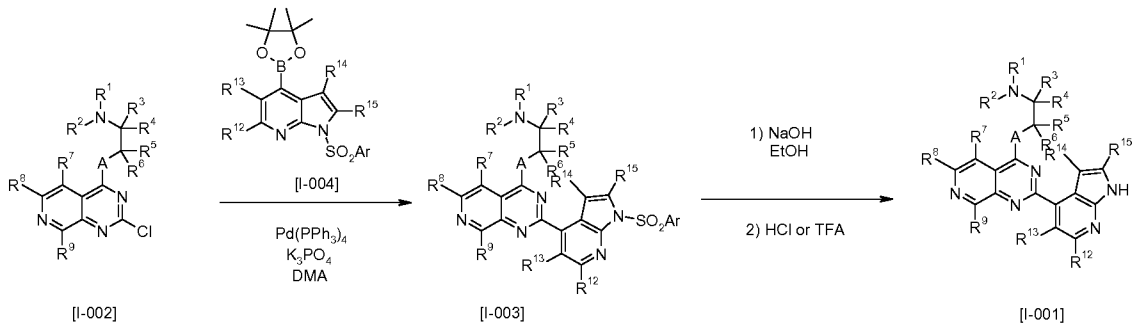
[I-001]

General synthesis of substituted substituted 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline derivatives of general formula [I-001] Scheme D1

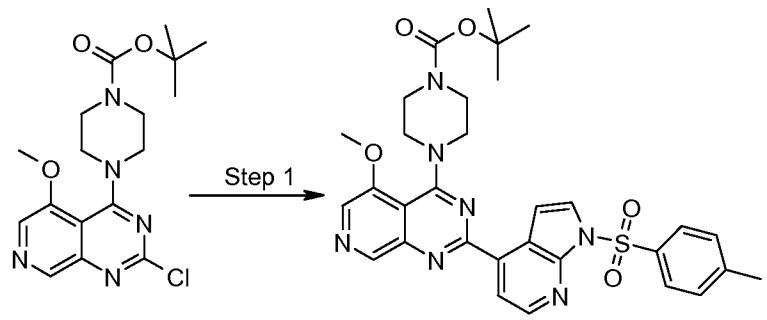
The 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline derivatives of general formula [I-003] were prepared by the reaction of a 2-Chloro-pyrido[3,4-d]pyrimidine derivative of general formula [I-002], prepared in scheme C2, in a Suzuki type palladium catalysed cross coupling reaction with boronic acid or boronate ester derivative of general formula [I-004] a palladium catalyst such as $Pd(PPh_3)_4$, a base such as K_2PO_4 in a polar aprotic solvent such as DMA or DMF at elavated temperature either by heating thermally or using a microwave reactor, to yield 4PPAZ derivative of general formula [I-003]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography. The intermediate arylsulphonate protected derivative of general formula [I-003] was then subjected to a deprotection reaction in the presence of a base such as sodium hydroxide in a polar protic solvent such as ethanol. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported

toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme D1



Synthesis of 5-Methoxy-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1200]

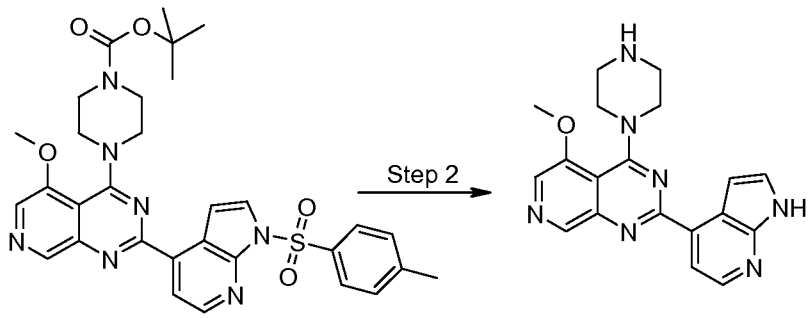


[C011] [D001]

4-{5-Methoxy-2-[1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [D001]

A solution of 4-(2-Chloro-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [C011 prepared in scheme C2] (250 mg, 0.671 mmol) in DMA (7.5 mL) was prepared. 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridine [D002] (374 mg, 0.940 mmol), $Pd(PPh_3)_4$ (77 mg, 0.067 mmol) and K_3PO_4 (2.68 mL of a 0.5 M solution in water) were added. The reaction mixture was heated to 150 °C in the microwave for 10 min. The reaction mixture was concentrated by rotovap and purified by column chromatography on silica, eluting with cyclohexane containing 0 - 100% EtOAc. The appropriate fractions were combined and concentrated to give the title compound [D001]] (115 mg, 28%) as a yellow solid. LCMS method: 5, RT 5.13 min, MI 616 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.92 (s, 1H), 8.53 (d, 1H), 8.37 (s, 1H), 8.26 (d, 1H), 8.05 (d, 1H), 8.02 (d, 1H), 7.77 (d, 1H), 7.64

– 7.60 (m, 1H), 7.57 – 7.53 (m, 1H), 7.43 (d, 2H), 4.09 (s, 3H), 3.67 (br. m, 4H), 3.56 (br. m, 4H), 1.43 (s, 9H).



[D001] [1200]

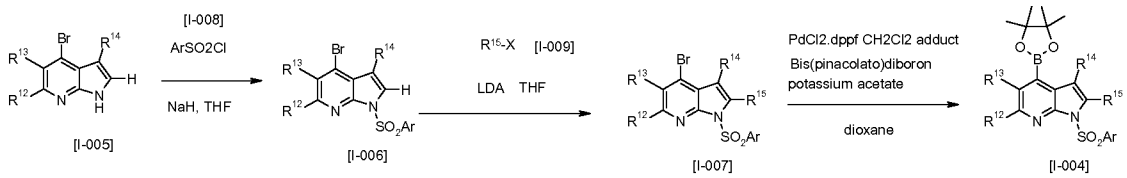
5-Methoxy-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1200]

A solution of 4-{5-Methoxy-2-[1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-1-carboxylic acid tert-butyl ester [D001] (100 mg, 0.162 mmol) in ethanol (4 mL) was prepared and NaOH (1 mL of a 5 M solution) was added. The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated by rotary evaporation and the residue dissolved in DCM (10 mL) and water (10 mL). The pH was adjusted to approx 7 by addition of ammonium chloride and the mixture extracted with DCM (3 x 10 mL). The combined organic extracts were dried (phase separator) and concentrated by rotary evaporation. The residue was purified by column chromatography on silica, eluting with cyclohexane containing 75 - 100% EtOAc. The appropriate fractions were combined and concentrated to give intermediate 4-[5-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester which was stirred in 4M HCl in dioxane (2 mL) at room temperature for 1 hour. The reaction mixture was concentrated by rotary evaporation, loaded onto a SCX cartridge, washed with methanol and eluted with 7N ammonia in methanol. The ammonia fraction was concentrated by rotary evaporation to give the title compound [1200] (29 mg, 49 %) as a yellow solid. LCMS method: 5, RT 2.23 min, MI 362 [M+H]; NMR: (1H, 500MHz, d6-dmso) 11.81 (1H, s), 8.89 (1H, s), 8.37 (1H, d, J = 5.0 Hz), 8.31 (1H, s), 8.09 (1H, d, J = 5.0 Hz), 7.63 - 7.62 (1H, m), 7.43 (1H, dd, J = 3.3, 1.8 Hz), 4.07 (3H, s), 3.66 - 3.64 (4H, m), 2.91 - 2.89 (4H, m).

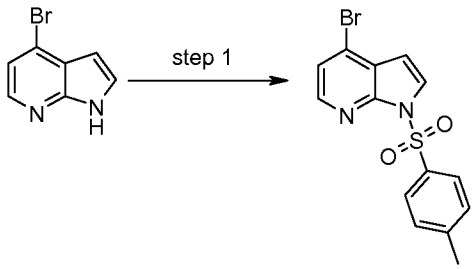
General synthesis of substituted boronic acid or boronate ester derivative of general formula [I-004] Scheme D2

The substituted boronic acid or boronate ester derivatives of general formula [I-004] were prepared by the reaction of a 4-Bromo-1H-pyrrolo[2,3-b]pyridine derivative of general formula [I-005] with an arylsuphonyl chloride derivative of general formula [I-008] with a base such as NaH in a polar aprotic solvent such as THF at low temperature. The 1-arylsulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine derivative of general formula [I-006] was then reacted with a strong base such as LDA, in a polar aprotic solvent such as THF at low temeperature and a alkylhalide derivative of general formula [I-009]. The C2 substituted 4-bromo-1H-pyrrolo[2,3-b]pyridine derivative of general formula [I-007] was then reacted in a palladium catalysed cross coupling reaction with a palladium catalyst such as $PdCl_2$ dppf, a boron agent such as bispinocolatodiboron, potassium acetate in a polar aprotic solvent such as dioxane at elavated temperature either by heating thermally or using a microwave reactor, to yield the substituted boronate ester derivative of general formula [I-004] which after reaction work up, typically by a liquid-liquid extraction was purified by column chromatography.

Scheme D2



Synthesis of 4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridine [D002]

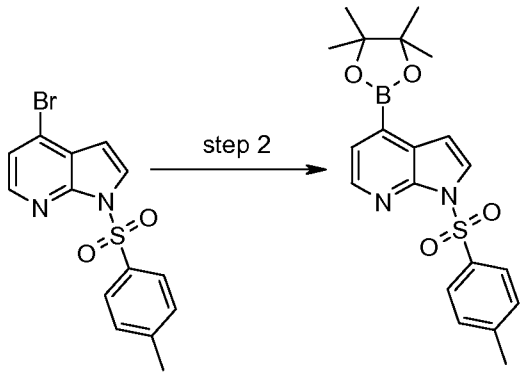


[D003]

4-Bromo-1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridine [D003]

4-Bromo-7-azaindole (3g, 15.22mmol) was weighed into a round bottom flask and dissolved in THF (50mL) under nitrogen. The reaction mixture was cooled to 0°C and treated portionwise with sodium hydride (60% in mineral oil, 0.67g, 16.75mmol), the addition was accompanied by fizzing. After the addition the reaction mixture was allowed

to stir for 30 minutes at room temperature and then treated with benzenesulfonyl chloride (2.14mL, 16.75mmol). The reaction mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction mixture was evaporated under reduced pressure and dissolved in DCM 30 mL, the organics were washed with 2x30 mL portions of 2M sodium carbonate, dried with MgSO4, filtered and evaporated to an orange oil. Purified by flash column chromatography eluting with 1:9 ethyl acetate:cyclohexane to provide the title compound as an off white solid (92%). LCMS method: 5, RT 5.36 min, MI 337 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.22 (d, 1H), 8.18 (d, 2H), 7.78 (d, 1H), 7.58 (t, 1H), 7.48 (t, 2H), 7.35 (d, 1H), 6.63 (d, 1H).

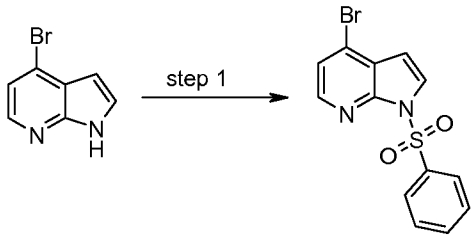


[D003] [D002]

4-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridine [D002]

4-Bromo-1-(toluene-4-sulfonyl)-1H-pyrrolo[2,3-b]pyridine (1.57g, 4.47mmol), Bis(pinacolato)diboron [D003] (2.71g, 10.72mmol), PdCl2.dppf CH2Cl2 adduct (0.365g, 0.45mmol) and potassium acetate (0.876g, 8.94mmol) were weighed into a microwave vial. Dioxane (30mL) was added and the reaction mixture was capped and heated at 130 °C in a microwave reactor for 30 minutes. The solvent was removed under reduced pressure and the residue was partitioned between ammonium chloride 20 mL and ethyl acetate 20 mL. The organics were dried with MgSO4, filtered and evaporated under reduced pressure to a brown oil. This was passed through a short column of silica eluting with 1:4 ethyl acetate:cyclohexane. The fractions were pooled and evaporated to yield the title compound [D002] as a pale yellow solid: LCMS method: 5, RT 4.77 min, MI 317 [M+H for boronic acid intermediate]

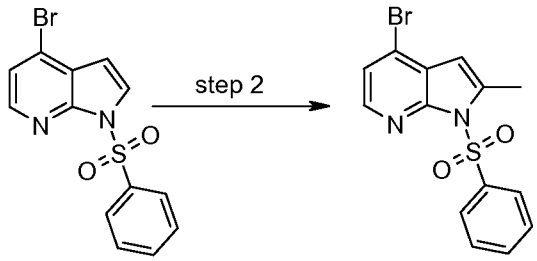
Synthesis of Benzenesulfonyl-2-methyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D004]



[D005]

1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine [D005]

4-Bromo-7-azaindole (3g, 15.22mmol) was weighed into a round bottom flask and dissolved in THF (50mL) under nitrogen. The reaction mixture was cooled to 0°C and treated portionwise with sodium hydride (60% in mineral oil, 0.67g, 16.75mmol), the addition was accompanied by fizzing. After the addition the reaction mixture was allowed to stir for 30 minutes at room temperature and then treated with benzenesulfonyl chloride (2.14mL, 16.75mmol). The reaction mixture was allowed to warm to room temperature and stirred for 2 hours. The reaction mixture was evaporated under reduced pressure and dissolved in DCM 30 mL, the organics were washed with 2x30 mL portions of 2M sodium carbonate, dried with MgSO4, filtered and evaporated to an orange oil. Purified by flash column chromatography eluting with 1:9 ethyl acetate: cyclohexane to provide the title compound [D005] as an off white solid (92%): LCMS method: 5, RT 5.36 min, MI 337 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.22 (d, 1H), 8.18 (d, 2H), 7.78 (d, 1H), 7.58 (t, 1H), 7.48 (t, 2H), 7.35 (d, 1H), 6.63 (d, 1H).

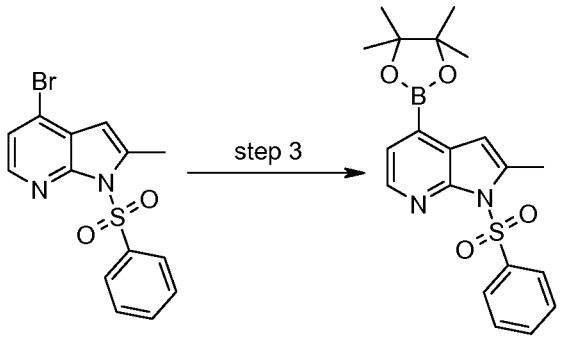


[D005] [D006]

1-Benzenesulfonyl-4-bromo-2-methyl-1H-pyrrolo[2,3-b]pyridine [D006]

To a solution of 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine [D005] (2g, 5.93mmol) in THF (50mL) at -78°C, LDA (2M, 5.9mL, 11.86mmol) was added dropwise. The solution was stirred 30min. The temperature was allowed to warm to 0oC and Methyl iodide (3.67mL, 59mmol) was then added dropwise and the solution was stirred 3h at 0°C and was allowed to stir to room temperature overnight. The reaction was quenched with aqueous ammonium chloride solution and extracted with DCM. The combined organic

layers were dried over MgSO4 and concentrated in vacuo. The crude was purified by SP1 (eluent, gradiant: Cyclohexane/AcOEt: 1/0 to 8/2). The fractions were collected and concentrated under reduced pressure to yield the title compound [D006] a white solid (87%). LCMS method: 5, RT 5.80 min, MI 351 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.12-8.15 (m, 3H), 7.56 (t, 1H), 7.47 (t, 2H), 7.29 (d, 1H), 6.34 (s, 1H), 2.74 (s, 3H).



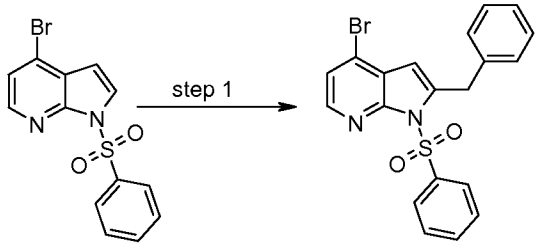
[D006] [D004]

Benzenesulfonyl-2-methyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D004][

Following the procedure described in schenme D2 replacing 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine with 1-Benzenesulfonyl-4-bromo-2-methyl-1H-pyrrolo[2,3-b]pyridine gave the title compound [D004] (72%%) as a pale yellow solid . LCMS method: 5, RT 6.19 min, MI 399 [M+H]; NMR: (1H, 500MHz, $CDCl_3$) 8.34 (d, 1H), 8.07 (d, 2H), 7.50 (t, 1H), 7.46 (d, 1H), 7.41 (t, 2H), 6.70 (s, 1H), 2.73 (s, 3H), 1.33 (s, 12H).

The following compounds were prepared according to Scheme D2:

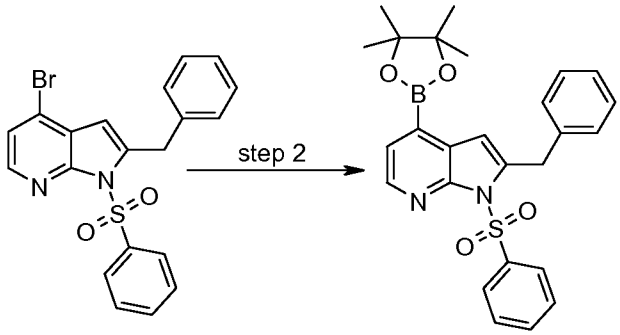
1-Benzenesulfonyl-2-benzyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D007]



[D008]

1-Benzenesulfonyl-2-benzyl-4-bromo-1H-pyrrolo[2,3-b]pyridine [D008]

Following the procedure described in scheme D2, 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine was reacted with benzyl bromide to give the title compound [D008] which was used crude in the next step. LCMS method: 5, RT 6.62 min, MI 427 [M+H].

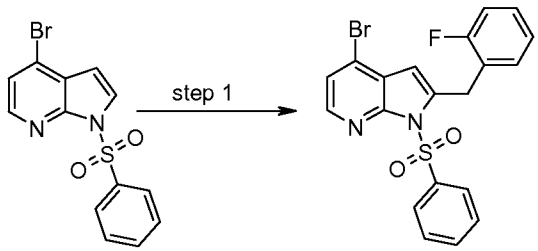


[D008] [D007]

1-Benzenesulfonyl-2-benzyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D007]

Following the procedure described in scheme D2 replacing 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine with 1-Benzenesulfonyl-2-benzyl-4-bromo-1H-pyrrolo[2,3-b]pyridine gave the title compound [D007] as a pale yellow solid: LCMS method: 5, RT 5.59 min, MI 392 [M+H, Boronic ester hydrolysed into the corresponding boronic acid in the LCMS conditions]; NMR: (1H, 500MHz, d6-dmso) 8.38 (d, 1H), 7.70 (dd, 1H), 7.49 (d, 1H), 7.42 (t, 1H), 7.23-7.30 (m, 7H), 6.75 (s, 1H), 4.54 (d, 2H), 1.34 (s, 12H).

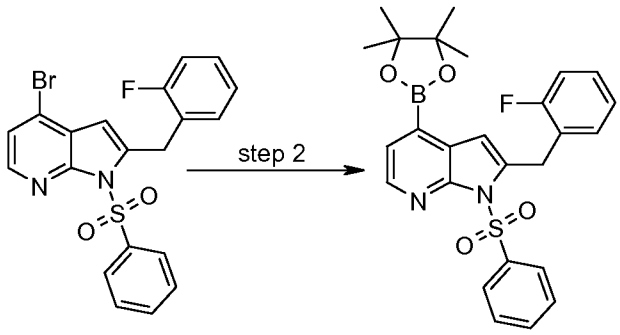
Synthesis of 1-Benzenesulfonyl-2-(2-fluoro-benzyl)-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D009]



[D010]

Step 1: 1-Benzenesulfonyl-4-bromo-2-(2-fluoro-benzyl)-1H-pyrrolo[2,3-b]pyridine [D010]

Following the procedure described in scheme D2, 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine was reacted with 2-fluorobenzylbromide to give the title compound [D010] (75%): LCMS method: 5, RT 6.45 min, MI 445 [M+H].

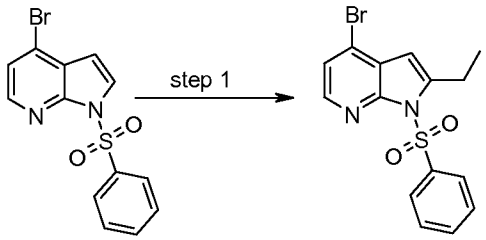


[D010] [D009]

Step 2: 1-Benzenesulfonyl-2-(2-fluoro-benzyl)-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D009]

Following the procedure described in scheme D2 replacing 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine with 1-Benzenesulfonyl-4-bromo-2-(2-fluoro-benzyl)-1H-pyrrolo[2,3-b]pyridine gave the title compound [D009] as a white solid . LCMS method: 5, RT 5.50 min, MI 411 [M+1, hydrolysed boronic ester to its corresponding boronic acid].

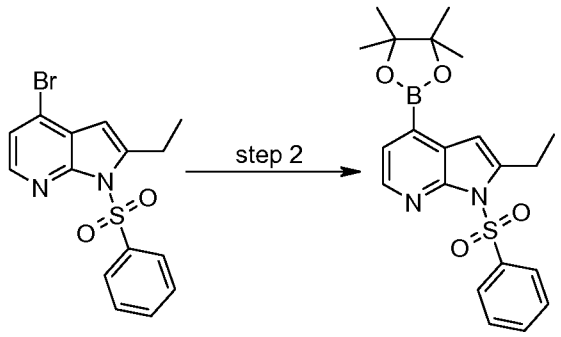
Synthesis of 1-Benzenesulfonyl-2-ethyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D011]



[D012]

1-Benzenesulfonyl-4-bromo-2-ethyl-1H-pyrrolo[2,3-b]pyridine [D012]

Following the procedure described in schemeD 2, 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine was reacted with iodoethane to give the title compound [D012] as a white solid: LCMS method: 5, RT 6.01 min, MI 351 [M+H]; NMR: (1H, 500MHz, d6-dmso) 8.11-8.15 (m, 3H), 7.56 (d, 1H), 7.45-7.48 (m, 2H), 7.30 (d, 1H), 6.39 (s, 1H), 3.19 (q, 2H), 1.42 (t, 3H).

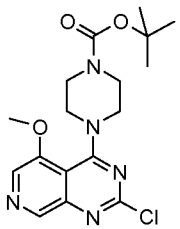
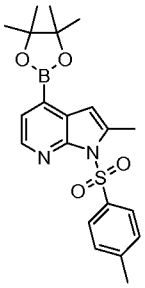
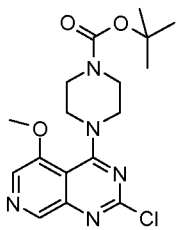
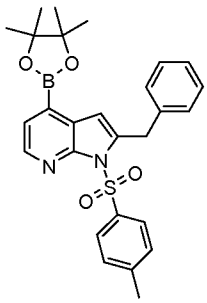


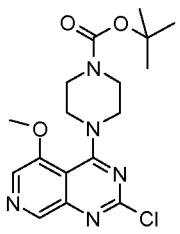
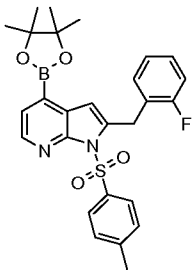
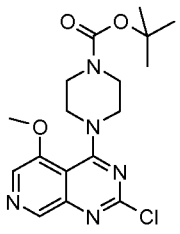
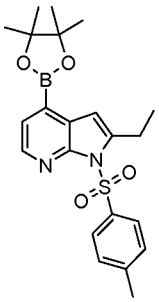
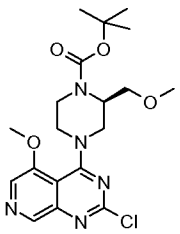
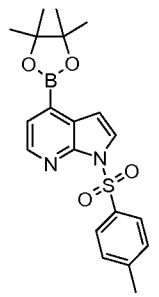
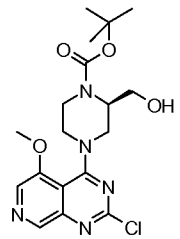
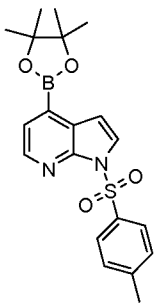
[D012] [D011]

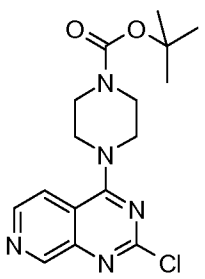
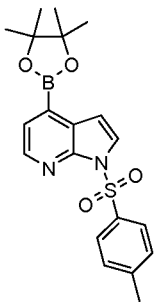
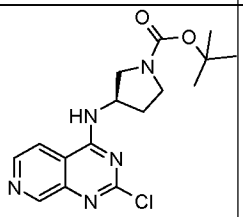
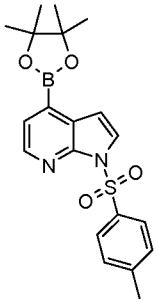
1-Benzenesulfonyl-2-ethyl-4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine [D011]

Following the procedure described in schemeD 2 replacing 1-Benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine with 1-Benzenesulfonyl-4-bromo-2-ethyl-1H-pyrrolo[2,3-b]pyridine gave the title compound [D011] as a pale yellow solid. LCMS method: 5, RT 6.42 min, MI 413 [M+H]; LCMS Method 1LCMS5, 6.42min, MI: 413 [M+1].

The following compounds were synthesised according to the general synthesis shown in scheme [D1]

Ex	Precursor	Boronic ester	Analysis		Name
			LCMS	NMR	
1201	 [C011]	 [D004]	Method 5: RT: 2.39 min, MI: 376 [M+H]	(1H, 500MHz, d6-dmso) 3.44 (brs, 4H), 3.86 (brs, 4H), 4.10 (s, 3H), 7.16 (s, 1H), 8.06 (d, 1H), 8.25 (d, 1H), 8.39 (s, 1H), 8.92 (brs, 2H), 8.98 (s, 1H), 11.77 (brs, 1H).	5-Methoxy-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1202	 [C011]	 [D007]	Method 5: RT: 3.49 min, MI: 452 [M+H]	(1H, 500MHz, d6-dmso) 3.19-3.39 (m, 3H, +H_2O), 3.77-3.83 (m, 4H), 4.08 (s, 3H), 4.16 (s, 2H), 7.08 (s, 1H), 7.24 (t, 1H), 7.32-7.40 (m, 4H), 8.05 (d, 1H), 8.26 (d, 1H),	2-(2-Benzyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-methoxy-4-piperazin-1-yl-pyrido[3,4-

				8.36 (s, 1H), 8.90 (s, 1H), 8.97 (brs, 2H), 11.86 (s, 1H).	d]pyrimidine
1203	 [C011]	 [D009]	Method 5: RT: 3.39 min, MI: 470 [M+H]	(1H, 500MHz, d6-dmso) 2.96 (brs, 4H), 3.60 (brs, 4H), 4.05 (s, 3H), 4.18 (s, 2H), 6.96 (s, 1H), 7.19-7.23 (m, 2H), 7.32-7.44 (m, 2H), 8.03 (s, 1H), 8.27 (d, 1H), 8.29 (s, 1H), 8.79 (s, 1H), 11.87 (brs, 1H).	2-[2-(2-Fluoro-benzyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1204	 [C011]	 [D011]			2-(2-Ethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1205	 [C019]	 [D002]	Method 5: RT: 2.53 min, MI: 406 [M+H]		5-Methoxy-4-((R)-3-methoxymethyl-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1206	 [C020]	 [D002]	Method 5: RT: 2.36 min, MI: 392 [M+H]	(1H, 500MHz, d6-dmso) 2.86-2.96 (m, 3H), 3.10 (d, 1H), 3.15-3.19 (m, 1H), 3.39-3.45 (m, 2H), 4.06 (s, 3H), 4.15-4.24 (m, 2H), 7.43-7.44 (m, 1H), 7.60-7.61 (m, 1H), 8.08 (d, 1H), 8.19 (s, 1H), 8.32 (s, 1H), 8.35	{(R)-4-[5-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol

				(d, 1H), 8.89 (s, 1H), 11.89 (brs, 1H).	
1207	 [C013]	 [D002]	Method 5: RT: 1.99 min, MI: 332 [M+H]	(1H, 500MHz, d6-dmso) 2.94-2.97 (m, 4H), 3.89-3.93 (m, 4H), 7.45 (t, 1H), 7.63 (t, 1H), 7.90 (d, 1H), 8.11 (d, 1H), 8.37 (d, 1H), 8.57 (d, 1H), 9.32 (s, 1H), 11.83 (brs, 1H).	4-Piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1208	 [C021]	 [D002]	Method 5: RT: 1.91 min, MI: 332 [M+H]	(1H, 500MHz, d6-dmso) 2.21-2.28 (m, 1H), 2.34-2.44 (m, 1H), 3.33-3.50 (m, 3H), 3.67-3.74 (m, 2H), 4.95-5.04 (m, 1H), 7.50 (d, 1H), 7.63 (t, 1H), 8.15 (d, 1H), 8.25 (d, 1H), 8.38 (d, 1H), 8.64 (d, 1H), 8.70 (d, 1H), 9.30 (s, 1H), 11.86 (s, 1H)	(R)-Pyrrolidin-3-yl-[2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine

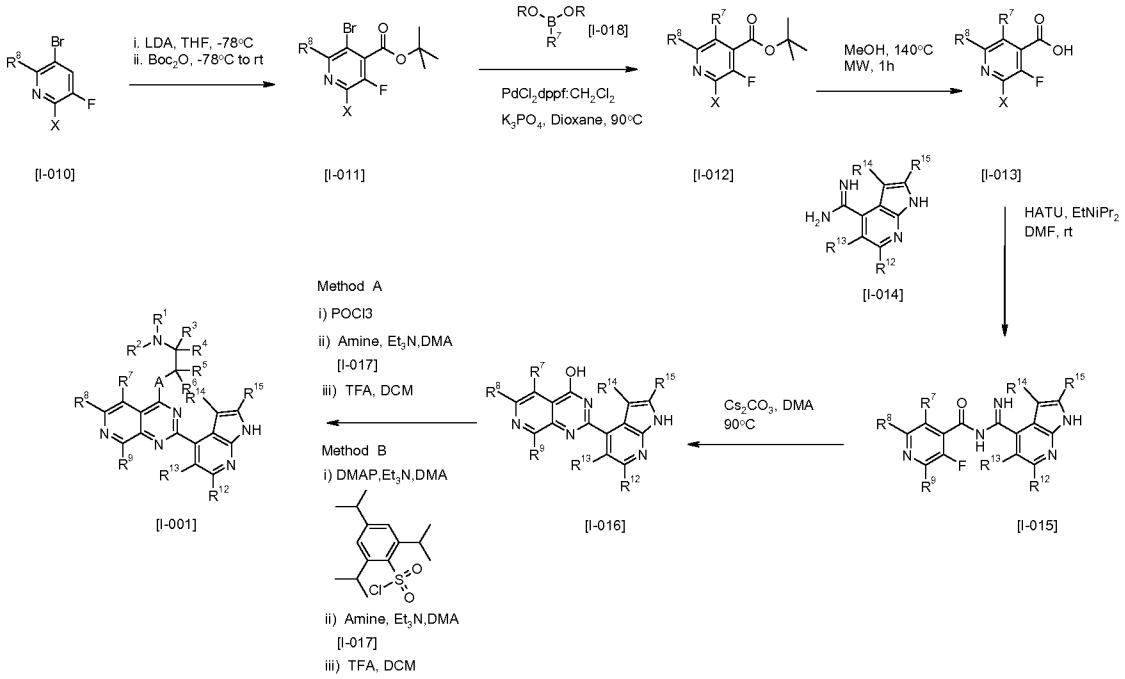
General synthesis of substituted substituted 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline derivatives of general formula [I-001] Scheme D3

The 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline derivatives of general formula [I-001] were prepared by the reaction of a halogenated pyridine derivative of general formula [I-010] with a strong base such as LDA, in a polar aprotic solovent such as THF, a symmetrical anhydride such as Di-tert-butyl dicarbonate at low temeperature to yield halo-substituted-isonicotinic acid tert-butly ester derivatives of general formula [I-011]. After reaction work up, typically by a liquid-liquid extraction the intermediate was purified by column chromatography. The halo-substituted-isonicotinic acid tert-butly ester derivative of general formula [I-011] was then subjected to a Suzuki type palladium catalysed cross coupling reaction with boronic acid or boronate ester derivative of general formula [I-018] a palladium catalyst such as $Pd(PPh_3)_4$, a base such as K_2PO_4 in a polar aprotic solvent such as DMA or DMF at elavated temperature either by heating thermally or using a microwave reactor, to yield the substituted-isonicotinic acid tert-butly ester

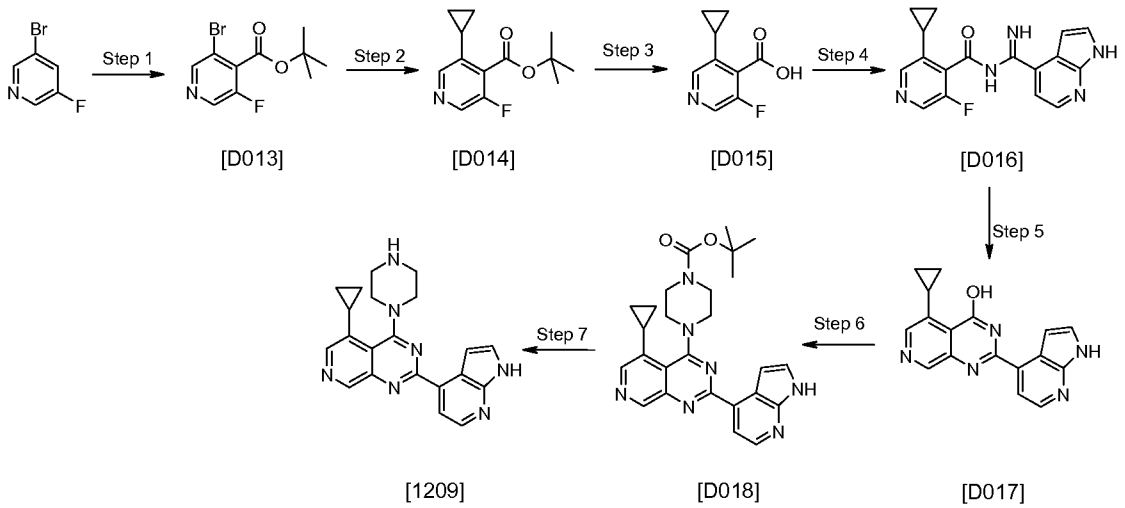
derivative of general formula [I-012]. After reaction work up, typically by a liquid-liquid extraction the intermediate was purified by column chromatography. The t-butylester inter intermediate [I-012] was then subjected to a deprotection reaction in the presence of a base such as sodium hydroxide in a polar protic solvent such as ethanol to yield the substituted-isonicotinic acid derivative of general formula [I-013], which was then subjected to a coupling reaction with a substituted 1H-pyrrolo[2,3-b]pyridine-4-carboxamidine derivative of general formula [I-014], with a suitable coupling agent such as O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) in a polar aprotic solvent such as DMA or DMF. The isonicotinoyl-amidine derivative of general formula [I-015] can then be cyclised to displace the relevant halogen group to yield the desired 2-(1H-pyrrolo[2,3-b]pyridine-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [I-016]. The 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline derivatives of general formula [I-001] were prepared by the reaction of a 2-(1H-pyrrolo[2,3-b]pyridine-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [I-016] with a chlorinatation agent such as phosphorous oxychloride to give compounds of general formula and the intermediate 4-chloro derivative was then further reacted with primary or secondary amino derivative of general formula [I-017], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-azaquinazoline derivatives of general formula [I-001] were prepared by the reaction of a -(1H-pyrrolo[2,3-b]pyridine-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [I-016] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- (1H-pyrrolo[2,3-b]pyridine-4-yl)-pyrido[3,4-d]pyrimidin--4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [G-117], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion

exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme D3



Synthesis of 5-Cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1209]



3-Bromo-5-fluoro-isonicotinic acid *tert*-butyl ester [D013]

To a solution of LDA (2M, 72mL, 144mmol) in THF (100mL) at -78°C was added dropwise via cannula a solution of 3-bromo-5-fluoropyridine (21.12g, 120mmol) in THF (50 mL) pre-cooled at -78°C. During the addition the internal temperature did not rise above -65°C. The dark red-brown solution was stirred for 1 hour. Di-*tert*-butyldicarbonate (52.4g, 240mmol) in THF (50 mL) was cooled to -10°C in a methanol/ice bath then added dropwise via cannula to the dark red-brown solution. The mixture was stirred for 2 hours then allowed to warm to room temperature and stir for 1 hour. Saturated aqueous ammonium chloride (100 mL) was added slowly and then water (200mL) and EtOAc (200mL) and the mixture was vigorously stirred for 45 minutes. The mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with EtOAc (200 mL). The THF and EtOAc layers were combined, dried over magnesium sulfate, filtered and evaporated. The recovered dark red-brown oil was purified by column chromatography (Cyclohexane/AcOEt: 1/0 to 97/3). Fractions containing desired material were concentrated in vacuo (14g, 85%). LCMS method: 5, RT 5.44 min, MI 277 [M+H]; NMR: (1H, 500MHz, CDCl3) 8.56 (s, 1H), 8.43 (s, 1H), 1.62 (s, 9H).

3-Cyclopropyl-5-fluoro-isonicotinic acid *tert*-butyl ester [D014]

A solution containing 3-Bromo-5-fluoro-isonicotinic acid *tert*-butyl ester [D013] (5.52g, 20mmol), potassium phosphate tribasic (12.74g, 60mmol) and cyclopropyl boronic acid (2.58g, 30mmol), in dioxane (100mL) was subjected to vacuum / argon balloon (three times). Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.408g, 0.5mmol) was added and the reaction heated at 96°C overnight under positive pressure of nitrogen. The mixture was cooled to room temperature and was filtered through a pad of 200g silica and washed with EtOAc (1L). The filtrate was concentrated in vacuo and the crude was purified by column chromatography (Cyclohexane/AcOEt: 98:2 to 96:4). The combined fractions were concentrated under reduced pressure to give the title compound [D014] as a colourless oil (3.42g, 72%). LCMS method: 5, RT 5.36 min, MI 238 [M+H]; NMR: (1H, 500MHz, CDCl3) 8.33 (s, 1H), 8.15 (s, 1H), 2.05-2.00 (m, 1H), 1.62 (s, 9H), 1.04-1.00 9m, 2H), 0.82-0.78 (m, 2H).

3-Cyclopropyl-5-fluoro-isonicotinic acid [D015]

In a microwave vial, 3-cyclopropyl-5-fluoro-isonicotinic acid *tert*-butyl ester [D014] (1.186g, 5mmol) was dissolved in methanol and then heated in microwave at 140°C for 1hr. The reaction was concentrated in vacuo to yield the title compound [D015] 0.84 g

(92%) of white crystalline solid. LC-MS: 1NJM406_1_28Jul2011; 1.51min, 87%; 182+; 1LCMS5.

3-Cyclopropyl-5-fluoro-N-[imino-(1H-pyrrolo[2,3-b]pyridin-4-yl)-methyl]-isonicotinamide [D016]

3-Cyclopropyl-5-fluoro-isonicotinic acid [D015] (0.681g, 3.76mmol), HATU (1.43g, 3.76mmol) and diisopropyethylamine (2.29mL, 13.16mmol) were stirred in DMF (5mL). After 1hr, 1H-Pyrrolo[2,3-b]pyridine-4-carboxamidine; acetic acid salt (0.92g, 3.76mmol) was added. Having stirred for 18hr the mixture was poured into water (180ml), stirred for 2 hours and then a white solid collected by filtration and washed with H2O to yield the title compound [D016] as a white solid (1.17g) was used without further purification. LCMS method: 5, RT 3.22 min, MI 324 [M+H].

5-Cyclopropyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [D017]

A mixture of N-[(2-Chloro-pyridin-4-yl)-imino-methyl]-3-cyclopropyl-5-fluoro-isonicotinamide [D016] (1.164g, 3.6mmol) and Cs2CO3 (1.18g, 3.60mmol) in DMA (12mL) was heated thermally at 90 °C overnight. The reaction mixture was poured into H2O (20ml) and acidified with dropwise addition of acetic acid at 0 °C. The beige precipitate (0.474, 43%) was collected by filtration and washed with H2O to yield the title compound [D017] which was used without further purification. LCMS method: 5, RT 4.58 min, MI 304 [M+H]; NMR: (1H, 500MHz, d6-dmso) 12.12 (brs, 1H), 9.09 (s, 1H), 8.54 (d, 1H), 8.37 (s, 1H), 7.90 (d, 1H), 7.83 (s, 1H), 7.36 (s, 1H), 3.56-3.64 (m, 1H), 1.24-1.30 (m, 2H), 1.08-1.14 (m, 2H).

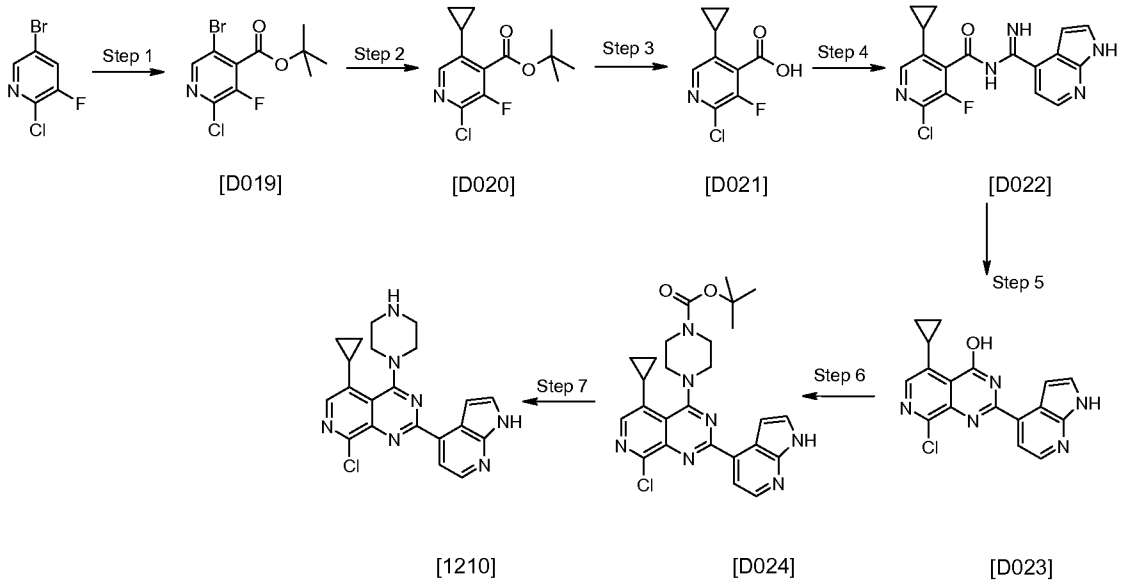
4-[5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [D018]

To a solution of 5-Cyclopropyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-o [D017]l (0.47g, 1.55mmol) in DMF (25mL) was added DIPEA (0.809mL, 4.65mmol) and DMAP (5mg). 2,4,6-Triisopropylbenzenesulfonyl chloride (0.563g, 1.86mmol) was then added and the mixture was stirred 2 hours. N-Boc-Piperazine (0.318g, 1.705mmol) was then added and the mixture was the stirred overnight. Water was added water (60-70mL) and the solution was stirred at RT for 15mins. The resulting solid was collected and washed twice with water. The solid was dissolved in DCM and purified by column chromatography (eluent: DCM/MeOH gradient 0% to 10% MeOH) to yield the title compound [D018] as a dark brown gum (0.6g, 82%) was used without further purification in the next step. LCMS method: 5, RT 5.85 min, MI 472 [M+H].

5-Cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1209]

To a solution of 4-[5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [D018] (0.6g, 1.27mmol) in DCM (15mL) was added HCl (4N, dioxane, 2mL) and the resultant bright yellow suspension was stirred at RT for 90mins. The solution was concentrated under reduced pressure and dissolved in MeOH and added to SCX-2 cartridge (10g), washed with MeOH/DCM (1:1, 40mL) and MeOH (20mL). Then the SCX-2 cartridge was washed with ammonia (7N in MeOH, 30mL). The ammonia washes were concentrated in vacuo and the material purified on the column chromatography (eluent DCM/MeOH gradient 0-20% MeOH/DCM). The fractions were combined and concentrated under reduced pressure to yield the title compound [1009]: LCMS method: 5, RT 2.65 min, MI 372 [M+H]; NMR: (1H, 500MHz, d6-dmso) 11.82 (brs, 1H), 9.13 (s, 1H), 8.36 (d, 1H), 8.10 (d, 1H), 7.62 (t, 1H), 7.45 (dd, 1H), 3.50-3.90 (m, 4H), 2.88-2.91 (m, 4H), 2.66-2.69 (m, 1H), 1.22-1.27 (m, 2H), 1.02-1.06

Synthesis of 8-Chloro-5-cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1210]



5-Bromo-2-chloro-3-fluoro-isonicotinic acid tert-butyl ester [D019]

Following the procedure described in scheme D3 1, 5-Bromo-2-chloro-3-fluoro-isonicotinic acid tert-butyl ester was prepared [D019] as acolourless oil by reaction of 5-bromo-2-chloro-3-fluoropyridine, LDA (2M), Di-*tert*-butyldicarbonate, and THF. LCMS method: 5, RT 6.25 min, MI 311 [M+H].

S2-Chloro-5-cyclopropyl-3-fluoro-isonicotinic acid tert-butyl ester [D020]

Following the procedure decribed in scheme D3, 5-Bromo-2-chloro-3-fluoro-isonicotinic acid tert-butyl ester was reacted with cyclopropyl boronic acid to give 2-Chloro-5-cyclopropyl-3-fluoro-isonicotinic acid tert-butyl ester [D020]. LCMS method: 5, RT 6.19 min, MI 272 [M+H].

2-Chloro-5-cyclopropyl-3-fluoro-isonicotinic acid [D021]

2-Chloro-5-cyclopropyl-3-fluoro-isonicotinic acid tert-butyl ester [D020] (815 mg, 3.00 mmol) was suspended in 2-propanol (9 mL) and HCl (5 mL of a 4M solution in dioxane) was added. The reaction mixture was heated to 50 °C overnight. The reaction mixture was concentrated under reduced pressure to the title compound [D021](530 mg, 82%) as a white crystalline solid which was used without purification. LCMS method: 5, RT 0.91 min, MI 216 [M+H].

2-Chloro-5-cyclopropyl-3-fluoro-N-[imino-(1H-pyrrolo[2,3-b]pyridin-4-yl)-methyl]-isonicotinamide [D022]

Follwing the procedure described in scheme D3, 2-chloro-5-cyclopropyl-3-fluoro-isonicotinic acid [D021] was reacted with 1H-Pyrrolo[2,3-b]pyridine-4-carboxamidine to give the title compound [D022]. LCMS method: 5, RT 4.45 min, MI 358 [M+H].

8-Chloro-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [D023]

Follwing the procedure described in scheme D3, 2-Chloro-5-cyclopropyl-3-fluoro-N-[imino-(1H-pyrrolo[2,3-b]pyridin-4-yl)-methyl]-isonicotinamide [D022] was reacted with Cs_2CO_3 to give the title compound [D023]. LCMS method: 5, RT 4.87 min, MI 306 [M+H].

4-[8-Chloro-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [D024]

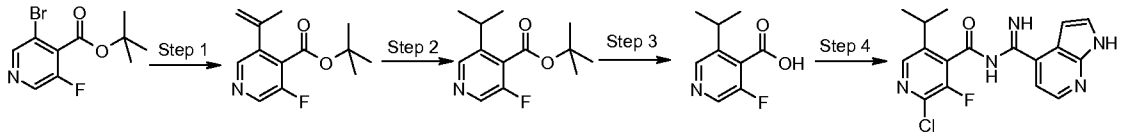
Follwing the procedure described in scheme D3, 8-Chloro-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [D023] was reacted with 1-Boc-piperazine to give the title compound [D024]. LCMS method: 5, RT 6.05 min, MI 506 [M+H].

8-Chloro-5-cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1210]

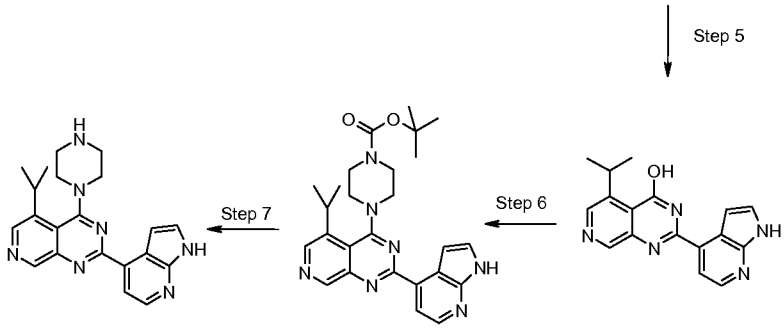
Follwing the procedure described in scheme D3, 8 4-[8-Chloro-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid

tert-butyl ester [D024] was reacted with 4N HCl in dioxane to give the title compound [1210]: LCMS method: 5, RT 3.22 min, MI 406 [M+H].

Synthesis of -Isopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1211]



[D013] [D025] [D026] [D027] [D028]



[1211] [D030] [D029]

3-Fluoro-5-isopropenyl-isonicotinic acid tert-butyl ester [D025]

Following the procedure described scheme D3, 3-Bromo-5-fluoro-isonicotinic acid *tert*-butyl ester [D013] was reacted with isopropenylboronic acid pinacol ester (contains phenothiazine as stabilizer), with dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct as catalyst to give 3-Fluoro-5-isopropenyl-isonicotinic acid tert-butyl ester [D025]. LCMS method: 5, RT 5.41 min, MI 238 [M+H].

3-Fluoro-5-isopropyl-isonicotinic acid tert-butyl ester [D026]

To a solution of 3-Fluoro-5-isopropenyl-isonicotinic acid tert-butyl ester [D025] in EtOH was added ammonium formate and palladium on charcoal (5% wt/wt) and the mixture was heated at 60oC overnight. More ammonium formate was added and the mixture was stirred for a further 45min at 60oC then was allowed to cool down to room temperature and was stirred overnight. The mixture was filtered through a celite pad and washed with EtOAc. Water was added to the filtrate and the layers were separated. The organic was dried over MgSO4 and concentrated in vacuo. The crude was purified by column chromatography (gradiant Cyclohexane/AcOEt: 1:0 to 92:8). The combined fractions were concentrated under reduced pressure to led the title compound [D026] as a pale yellow oil

(0.34g, 37%). LCMS method: 5, RT 5.55 min, MI 240 [M+H]; NMR: (1H, 500MHz, CDCl3) 8.42 (1H, s), 8.35 (1H, s), 3.09 (1H, sept), 1.60 (9H, s), 1.33 (6H, d).

3-Fluoro-5-isopropyl-isonicotinic acid [D027]

To a solution of 3-Fluoro-5-isopropyl-isonicotinic acid tert-butyl ester [D026] (0.335g, 1.4mmol) in isopropyl alcohol (5mL), a solution of HCl (4N in dioxane, 1mL) was added and the solution was warmed to 50°C overnight. LC-MS implies some progress but not complete. HCl (4N in dioxane, 1mL) was added again and left at 50°C overnight. The reaction is still not complete so more HCl (4N in dioxane, 1mL) was added and left through the day (~6-7hrs). The solution was concentrated in vacuo to yield the title compound [D027] an off-white solid which was used without further purification and analysis.

3-Fluoro-N-[imino-(1H-pyrrolo[2,3-b]pyridin-4-yl)-methyl]-5-isopropyl-isonicotinamide [D028]

Following the procedure described in scheme D3, 3-Fluoro-5-isopropyl-isonicotinic acid was reacted [D027] with , 1H-Pyrrolo[2,3-b]pyridine-4-carboxamidine to give3-Fluoro-N-[imino-(1H-pyrrolo[2,3-b]pyridin-4-yl)-methyl]-5-isopropyl-isonicotinamide [D028]. LCMS method: 5, RT 3.67 min, MI 326 [M+H].

5-Isopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [D029]

Following the procedure described in scheme D3, 3-Fluoro-N-[imino-(1H-pyrrolo[2,3-b]pyridin-4-yl)-methyl]-5-isopropyl-isonicotinamide [D028] was treated with Cs_2CO_3 to give 5-Isopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [D029] as a brown solid. LCMS method: 5, RT 4.87 min, MI 306 [M+H].

4-[5-Isopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [D030]

Following the procedure described in scheme D3, 5-Isopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [D029] was treated with 1-Boc-piperazine to give the title compound [D030] as a brown solid. LCMS method: 5, RT 5.78 min, MI 474 [M+H].

5-Isopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine [1211]

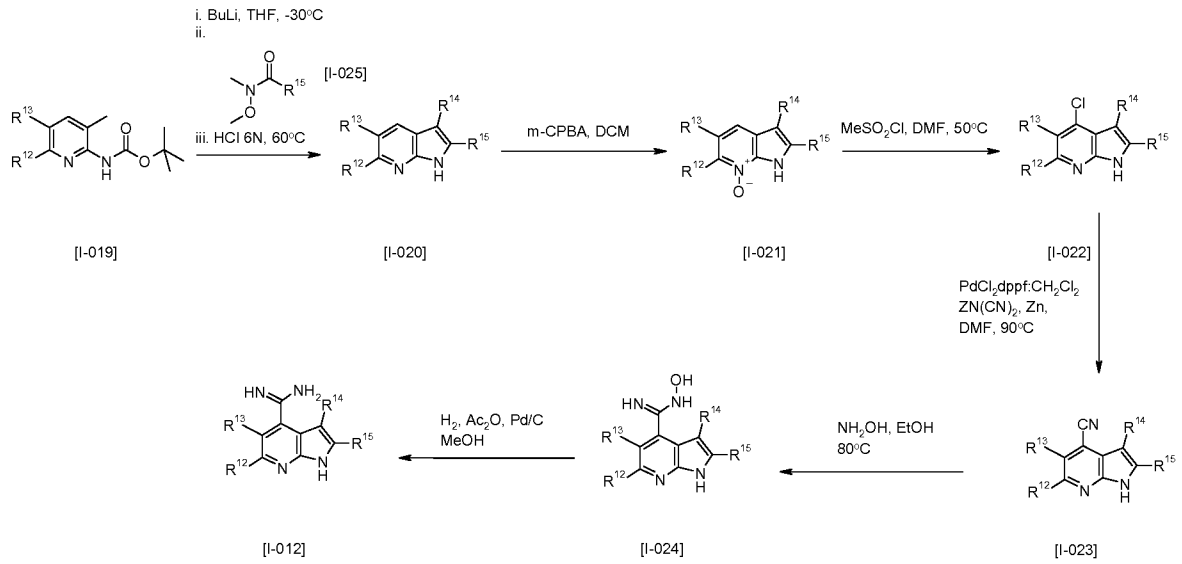
Following the procedure described in scheme D3, 4-[5-Isopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [D030] was treated with 4N HCl to give the title compound[1211] as a brown solid. LCMS method: 5, RT 2.82 min, MI 374 [M+H], NMR: (1H, 500MHz, CDCl3) 9.28 (1H,

s), 9.0 (1H, br s), 8.61 (1H, s), 8.46 (1H, s), 8.23 (1H, d), 7.63 (1H, s), 7.47 (1H, s), 4.07 (1H, m), 3.86 (2H, m), 3.49 (2H, m), 3.11 (4H, m), 1.25 (6H, d).

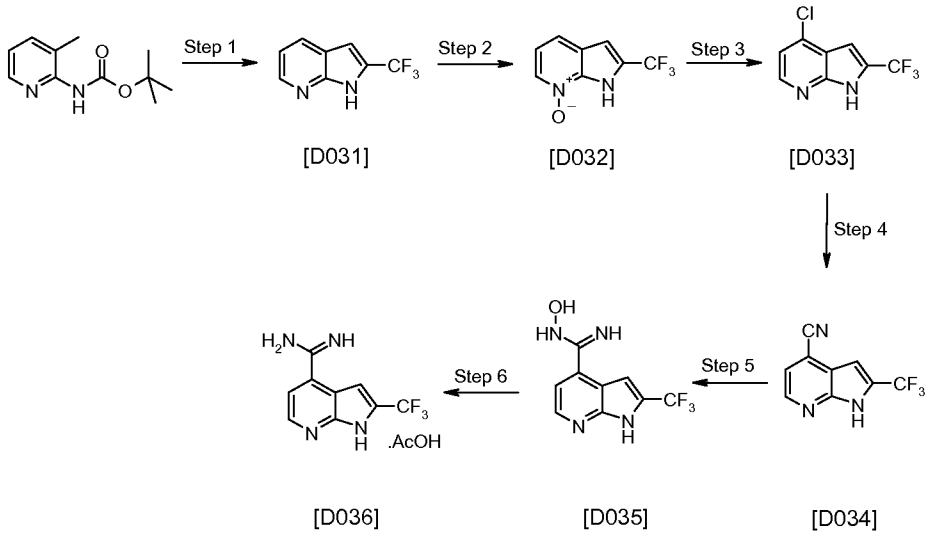
General synthesis of substituted 1H-pyrrolo[2,3-b]pyridine-4-carboxamidine derivative of general formula [I-012] Scheme D4

The substituted 1H-pyrrolo[2,3-b]pyridine-4-carboxamidine derivatives of general formula [I-012] were prepared by the reaction of 2-methyl pyridine-2-yl carbamic acid tert butyl ester derivative of general formula [I-019] with a strong base such as nBuLi, in a polar aprotic solovent such as THF, and a substituted Weinreb amide derivative of general formula [I-025] at low temeperature followed by reaction with a mineral acid such as hydrochloric acid at elevated temperature to yield the 1-H-pyrrolo[2,3-b]pyridine derivative of general formula [I-020] , after reaction work up, typically by a liquid-liquid extraction the intermediate was purified by column chromatography. The 1-H-pyrrolo[2,3-b]pyridine derivative of general formula [I-020] was then subjected to a pyridine N-oxidation reaction with an oxidising reagent such as mCPBA in a solvent such as DCM. The intermediate 1-H-pyrrolo[2,3-b]pyridine-7-oxide derivative of general formula [I-021] was then reacted with a chlorinating agent such as methansulfonyl chloride, in a polar aprotic solvent such as DMF at elevated temperature, after reaction work up, typically by a liquid-liquid extraction the intermediate was purified by column chromatography. The intermediate 4-chloro-1H-pyrrolo[2,3-b]pyridine derivative of general formula [I-022] was then submitted to a palladium catalysed cross coupling reaction with a cyanide species such as zinc cyanide, a palladium catalyst such as dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct, zinc dust, in a polar aprotic solvent such as DMF at elevated temperature, after reaction work up, typically by a liquid-liquid extraction the intermediate was purified by column chromatography. The intermediate 1H-pyrrolo[2,3-b]pyridine-4-carbonitrile derivative of general formula [I-023] was then reacted with hydroxylamine (50% wt/wt in water) and a polar protic solvent such as EtOH at elevated temperature. The intermediate N-hydroxy-1H-pyrrolo[2,3-b]pyridine-4-carboxamide of general formula [I-024] was then subjected to a hydrogenolysis reaction with acetic anhydride in a polar protic solvent such as methanol a palladium catalyst such as palladium on activated charcoal under a atmosphere of hydrogen gas, to yield the substituted 1H-pyrrolo[2,3-b]pyridine-4-carboxamidine derivative of general formula [I-012] Scheme D4.

Scheme D4



Synthesis of 2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine; acetic acid salt [D036]



Step 1: 2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine [D031]

To a solution of (3-Methyl-pyridin-2-yl)-carbamic acid tert-butyl ester (5g, 24mmol) in THF (50mL) at -30oC was added BuLi (2.5M, 28.5mL, 72mmol) and the reaction mixture was warmed to 0oC and stirred for 90min. A solution of 2,2,2-Trifluoro-N-methoxy-N-methyl-acetamide (2.9mL, 24mmol) in THF (10mL) was slowly added and the reaction was stirred at 0oC for 3h. The reaction mixture was slowly treated with HCl (30mL, 6M) followed by heating at 60oC for 18h. The reaction mixture was cooled, the layers were separated and the aqueous layer was made basic with NaOH (5M) and extracted twice

with AcOEt. The combined organic layers (plus the one from the first extraction) were dried over MgSO4, concentrated and the residue was purified by Column chromatography (eluent Cyclohexane/AcOEt 1/0 to 8/2) to afford the title compound [D031] as a yellow solid (1.2g, 27%): LCMS method: 5, RT 4.44 min, MI 187 [M+H], NMR: (1H, 500MHz, d6-dmso) 14.33 (brs, 1H), 8.49 (d, 1H), 8.09 (d, 1H), 7.27 (dd, 1H), 6.90 (s, 1H).

2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine 7-oxide [D032]

To a solution of 2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine [D031] (1.2g, 6.45mmol) in DCM (10mL), 3-Chloroperoxybenzoic acid (1.22g, 7.09mmol) was added and the mixture was stirred overnight. A saturated solution of NaHCO3 was added and the layers were separated. The organic was dried over MgSO4 and concentrated under reduced pressure. To yield the title compound [D032] as yellow solid (0.82g, 63%) was used without further purification. LCMS method: 5, RT 3.43 min, MI 203 [M+H], NMR: (1H, 500MHz, d6-dmso) 8.34 (d, 1H), 7.76 (d, 1H), 7.19 (d, 1H), 7.18 (s, 1H),

4-Chloro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridine [D033]

To a solution of 2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine 7-oxide [D032] (0.82g, 4.05mmol) in DMF (10mL) at 50oC , methane sulfonyl chloride (1.57mL, 20.28mmol) was added dropwise. The solution was stirred 3h at 50°C. The reaction was then cooled to room temperature and water (5mL) was added. A solution of 5M NaOH was added and the solid was collected, dried using an azeotrope with toluene to yield the title compound [D032] which was used without further purification. LCMS: 1LCMS5 5.77min, 221-223 [M+1, Cl pattern].

2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile [D034]

A seaablel vial was charged with 4-Chloro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridine [D033] (0.6g, 2.72mmol), Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.222g, 0.27mmol), zinc cyanide (0.958g, 8.16mmol), zinc (dust, 0.036g, 0.54mmol) and DMF (15mL). The vial was capped and heated at 90oC overnight. The reaction was poured in water and extracted with AcOEt. The aqueous layer was extracted again with AcOEt and the organics were combined, washed with water and brine and dried over MgSO4 to yield the title compound [D043] which was used without further purification: LCMS method: 5, RT 4.98 min, MI 212 [M+H].

N-Hydroxy-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D035]

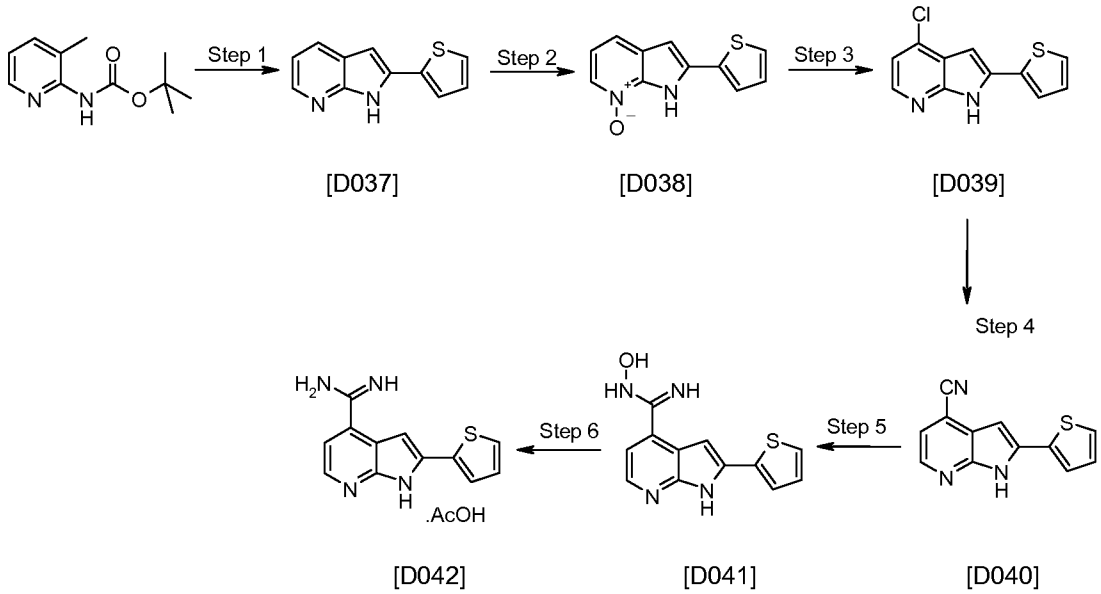
A mixture of 2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile [D034] (0.68g, 3.22mmol) and hydroxylamine (50% wt/wt in water, 0.205mL, 6.44mmol) and EtOH (5mL) was heated at 80°C overnight. Solvent was then evaporated and the mixture

azeotroped twice with toluene under vacuum. To yield the title compound [D035] as a yellow solid (0.78g, 99%) which was used in the next step without further purification: LCMS method: 5, RT 2.22 min, MI 245 [M+H], NMR: (1H, 500MHz, d6-dmso): 13.14 (brs, 1H), 10.40 (s, 1H), 8.70 (s, 1H), 7.70 (s, 1H), 7.56 (d, 1H), 6.27 (s, 2H).

2-Trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine; compound with acetic acid [D036]

To a suspension of N-Hydroxy-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D035] (0.43g, 1.76mmol) in MeOH (10mL) was added dropwise acetic anhydride (0.175mL, 1.85mmol) at room temperature. The suspension was stirred 15min and palladium on charcoal (5% wt/wt, 0.1g) was added. The vessel was seal and hydrogen (balloon) was bubble in the mixture for 10min and left stirring at RT under hydrogen atmosphere overnight. The mixture was filtered through celite and concentrated in vacuo to yield the title compound [D036] as a yellow solid (0.51g, 100%) which was used without further purification. LCMS method: 5, RT 4.45 min, MI 229 [M+H], NMR: (1H, 500MHz, d6-dmso) 1.79 (s, 3H, CH_3CO_2H), 8.50 (s, 1H), 7.35 (s, 1H), 7.03 (s, 1H).

Synthesis of 2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine acetic acid salt [D042]



2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine [D037]

Was prepared, following the procedure described in scheme D4, step 1, by reaction of (3-Methyl-pyridin-2-yl)-carbamic acid tert-butyl ester, thiophene-2-carboxylic acid methoxy-methyl-amide, BuLi and THF to give the title compound as a yellow solid. LCMS method: 5, RT 4.79 min, MI 201 [M+H].

2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine 7-oxide [D038]

Was prepared, following the procedure described in scheme D4, step 2, by reaction of 2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine [D037], m-CPBA and DCM to give the title compound as a yellow solid. LCMS method: 5, RT 3.38 min, MI 217 [M+H].

4-Chloro-2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine [D039]

Was prepared, following the procedure described in scheme D4, step 3, by reaction of 2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine 7-oxide [D038], methane sulfonyl chloride and DMF to give the title compound as a yellow solid. LCMS method: 5, RT 6.05 min, MI 235 [M+H].

2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile [D040]

Was prepared, following the procedure described in scheme D4, step 4, by reaction of 4-Chloro-2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine [D039], PdCl2dppf:CH2Cl2, Zinc cyanide, zinc dust and DMA to give the title compound as a yellow solid. LCMS method: 5, RT 5.28 min, MI 226 [M+H].

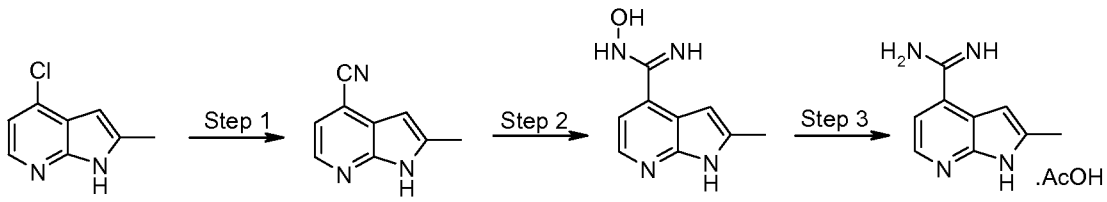
N-Hydroxy-2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D041]

Was prepared, following the procedure described in scheme D4, step 5, by reaction of 2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile [D040], hydroxylamine and EtOH to give the title compound as a yellow solid. LCMS method: 5, RT 2.38 min, MI 259 [M+H].

2-Thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine acetic acid salt [D042]

Was prepared, following the procedure described in scheme D4, step 6, by reaction of N-Hydroxy-2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidineacetic anhydride [D041], Pd/C, hydrogen and MeOH to give the title compound as a yellow solid. LCMS method: 5, RT 4.45 min, MI 243 [M+H].

Synthesis of 2-methyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine acetic acid salt [D045]



[D043] [D044] [D045]

2-Methyl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile [D043]

Was prepared, following the procedure described in scheme D4, step 4, by reaction of 4-Chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine, PdCl2dppf:CH2Cl2, Zinc cyanide, zinc dust and DMA to give the title compound as a white solid. LCMS method: 5, RT 4.17 min, MI 158 [M+H].

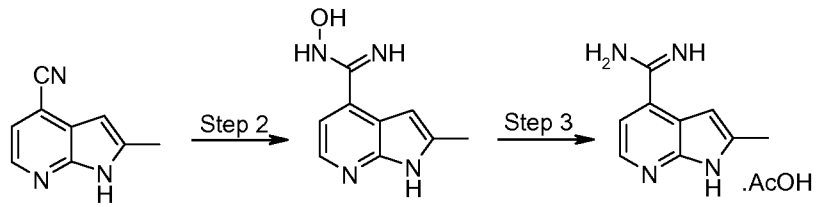
N-Hydroxy-2-methyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D044]

Was prepared, following the procedure described in scheme D4, step 5, by reaction of 2-Methyl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile [D043], hydroxylamine and EtOH to give the title compound as a yellow solid. LCMS method: 5, RT 1.92 min, MI 191 [M+H].

2-methyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine acetic acid salt [D045]

Was prepared, following the procedure described in scheme D4, step 6, by reaction of N-Hydroxy-2-methyl-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D044], acetic anhydride, Pd/C, hydrogen and MeOH to give the title compound as a yellow solid. LCMS method: 5, RT 2.44 min, MI 175 [M+H].

For example Synthesis of 21H-pyrrolo[2,3-b]pyridine-4-carboxamidine acetic acid salt [D047]



[D046] [D047]

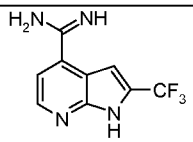
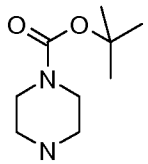
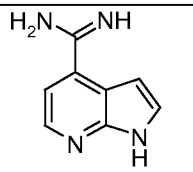
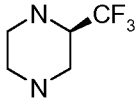
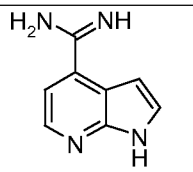
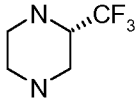
N-Hydroxy -1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D047]

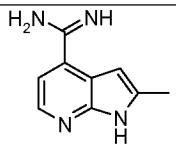
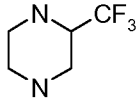
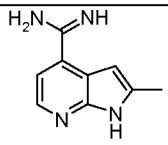
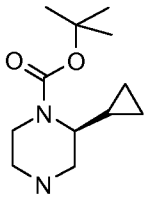
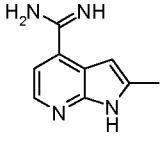
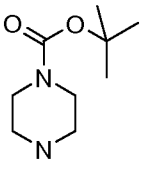
Was prepared, following the procedure described in scheme D4, step 5, by reaction of 1H-pyrrolo[2,3-b]pyridine-4-carbonitrile, hydroxylamine and EtOH to give the title compound as a yellow solid. LCMS method: 5, RT 1.24 min, MI 162 [M+H].

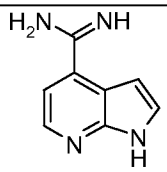
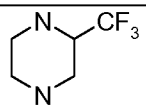
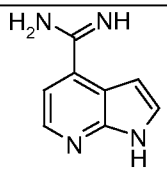
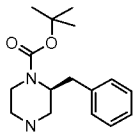
2-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine acetic acid salt [D047]

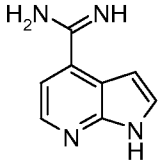
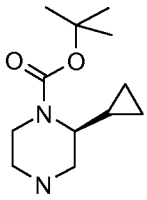
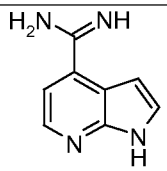
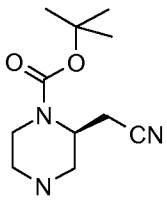
Was prepared, following the procedure described in scheme D4, step 6, by reaction of N-Hydroxy-1H-pyrrolo[2,3-b]pyridine-4-carboxamidine [D047], acetic anhydride, Pd/C, hydrogen and MeOH to give the title compound as a yellow solid. LCMS method: 5, RT 1.23 min, MI 161 [M+H], NMR: (1H, 500MHz, d6-dmso) 8.38 (1H, d), 7.71 (1H, d), 7.30 (1H, d), 6.58 (1H, d), 1.80 (8H, s)

Following the procedures described in Example AZA-9, the following compounds were prepared from 3-Cyclopropyl-5-fluoro-isonicotinic acid:

Ex	SM [I-013]	Amidine [I-014]	Amine [I-017]	Analysis		Name
				LCMS	NMR	
1212	[D015]	 [D036]		Method 5: RT: 3.59 min, MI: 440 [M+H]	1H NMR (DMSO, 500 MHz) 13.17 (s, 1H), 9.19 (s, 1H), 8.63 (d, 1H), 8.25 (d, 1H), 8.19 (s, 1H), 7.95 (s, 1H), 4.10-3.77 (m, 8H), 2.75-2.69 (m, 1H), 1.28-1.22 (m, 2H), 1.13-1.07 (m, 2H).	[5-Cyclopropyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1213	[D015]	 [D047]		Method 5: RT: 5.02 min, MI: 440 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 11.49 (1H, br. s), 9.10 (1H, s), 8.39 (1H, d, J = 5.0 Hz), 8.16 (1H, s), 8.10 (1H, d, J = 5 Hz), 7.57 (1H, t, J = 2.9 Hz), 7.46 (1H, dd, J = 3.3, 1.9 Hz) 4.43 (1H, br. d, J = 12.8 Hz), 4.01 - 3.96 (1H, m), 3.77 - 3.72 (1H, m), 3.48 - 3.38 (2H, m), 3.10 - 3.07 (1H, m), 2.93 - 2.85 (1H, m), 2.75 - 2.70 (1H, m), 1.34 - 1.20 (2H, m), 1.08 - 0.96 (2H, m).	5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-((R)-3-trifluoro-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
1214	[D015]	 [D047]		Method 5: RT: 5.03 min, MI: 440	(1H, 400MHz, d6-dmso 90 °C) 11.49 (1H, brs), 9.10 (1H, s), 8.39 (1H, d), 8.16 (1H, s), 8.10 (1H, d), 7.57 (1H, t), 7.46	5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-((S)-3-trifluoro-

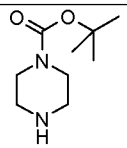
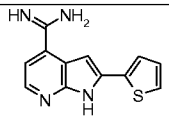
				[M+H]	(1H, dd) 4.43 (1H, br. d), 4.01 - 3.96 (1H, m), 3.77 - 3.72 (1H, m), 3.48 - 3.38 (2H, m), 3.10 - 3.07 (1H, m), 2.93 - 2.85 (1H, m), 2.75 - 2.70 (1H, m), 1.34 - 1.20 (2H, m), 1.08 - 0.96 (2H, m).	methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
1215	[D015]	 [D045]		Method 5: RT: 5.27 min, MI: 454 [M+H]	1H NMR (DMSO, 500MHz), 11.67 (brs, 1H), 9.07 (brs, 1H), 8.24 (d, 1H), 8.10 (s, 1H), 8.03 (d, 1H), 7.16 (s, 1H), 4.72-4.18 (m, 1H), 4.05-3.88 (m, 1H), 3.85-3.61 (m, 1H), 3.31 (s, 3H), 3.18-2.72 (m, 4H), 1.33-1.14 (m, 2H), 1.06-0.95 (m, 1H).	5-Cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-(3-trifluoro-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
1216	[D015]	 [D045]		Method 5: RT: 3.20 min, MI: 426 [M+H]	1H NMR (DMSO, 500MHz) 11.68 (brs, 1H), 9.07 (brs, 1H), 8.24 (d, 1H), 8.13 (d, 1H), 8.11 (d, 1H), 7.17 (s, 1H), 4.34-4.08 (m, 2H), 3.60-3.46 (m, 2H), 3.18-2.84 (m, 2H), 3.01 (s, 3H), 1.04-0.88 (m, 3H), 0.60-0.25 (m, 5H).	5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1217	[D015]	 [D045]		Method 5: RT: 2.80 min, MI:	(1H, 500MHz, d6-dmso) 11.64 (s, 1H), 9.03 (s, 1H), 8.22 (d, 1H), 8.06 (s, 1H), 8.02 (d, 1H),	5-Cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-

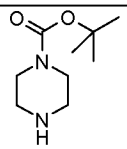
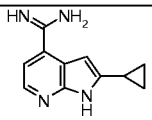
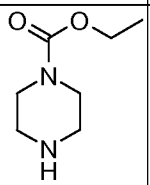
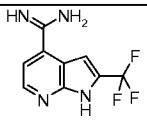
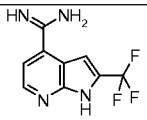
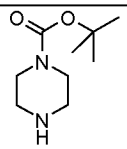
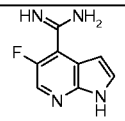
				386 [M+H]	7.15 (s, 1H), 3.08 (very broad m, 4H), 2.87-2.92 (m, 4H), 2.65-2.70 (m, 1H), 2.47 (s, 3H), 1.22-1.26 (m, 2H), 1.02-1.07 (m, 2H),	yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1218	[D015]	 [D047]		Method 5: RT: 5.03 min, MI: 440 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 11.49 (1H, br. s), 9.10 (1H, s), 8.39 (1H, d, J = 5.0 Hz), 8.16 (1H, s), 8.10 (1H, d, J = 5 Hz), 7.57 (1H, t, J = 2.9 Hz), 7.46 (1H, dd, J = 3.3, 1.9 Hz) 4.43 (1H, br. d, J = 12.8 Hz), 4.01 - 3.96 (1H, m), 3.77 - 3.72 (1H, m), 3.48 - 3.38 (2H, m), 3.10 - 3.07 (1H, m), 2.93 - 2.85 (1H, m), 2.75 - 2.70 (1H, m), 1.34 - 1.20 (2H, m), 1.08 - 0.96 (2H, m).	5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
1219	[D015]	 [D047]		Method 5: RT: 3.53 min, MI: 462 [M+H]	(1H, 500MHz, d6-dmso) 11.47 (1H, brs), 9.05 (1H, s), 8.35 (1H, d), 8.06 (1H, s), 7.95 (1H, d), 7.56 - 7.55 (1H, br. m), 7.43 (1H, d), 7.34 - 7.30 (2H, m), 7.27 - 7.24 (3H, m), 4.27 (1H, dr. d), 4.20 - 4.17 (1H, m), 3.39 - 3.33 (1H, m), 3.21 - 3.17 (1H, m), 3.14 - 3.04 (2H,	4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine

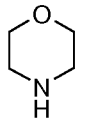
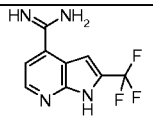
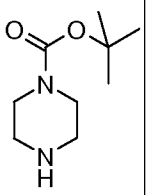
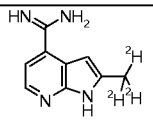
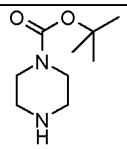
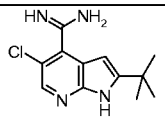
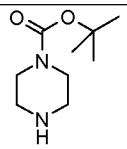
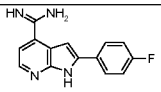
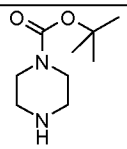
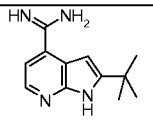
					m), 2.96 - 2.82 (2H, m), 2.77 - 2.72 (1H, m), 2.63 - 2.56 (1H, m), 1.23 - 1.15 (2H, m), 0.94 - 0.87 (2H, m).	
1220	[D015]	 [D047]		Method 5: RT: 3.09 min, MI: 412 [M+H]	(1H, 500MHz, d6-dmso) 11.52 (1H, s, brs), 9.13 (1H, s), 8.41 (1H, d), 8.20 (1H, s), 8.11 (1H, d), 7.60 (1H, d), 7.47 (1H, d), 4.44 - 4.41 (1H, br. m), 4.28 - 4.24 (1H, br. m), 3.74 - 3.68 (1H, br. m), 3.60 - 3.53 (1H, m), 3.36 - 3.33 (1H, m), 3.14 - 3.07 (1H, m), 2.80 - 2.68 (2H, m), 1.30 - 1.24 (2H, m), 1.12 - 1.04 (2H, m), 1.02 - 0.97 (1H, m), 0.66 - 0.59 (3H, m), 0.46 - 0.41 (1H, m).	5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1221	[D015]	 [D047]		Method 5: RT: 2.94 min, MI: 411 [M+H]	(1H, 400MHz, d6-dmso 90 °C) 11.46 (1H, brs), 9.08 (1H, s), 8.38 (1H, d), 8.15 (1H, s), 8.13 (1H, d), 7.57 - 7.55 (1H, m), 7.48 (1H, dd), 4.34 - 4.32 (1H, m), 4.13 - 4.10 (1H, m), 3.31 - 3.25 (1H, m), 3.21 - 3.16 (1H, m), 3.11 - 3.01 (2H, m), 2.95 - 2.86 (2H, m), 2.72 - 2.69 (1H, m), 2.61 - 2.58 (1H, m), 1.30 -	{(S)-4-[5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile

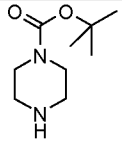
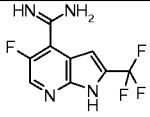
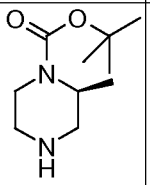
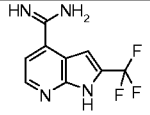
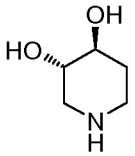
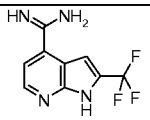
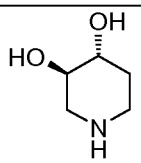
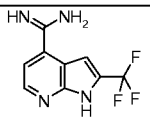
					1.23 (2H, m), 1.03 - 0.98 (2H, m).	

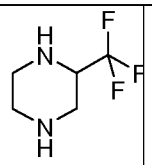
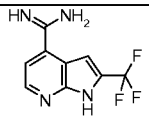
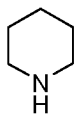
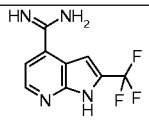
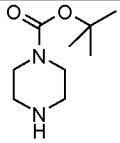
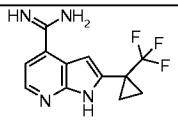
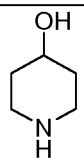
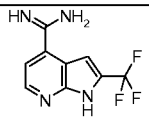
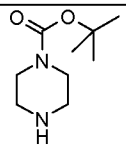
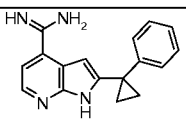
The following compounds were synthesised according to the general synthesis shown in scheme [B4]

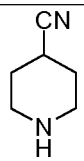
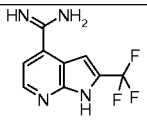
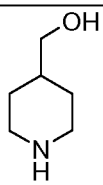
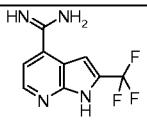
Ex	Amine 1	Amidine 2	Analysis		Name
			LCMS	NMR	
1222			method 5: RT 3.59 min, MI: 454 [MH+]	($CDCl_3$, 500MHz), 12.06 (brs, 1H), 9.12 (s, 1H), 8.47 (d, 1H), 8.23 (d, 1H), 8.06 (s, 1H), 7.80 (s, 1H), 7.57 (d, 1H), 7.39 (d, 1H), 7.19 (dd, 1H), 4.02 -3.61 (m, 4H), 3.12-3.06 (m, 4H), 2.80-2.74 (m, 1H), 1.30-1.26 (m, 2H), 1.05-1.01	5-Cyclopropyl-4-piperazin-1-yl-2-(2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine

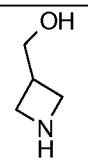
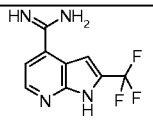
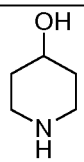
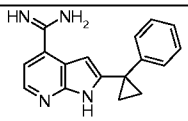
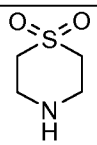
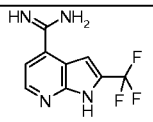
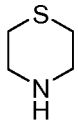
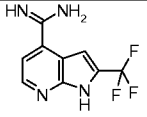
1223			method 5: RT 3.21 min, MI: 412 [MH+]	1H NMR (400 MHz, 90 ºC, d6-DMSO) 11.27 (1H, br s), 9.04 (1H, s), 8.23 (1H, d, J = 5.1 Hz), 8.11 (1H, s), 8.02 (1H, d, J = 5.1 Hz), 7.10 (1H, s), 3.74 - 3.72 (4H, m), 2.95 - 2.92 (4H, m, overlapping with water signal), 2.74 - 2.67 (1H, m), 2.18 - 2.12 (1H, m), 1.28 - 1.23 (2H, m), 1.09 - 1.04 (2H, m), 1.00 - 0.96 (2H, m), 0.95 - 0.91 (2H, m).	5-Cyclopropyl-2-(2-cyclopropyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1224			method 5: RT 4.98 min, MI: 512 [MH+]	(DMSO) 13.11 (brs, 1H), 9.12 (s, 1H), 8.60 (d, 1H), 8.23 (d, 1H), 8.14 (s, 1H), 7.94 (s, 1H), 40.08-4.05 (m, 1H), 3.95-3.55 (m, 8H), 1.26- 1.17 (m, 2H), 1.56-1.00 (m, 2H).	4-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid ethyl ester
1225	--		method 5: RT 5.77 min, MI: 372 [MH+]	(DMSO) 8.97 (s, 1H), 8.62 (d, 1H), 8.24 (s, 1H), 7.88 (d, 1H), 7.67 (s, 1H), 3.45-3.39 (m, 1H), 1.12-1.08 (m, 2H), 0.97-0.92 (m, 2H).	5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol
1226			method 5: RT 2.10 min, MI: 390 [MH+]	1H NMR (500 MHz, d6-DMSO) 11.92 (1H, s), 8.98 (1H, s), 8.32 (1H, d, J = 3.5 Hz), 8.12 (1H, s), 7.65 (1H, t, J = 2.9 Hz), 6.94 (1H, dd, J = 3.4, 2.0 Hz), 3.84 - 3.49 (4H, br m), 2.85 (4H, br s), 2.67 - 2.62 (1H, m), 1.29 - 1.26 (2H, m), 1.07 - 1.04 (2H, m).	5-Cyclopropyl-2-(5-fluoro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

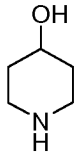
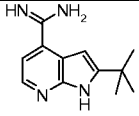
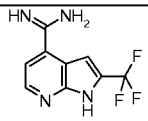
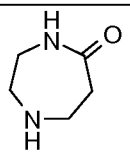
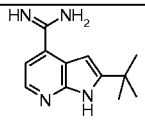
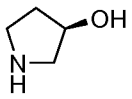
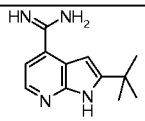
1227			method 5: RT 6.01 min, MI: 441 [MH+]	(DMSO) 13.11 (s, 1H), 9.12 (s, 1H), 8.62 (s, 1H), 8.22 (d, 1H), 8.13 (s, 1H), 7.93 (s, 1H), 3.80-3.60 (m, 8H), 2.72-2.67 (m, 1H), 1.28-1.23 (m, 2H), 1.06-1.03 (m, 2H).	5-Cyclopropyl-4-morpholin-4-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1228			method 5: RT 2.16 min, MI: 389 [MH+]	1H NMR (400 MHz, d6-DMSO, 90 ºC) 11.28 (1H, s), 9.04 (1H, s), 8.24 (1H, d, J = 5.2 Hz), 8.11 (1H, s), 8.03 (1H, d, J = 5.2 Hz), 7.16 (1H, d, J = 1.5 Hz), 3.74 - 3.72 (4H, m), 2.95 - 2.93 (4H, m, overlapping with water signal), 2.74 - 2.69 (1H, m), 1.28 - 1.23 (2H, m), 1.01 - 0.97 (2H, m).	5-Cyclopropyl-4-piperazin-1-yl-2-(2-triduteriomethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1229			method 5: RT 3.44 min, MI: 462 [MH+]	1H NMR (d6-DMSO, 500MHz), 11.87 (1H, s), 8.94 (1H, s), 8.22 (1H, s), 8.11 (1H, s), 3.75-3.55 (4H, m), 2.82 (4H, br s), 2.64-2.59 (1H, m), 1.27 (2H, ddd), 1.05 (2H, ddd)	2-(2-tert-Butyl-5-chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1230			method 5: RT: 4.02 min, MI: 466 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 ºC) 9.13 (1H, s), 8.38 (1H, d, J = 5.1 Hz), 8.14 (1H, s), 8.11 (1H, d, J = 5.1 Hz), 8.07 - 8.03 (2H, m), 7.84 (1H, s), 7.32 (2H, t, J = 8.9 Hz), 3.78 - 3.76 (4H, m), 2.97 - 2.94 (4H, m, overlapping with water signal), 2.77 - 2.70 (1H, m), 1.30 - 1.25 (2H, m), 1.02 - 0.98 (2H, m).	5-Cyclopropyl-2-[2-(4-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1231			method 5: RT: 3.51min, MI: 428 [M+H]	(1H, d6-DMSO, 500MHz) 11.71 (1H, br s), 9.03 (1H, s), 8.26 (1H, d), 8.07 (1H, s), 8.02 (1H, d), 7.18 (1H, d), 3.81 (2H, v br s), 3.62 (2H, v br s), 2.90 (4H, br	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

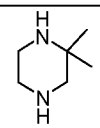
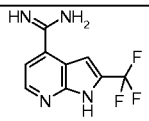
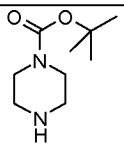
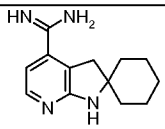
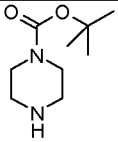
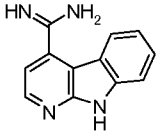
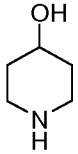
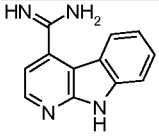
				s), 2.70-2.65 (1H, m), 1.41 (9H, s), 1.28-1.22 (2H, m), 1.04-1.01 (2H, dt).	
1232			method 5: RT 2.48 min, MI: 458 [MH+]	1H NMR (400 MHz, d6-DMSO, 90 ºC) 9.02 (1H, s), 8.54 (1H, d, J = 3.6 Hz), 8.18 (1H, s), 7.51 - 7.49 (1H, m), 3.74 - 3.72 (4H, m), 2.92 - 2.89 (4H, m), 2.68 - 2.62 (1H, m), 1.31 - 1.26 (2H, m), 1.04 - 1.01 (2H, m).	5-Cyclopropyl-2-(5-fluoro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
1233			method 5: RT: 3.63min, MI=454 [M+H]		5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1234			471.1 (M+H)	($CDCl_3$) 13.11 (br s, 1H), 9.06 (s, 1H), 8.62 (d, J = 5.0 Hz, 1H), 8.25 (d, J = 5.0 Hz, 1H), 8.10 (s, 1H), 7.98 (d, J = 1.0 Hz, 1H), 5.09-4.67 (m, 1H), 4.67-4.17 (m, 2H), 4.03-3.68 (m, 4H), 3.68-3.38 (m, 2H), 2.63-2.53 (m, 1H), 2.06 (br s, 1H), 1.70 (br s, water), 1.49-0.80 (m, 4H)	(+/-)-(cis)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol
1235			471.1 (M+H)	($CDCl_3$): 13.09 (br s, 1H), 9.07 (s, 1H), 8.62 (d, J = 5.0 Hz, 1H), 8.25 (d, J = 5.0 Hz, 1H), 8.11 (s, 1H), 7.98 (d, J = 1.0 Hz, 1H), 5.22-4.71 (m, 2H), 4.22-3.74 (m, 3H), 3.62-3.34 (m, 3H), 2.60-2.53 (m, 1H), 2.30-1.81 (m, 1H), 1.71-1.13 (m, 3H), 1.12-0.95 (m, 2H)	(+/-)- (trans)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol

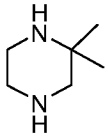
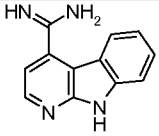
1236			method 5: RT: 4.74min, MI 508 [M+H]	1H NMR (DMSO, 500MHz) 13.14 (s, 1H), 9.12 (s, 1H), 8.61 (d, 1H), 8.21 (d, 1H), 8.14 (s, 1H), 7.91 (s, 1H), 4.70-4.21 (m, 1H), 4.04-3.96 (m, 1H), 3.87-3.46 (m, 2H), 3.19-2.96 (m, 3H), 1.37-1.17 (m, 2H), 1.14-0.96 (m, 2H).	5-Cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1237			439.49		5-Cyclopropyl-4-piperidin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1238			method 5: RT: 5.31 min, MI 480 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 11.66 (1H, br s), 9.04 (1H, s), 8.39 (1H, d, J = 5.0 Hz), 8.13 (1H, s), 8.10 (1H, d, J = 5.0 Hz), 7.55 (1H, s), 3.76 - 3.73 (4H, m), 2.94 - 2.91 (4H, m, partly obscured by water signal), 2.73 - 2.66 (1H, m), 1.49 - 1.48 (2H, m), 1.47 - 1.46 (2H, m), 1.29 - 1.24 (2H, m), 1.01 - 0.97 (2H, m).	5-Cyclopropyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine
1239			method 5: RT 6.34min, MI=455 [M+H]	(DMSO), 13.12 (s, 1H), 9.08 (s, 1H), 8.61 (d, 1H), 8.23 (d, 1H), 8.10 (s, 1H), 7.96 (s, 1H), 4.84-4.70 (m, 1H), 4.14-4.04 (m, 1H), 3.88-3.75 (m, 1H), 3.68-3.40 (m, 2H), 1.95-1.84 (m, 1H), 1.67-1.39 (m, 2H), 1.31-1.20 (m, 2H), 1.17-0.99 (m, 4H).	1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol
1240			method 5: RT: 3.82 min, MI:	1H NMR (400 MHz, d6-DMSO, 90 °) 11.28 (1H, br s), 8.96 (1H, s), 8.27 (1H, d, J = 5.1 Hz), 8.09 (1H, s), 8.05 1H, d, J = 5.1 Hz), 7.45 - 7.43 (2H,	5-Cyclopropyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-

			488 [M+H]	m), 7.38 - 7.34 (2H, m), 7.29 - 7.26 (1H, m), 7.02 (1H, m), 3.63 - 3.60 (4H, m), 2.88 - 2.85 (4H, m), 2.70 - 2.64 (1H, m), 1.60 - 1.57 (2H, m), 1.40 - 1.37 (2H, m), 1.27 - 1.22 (2H, m), 1.00 - 0.96 (2H, m).	yl-pyrido[3,4-d]pyrimidine
1241			method 5: RT 5.38min, MI= 464 [M+H]	(DMSO, 90°C), 12.78 (brs, 1H), 9.12 (s, 1H), 8.62 (d, 1H), 8.24 (d, 1H), 8.18 (s, 1H), 7.95 (d, 1H), 4.04-3.98 (m, 2H), 3.72-3.66 (m, 2H), 3.22-3.15 (m, 1H), 2.72-2.65 (m, 1H), 2.15-2.08 (m, 2H), 2.00-1.91 (m, 2H), 1.31-1.26 (m, 2H), 1.03-0.99 (m, 2H).	1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile
1242			method 5: RT: 5.29min, MI=469 [M+H]	(DMSO, 90°C), 12.76 (brs, 1H), 9.08 (s, 1H), 8.61 (d, 1H), 8.25 (d, 1H), 8.16 (s, 1H), 7.96 (d, 1H), 4.38-4.35 (m, 2H), 4.12 (t, 1H), 3.37-3.28 (m, 4H), 2.69-2.62 (m, 1H), 1.91-1.73 (m, 3H), 1.46-1.34 (m, 2H), 1.29-1.25 (m, 2H), 1.02-0.98 (m, 2H).	{1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol

1243			method 5: RT 4.57min, MI: 441 [M+H]	(DMSO, 90°C), 9.03 (s, 1H), 8.60 (d, 1H), 8.26 (d, 1H)m, 8.19 (s, 1H), 7.96 (d, 1H), 4.53 (t, 2H), 4.26 (dd, 2H), 3.62 (d, 2H), 3.00-2.87 (m, 2H), 1.32-1.28 (m, 2H), 0.97-0.93 (m, 2H).	{1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol
1244			method 5: RT = 5.05 min, MI: 503 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 ºC) 11.27 (1H, s), 8.95 (1H, s), 8.26(1H, d, J = 5.1 Hz), 8.09 (1H, s), 8.05 (1H, d, J = 5.1 Hz), 7.45 - 7.42 (2H, m), 7.37 - 7.34 (2H, m), 7.29 - 7.25 (1H, m), 7.05 (1H, d, J = 2.2 Hz), 4.40 (1H, d, J = 4.3 Hz), 4.01 - 3.95 (2H, m), 3.83 - 3.77 (1H, m), 3.45 - 3.38 (2H, m), 2.66 - 2.61 (1H, m), 1.90 - 1.83 (2H, m), 1.59 - 1.49 (4H, q and m overlapping), 1.39 - 1.37 (2H, m), 1.26 - 1.21 (2H, m), 0.99 - 0.95 (2H, m).	1-{5-Cyclopropyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol
1245			method 5: RT 4.51min, MI: 489 [M+H]	1H NMR (DMSO, 500MHz) 13.15 (s, 1H), 9.19 (s, 1H), 8.63 (d, 1H), 8.25 (d, 1H), 8.16 (s, 1H), 7.97 (s, 1H), 4.41-4.01 (m, 4H), 3.41-3.34 (m, 4H), 2.73-2.66 (m, 1H), 1.32-1.23 (m, 2H), 1.09-1.02 (m, 2H).	5-Cyclopropyl-4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1246			method 5: RT 5.95min, MI=457 [M+H]	1H NMR (DMSO, 500MHz) 13.12 (s, 1H), 9.10 (s, 1H), 8.61 (d, 1H), 8.22 (d, 1H), 8.11 (s, 1H), 7.94 (s, 1H), 4.09-4.01 (m, 4H), 2.83-2.73 (m, 4H), 2.63-2.57 (m, 1H), 1.31-1.23 (m, 2H), 1.06-0.98 (m, 2H).	5-Cyclopropyl-4-thiomorpholin-4-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine

1247			method 5: RT: 5.61 min, MI: 443 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 11.31 (1H, br s), 9.03 (1H, s), 8.27 (1H, d, J = 5.2 Hz), 8.11 (1H, s), 8.06 (1H, d, J = 5.2 Hz), 7.24 - 7.23 (1H, m), 4.42 (1H, d, J = 4.1 Hz), 4.18 - 4.08 (2H, m), 3.88 - 3.83 (1H, m), 3.60 - 3.53 (2H, m), 2.71 - 2.65 (1H, m), 1.95 - 1.91 (2H, m), 1.65 - 1.57 (2H, m), 1.46 (9H, s), 1.28 - 1.23 (2H, m), 1.00 - 0.96 (2H, m).	1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol
1248			method 5: RT: 5.62min, MI: 411 [M+H]	1H NMR (DMSO, 500MHz) 13.09 (brs, 1H), 9.02 (s, 1H), 8.59 (d, 1H), 8.24 (d, 1H), 8.13 (s, 1H), 7.95 (s, 1H), 7.47 (t, 4H), 2.43-2.33 (m, 3H), 1.31-1.24 (m, 2H), 0.99-0.92 (m, 2H).	4-Azetidin-1-yl-5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1249			method 5: RT: 1.76 min, MI: 456 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 11.31 (1H, s), 9.05 (1H, s), 8.28 (1H, d, J = 5.0 Hz), 8.15 (1H, s), 8.06 (1H, d, J = 5.0 Hz), 7.29 - 7.26 (1H, m), 7.19 (1H, d, J = 2.3 Hz), 4.03 - 4.00 (2H, m), 3.96 - 3.94 (2H, m), 3.39 - 3.35 (2H, m), 2.77 - 2.74 (2H, m), 2.65 - 2.58 (1H, m), 1.47 (9H, s), 1.28 - 1.23 (2H, m), 0.99 - 0.95 (2H, m).	1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-[1,4]diazepan-5-one
1250			method 5: RT: 4.78 min, MI: 429 [M+H]	1H NMR (500MHz, d6-DMSO), 11.67 (1H, br d, J = 1.8 Hz), 8.92 (1H, s), 8.25 (1H, d, J = 5.2 Hz), 8.07 (1H, s), 8.06 (1H, d, J = 5.2 Hz), 7.22 (1H, d, J = 2.3 Hz), 4.95 (1H, br , J = 2.9 Hz), 4.35 (1H, br s), 4.19 - 4.13 (1H, m), 4.09 - 4.04 (1H, s), 3.77 - 3.72 (1H, m), 3.48 (1H, d, J = 11.3 Hz), 2.35 - 2.28 (1H, m), 2.05 - 1.98	(R)-1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-ol

				(1H, m), 1.90 - 1.86 (1H, m), 1.34 - 1.29 (1H, m), 1.20 - 1.14 (1H, m), 1.20 - 1.14 (1H, m), 1.04 - 0.99 (1H, m), 0.94 - 0.89 (1H, m).	
1251			method 5: RT: 3.79min, MI: 468 [M+H]	1H NMR (DMSO, 500MHz) 13.10 (brs, 1H), 9.06 (s, 1H), 8.61 (d, 1H), 8.23 (d, 1H), 8.11 (s, 1H), 7.96 (s, 1H), 4.02-3.75 (m, 1H), 3.70-3.53 (m, 2H), 3.38-3.25 (m, 2H), 2.98-2.85 (m, 2H), 1.29-0.70 (m, 10H).	5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
1252			442	1H NMR (400 MHz, d6-DMSO, 90 ºC) 8.96 (1H, s), 8.10 (1H, s), 7.82 (1H, d, J = 5.5 Hz), 7.34 (1H, d, J = 5.5 Hz), 6.42 (1H, s), 3.70 - 3.67 (2H, m), 3.09 - 3.106 (2H, m), 2.90 - 2.88 (2H, m), 2.70 - 2.66 (3H, m), 1.73 - 1.58 (7H, m), 1.55 - 1.45 (4H, m), 1.28 - 1.20 (3H, m), 0.99 - 0.95 (2H, m).	4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)spiro[1,3-dihydropyrrolo[2,3-b]pyridine-2,1'-cyclohexane]
1253			422 (M+H)	^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.08 (s, 1H), 9.17 (s, 1H), 8.83 (br s, 1H), 8.68 (d, 1H, J = 8.4 Hz), 8.59 (d, 1H, J = 5.1 Hz), 8.26 (s, 1H), 7.89 (d, 1H, J = 5.1 Hz), 7.55 (d, 1H, J = 7.9 Hz), 7.49 (m, 1H), 7.18 (m, 1H), 3.68 (br s, 4H), 3.34 (br s, 4H), 2.77 (m, 1H), 1.30 (m, 2H), 1.14 (m, 2H).	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole
1254			437 (M+H)	^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.12 (s, 1H), 9.07 (s, 1H), 8.60 (d, 1H, J = 5.0 Hz) 8.54 (d, 1H, J = 8.1 Hz), 8.22 (s, 1H), 7.84 (d, 1H, J = 5.0 Hz), 7.56 (d, 1H, J = 8.0 Hz), 7.49 (m, 1H), 7.17 (m, 1H), 4.11 (m, 3H), 3.58	1-[5-Cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol

				(br s, 2H), 2.61 (m, 1H), 1.89 (m, 2H), 1.55 (m, 2H), 1.92 (m, 2H), 1.21 (m, 2H).	
1255			450 (M+H)	^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.09 (s, 1H), 9.17 (s, 1H), 9.05 (br s, 2H), 8.67 (d, 1H, J = 8.1 Hz), 8.60 (d, 1H, J = 5.1 Hz), 8.29 (s, 1H), 7.93 (d, 1H, J = 5.1 Hz) 7.55 (d, 1H, J = 7.9 Hz), 7.49 (m, 1H), 7.18 (m, 1H), 3.93 (m, 4H), 3.39 (m, 2H), 2.61 (m, 1H), 1.01-1.48 (m, 10H).	4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole

Example 1253. 4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole trifluoroacetic acid salt

1253a) A mixture of azeotropically dried (xylene) 4-chloro-9H-pyrido[2,3-b]indole (1.31 g, 6.46 mmol), zinc cyanide (1.21 g, 10.3 mmol), zinc (0.145 g, 2.22 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.479 g, 0.523 mmol) and 1,1'-bis(diphenylphosphino)ferrocene (0.375 g, 0.676 mmol) in N,N-dimethylformamide (27 mL) was vacuum degassed then heated at 100 °C under an atmosphere of argon overnight. The mixture is cooled and poured into water:ethyl acetate (2:1, 150 mL). The layers were separated, the aqueous extracted with ethyl acetate (2X50 mL) and the combined organic extracts are diluted with hexane (15 mL) and brine (100 mL). The fine suspension of solids was removed by filtration of the aqueous layer through Celite, washing with methanol and ethyl acetate. The organic extracts and aqueous/organic rinsate were combined, separated and the organic layer washed with additional brine (100 mL), dried over magnesium sulfate, filtered and concentrated in vacuo onto silica gel (12 g) prior to purification on silica gel (80 g, 5-35% ethyl acetate:hexane). 9H-Pyrido[2,3-b]indole-4-carbonitrile was isolated as a yellow solid (0.830 g, 66% yield). LCMS (ESI): 194 $(M+H)^+$; ^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.45 (s, 1H), 8.63 (d, 1H, J = 5.0 Hz), 8.32 (d, 1H, J = 8.0 Hz), 7.68 (d, 1H, J = 5.0 Hz), 7.64 (m, 2H), 7.40 (m, 1H); ^{13}C-NMR (DMSO-d_6, 100 MHz): δ 151.6, 146.2, 139.7, 128.6, 121.1, 120.5, 117.9, 116.9, 116.7, 114.1, 112.0, 109.8.

1253b) Lithium hexamethyldisilazide in tetrahydrofuran(1.0 M, 7.0 mL, 7.0 mmol) was added to a suspension of 9H-pyrido[2,3-b]indole-4-carbonitrile (0.422 g, 2.18 mmol) in tetrahydrofuran (12.0 mL, 148 mmol) at room temperature under an atmosphere of nitrogen. Additional lithium hexamethyldisilazide in tetrahydrofuran (1.0 M, 7 mL) was added at 48 h to drive the reaction to completion. After stirring a total of 72 h, the mixture was diluted with water (50 mL) and the resultant solids were collected by filtration, washed with water and dried on a Buchner funnel and in vacuo. 9H-Pyrido[2,3-b]indole-4-carboxamidine was isolated as beige solids (0.297 g, 65% yield) and was used without further purification. LCMS (ESI): 211 $(M+H)^+$.

1253c) 9H-Pyrido[2,3-b]indole-4-carboxamidine (0.295 g, 1.40 mmol), N,N,N',N'-tetramethyl-O-(7-azabenzotriazol-1-yl)uronium hexafluorophosphate (0.806 g, 2.12 mmol), 3-cyclopropyl-5-fluoro-isonicotinic acid (0.320 g, 1.76 mmol) and N,N-diisopropylethylamine (0.750 mL, 4.30 mmol) were combined in N,N-dimethylformamide (8.0 mL) and stirred for 90 min. The mixture was poured into ethyl acetate (50 mL) and washed with water (2X5 mL). The combined aqueous wash was extracted with ethyl acetate (3X15 mL) which was combined with the first organic extract, washed with brine (30 mL), dried over sodium sulfate, filtered and concentrated in vacuo. The crude 3-cyclopropyl-5-fluoro-N-[imino-(9H-pyrido[2,3-b]indol-4-yl)-methyl]-isonicotinamide was combined with cesium carbonate (0.914 g, 2.81 mmol) in N,N-dimethylformamide (14.0 mL) and was heated at 90 °C under an atmosphere of nitrogen overnight. The mixture was concentrated in vacuo onto silica gel (4.5 g) then purified (silica gel 40 g, 0-10% MeOH:DCM) to afford 5-cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-3H-pyrido[3,4-d]pyrimidin-4-one (0.230 g; Yield = 46.4%). LCMS (ESI): 354 $(M+H)^+$.

1253d) 5-Cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-3H-pyrido[3,4-d]pyrimidin-4-one (18 mg, 0.051 mmol), 2,4,6-triisopropylbenzenesulfonyl chloride (17.5 mg, 0.0578 mmol), 4-dimethylaminopyridine (1.0 mg, 0.0082 mmol) and triethylamine (35.0 µL, 0.251 mmol) in N,N-dimethylformamide (1.00 mL) was stirred under an atmosphere of nitrogen at room temperature for 1h, then a solution of piperazine (74.0 mg, 0.859 mmol) in N,N-dimethylformamide (1.0 mL) was added and stirring was continued for 3 h. The mixture was concentrated in vacuo and purified by preparative HPLC (0-45% acetonitrile:water, 0.1% trifluoracetic acid) to afford 4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole trifluoroacetic acid salt (10.0 mg; Yield = 37%;) as a yellow lyophilate. LCMS (ESI): 422 $(M+H)^+$; ^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.08 (s, 1H), 9.17 (s, 1H), 8.83 (br s, 1H), 8.68 (d, 1H, J = 8.4 Hz), 8.59 (d, 1H, J = 5.1

Hz), 8.26 (s, 1H), 7.89 (d, 1H, J = 5.1 Hz), 7.55 (d, 1H, J = 7.9 Hz), 7.49 (m, 1H), 7.18 (m, 1H), 3.68 (br s, 4H), 3.34 (br s, 4H), 2.77 (m, 1H), 1.30 (m, 2H), 1.14 (m, 2H).

Example 1254. 1-[5-cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol trifluoroacetic acid salt

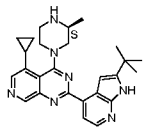
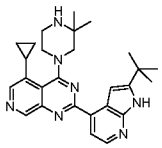
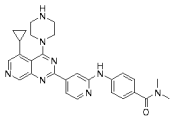
Analogous to Example 1253d, 5-cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-3H-pyrido[3,4-d]pyrimidin-4-one (44.0 mg, 0.124 mmol) was reacted with piperidin-4-ol (34.0 mg, 0.336 mmol) to afford 1-[5-cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol trifluoroacetic acid salt (32 mg; Yield = 47%) as a yellow lyophilate. LCMS (ESI): 437 $(M+H)^+$; ^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.12 (s, 1H), 9.07 (s, 1H), 8.60 (d, 1H, J = 5.0 Hz) 8.54 (d, 1H, J = 8.1 Hz), 8.22 (s, 1H), 7.84 (d, 1H, J = 5.0 Hz), 7.56 (d, 1H, J = 8.0 Hz), 7.49 (m, 1H), 7.17 (m, 1H), 4.11 (m, 3H), 3.58 (br s, 2H), 2.61 (m, 1H), 1.89 (m, 2H), 1.55 (m, 2H), 1.92 (m, 2H), 1.21 (m, 2H).

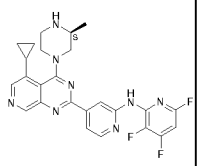
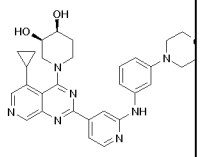
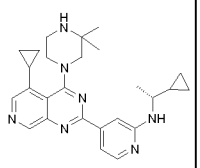
Example 1255. 4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin- 2-yl]-9H-pyrido[2,3-b]indole trifluoroacetic acid salt

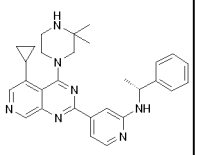
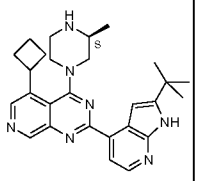
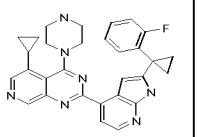
Analogous to Example 1253d, 5-cyclopropyl-2-(9H-pyrido[2,3-b]indol-4-yl)-3H-pyrido[3,4-d]pyrimidin-4-one (52.5 mg, 0.148 mmol) was reacted with 2,2-dimethylpiperazine (31.4 mg, 0.275 mmol) to afford 4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin- 2-yl]-9H-pyrido[2,3-b]indole trifluoroacetic acid salt (17.5 mg; Yield = 21%) as a yellow lyophilate. LCMS (ESI): 450 $(M+H)^+$; ^{1}H-NMR (DMSO-d_6, 400 MHz): δ 12.09 (s, 1H), 9.17 (s, 1H), 9.05 (br s, 2H), 8.67 (d, 1H, J = 8.1 Hz), 8.60 (d, 1H, J = 5.1 Hz), 8.29 (s, 1H), 7.93 (d, 1H, J = 5.1 Hz) 7.55 (d, 1H, J = 7.9 Hz), 7.49 (m, 1H), 7.18 (m, 1H), 3.93 (m, 4H), 3.39 (m, 2H), 2.61 (m, 1H), 1.01-1.48 (m, 10H).

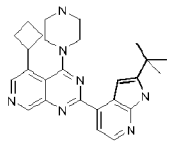
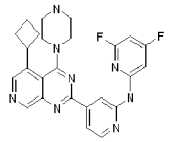
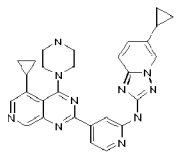
The following compounds were synthesized according to the general syntheses shown in any of the Scheme(s) provided above using analogous procedures, starting materials and intermediates.

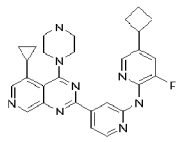
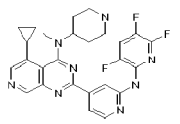
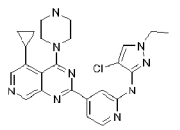
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	

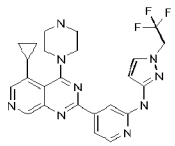
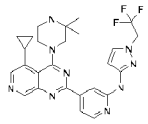
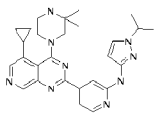
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2001		[D4],[D3]	Method 5: RT: 3.66min, MI: 442 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 ºC) 11.32 (1H, s), 9.03 (1H, s), 8.27 (1H, d, J = 5.1 Hz), 8.11 (1H, s), 8.04 (1H, d, J = 5.1 Hz), 7.21 (1H, d, J = 2.2 Hz), 4.21 - 4.16 (2H, m), 3.23 - 3.16 (1H, m), 3.06 - 3.01 (1H, m), 2.94 - 2.82 (3H, m), 2.74 - 7.66 (1H, m), 1.28 - 1.23 (2H, m), 1.07 (3H, d, J = 6.0 Hz), 1.02 - 0.98 (2H, m).	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
2002		[D4],[D3]	Method 5: RT:3.75 min, MI:456 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 ºC) 11.38 (1H, br s), 9.11 (1H, s), 8.30 (1H, d, J = 5.0 Hz), 8.21 (1H, s), 8.07 (1H, d, J = 5.0 Hz), 7.19 (1H, d, J = 2.3 Hz) 3.97 - 3.94 (2H, m), 3.89 (2H, s), 3.35 - 3.32 (2H, m), 2.67 - 2.60 (1H, m), 1.31 - 1.26 (8 H, m), 1.05 - 1.00 (2H, m).	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
2003		[B4]	Method 5: RT: 3.05min, MI: 495.42 [M+H]	1H NMR (500MHz, DMSO) 9.06 (1H, s), 8.37 (1H, d), 8.17 (1H, s), 7.98 (1H, s), 7.82 (1H, s), 7.80 (1H, s), 7.76 (1H, dd), 7.38 (2H, d), 3.92 (4H, s, br), 3.32 (4H, s, br), 2.97 (6H, s), 2.70-2.66 (1H, m), 1.26-1.24 (2H, m), 1.08-1.07 (2H, m).	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-N,N-dimethyl-benzamide

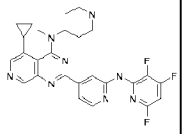
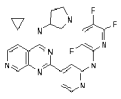
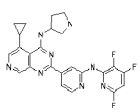
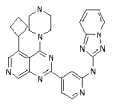
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2004		[B4]	Method 5: RT: 2.74min, MI: 493 [M+H]	1H NMR (DMSO, 500MHz) 10.13 (1H, s), 9.07 (1H, s), 8.93 (2H, s), 8.48 (1H, s), 8.19 (1H, s), 8.02 (1H, s), 7.02 (1H, m), 4.34 (2H, m), 3.72 (1H, m), 3.48 (4H, m), 3.09 (1H, m),1.25 (5H, m), 1.09 (2H, m).	{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine
2005		[B4]	LCMS: Purity: 90%, RT: min, MI: 540.289978	(CDCl3) d: 9.06 (s, 1H), 8.31 (br d, J = 4.4 Hz, 1H), 8.03 (br s, 2H), 7.76 (dd, J = 5.3; 1.3 Hz, 1H), 7.06 (app t, J = 2.0 Hz, 1H), 6.91 (br s, 2H), 6.65 (dd, J = 8.2; 2.0 Hz, 1H), 4.59-3.90 (br m, 4H), 3.89-3.84 (m, 4H), 3.84-3.51 (br s, 2H), 3.22-3.16 (m, 4H), 2.62-2.51 (m, 1H), 1.90-1.50 (br m, 3H), 1.27-1.21 (m, 2H), 0.99-0.95 (m, 2H)	(+/-)-*cis*-1-{5-Cyclopropyl-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-3,4-diol
2006		[B4]	LCMS: Purity: 92%, RT: min, MI: 444.28 (M+H)	(dmso-d6) 9.08 (br s, 2H), 8.83 (br s, 1H), 8.81 (s, 1H), 8.00 (s, 1H), 7.83 (br s, 1H), 7.77 (d, J = 6.7 Hz, 1H), 7.47 (dd, J = 6.7; 1.5 Hz, 1H), 5.98 (br s, exch. H's), 3.69 (br s, 4H), 3.26 (br s, 1H), 3.09 (br s, 2H), 2.25-2.17 (m, 1H), 1.12 (br s, 2H), 1.05 (d, J = 6.4 Hz, 3H), 1.05-0.95 (m, 4H), 0.94-0.70 (m, 5H), 0.40-0.35 (m, 3H), 0.05-(-0.03) (m, 1H)	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-((R)-1-cyclopropyl-ethyl)-amine

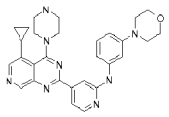
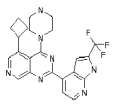
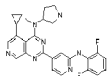
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2007		[B4]	LCMS: Purity: 94%, RT: min, MI: 480.28 (M+H)	(dmso-d6) 9.39 (br s, 3H), 9.09 (s, 1H), 8.28 (s, 1H), 8.13 (d, J = 6.5 Hz, 1H), 8.10 (br s, 1H), 7.79 (d, J = 6.5 Hz, 1H), 7.51 (d, J = 7.4 Hz, 2H), 7.44 (app t, J = 7.4 Hz, 2H), 7.33 (app t, J = 7.4 Hz, 1H), 5.17 (br s, 1H), 4.20-3.80 (m, 4H), 3.38 (br s, 2H), 2.52-2.47 (m, 1H), 1.63 (d, J = 6.7 Hz, 3H), 1.60-1.00 (m, 10H)	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-((R)-1-phenyl-ethyl)-amine
2008		[D4],[D3]	Method 5: RT: 3.98min, MI: 456.43 [M+H]	1H NMR (d6-DMSO, 400MHz, 90°C) 11.34 (1H, s), 9.11 (1H, s), 8.67 (1H, s), 8.28 (1H, d), 8.05 (1H, d), 7.20 (1H, s), 4.36 (1H, m), 3.98 (2H, m), 3.10 (1H, m), 3.02 (2H, m), 2.96 (2H, m), 2.54 (2H, s), 2.22 (2H, m), 2.17(1H, m), 1.97 (1H, m), 1.47 (9H, s), 1.07 (3H, d).	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
2009		[D4],[D3]	Method 5: RT: 3.99min, MI: 506 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 11.18 (1H, br s), 8.90 (1H, s), 8.25 (1H, d, J = 5.1 Hz), 8.08 (1H, s), 8.04 (1H, d, J = 5.1 Hz), 7.61 (1H, dt, J = 7.7, 1.8 Hz), 7.43 - 7.38 (1H, m), 7.25 (1H, dt, J = 7.5, 1.2 Hz), 7.21 - 7.16 (1H, m), 6.88 (1H, s), 3.60 - 3.57 (4H, m), 2.89 - 2.86 (4H, m), 2.68 - 2.64 (1H, m), 1.69 - 1.66 (2H, m), 1.40 - 1.37 (2H, m), 1.26 - 1.21 (2H, m), 0.98 - 0.95 (2H, m).	5-Cyclopropyl-2-{2-[1-(2-fluoro-phenyl)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridin-4-yl}-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

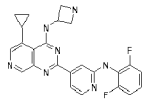
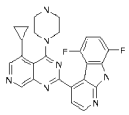
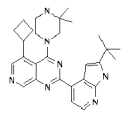
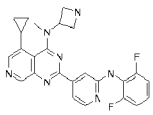
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2010		[D4],[D3]	Method 5: RT: 3.90min, MI: 442.48 [M+H]	1H NMR (d6-DMSO, 500MHz) 11.71 (1H, s), 9.07 (1H, s), 8.65 (1H, s), 8.26 (1H, d), 8.04 (1H, d), 7.17 (1H, s), 4.24 (1H, m), 3.84 (1H, m), 3.56 (1H, m), 3.38 (1H, m), 3.36 (1H, m), 2.94 (2H, s), 2.41 (2H, m), 2.15 (2H, m), 2.12 (1H, m), 2.04 (1H, m), 1.41 (9H, s), 1.10 (3H, s), 0.75 (3H, s).	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2011		[B4]	LCMS: Purity: 97%, RT: min, MI: 475.19 (MH)+,	(400 MHz, d6-DMSO,δ): 10.45 (s, 1H), 9.15 (s, 1H), 8.90-8.75 (m, 3H), 8.62 (s, 1H), 8.47 (d, J=5.3 Hz, 1H), 7.92 (dd, J=5.2, 1.3 Hz, 1H), 7.80 (dd, J=11.2, 1.6 Hz, 1H), 6.69 (dt, J=8.5, 1.6 Hz, 1H), 4.25 (pent, J=8.8 Hz, 1H), 3.89-3.84 (m, 4H), 3.40-3.17 (m, 4H), 2.52-2.42 (m, 2H), 2.28-2.03 (m, 3H), 1.97-1.87 (m, 1H).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-2-yl)-amine
2012		[B4]	LCMS: Purity: 96%, RT: min, MI: 505.25 (MH)+	(400 MHz, d6-DMSO,δ): 10.63 (br s, 1H), 9.15 (s, 1H), 9.12 (s, 1H), 8.89 (br s, 2H), 8.68 (s, 1H), 8.45 (d, J=5.8 Hz, 1H), 8.21 (s, 1H), 7.94 (dd, J=5.4, 1.3 Hz, 1H), 7.60 (d, J=9.0 Hz, 1H), 7.42 (dd, J=9.2, 1.7 Hz, 1H), 3.96 (br s, 4H), 3.36 (br s, 4H), 2.76-2.68 (m, 1H), 2.12-2.05 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H), 1.04-0.98 (m, 2H), 0.85-0.80 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine

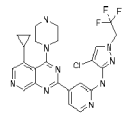
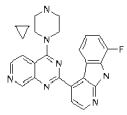
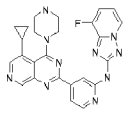
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2013		[B4]	LCMS : Purity: 97%, RT: min, MI: 497.24 (MH)+	(400 MHz, d6-DMSO,δ): 10.26 (br s, 1H), 9.10 (s, 1H), 8.90 (br s, 2H), 8.83 (s, 1H), 8.44 (d, J=5.7 Hz, 1H), 8.22 (s, 1H), 8.07 (d, J=1.5 Hz, 1H), 8.01 (d, J=5.6 Hz, 1H), 7.83 (d, J=11.2 Hz, 1H), 3.94 (br s, 4H), 3.61 (pent, J=8.7 Hz, 1H), 3.34 (br s, 4H), 2.72-2.65 (m, 1H), 2.37-2.28 (m, 2H), 2.22-2.11 (m, 2H), 2.08-1.95 (m, 1H), 1.91-1.82 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	(5-Cyclobutyl-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2014		[B4]	LCMS : Purity: >95%, RT: min, MI: 507 (M+H)	1H-NMR DMSO 9.69 (br s, 1H), 8.93 (s, 1H), 8.60 (s, 1H), 8.40 (m, 1H), 8.27 (m, 1H), 8.12 (s, 1H), 7.91 (m, 1H), 4.62 (br m, 1H), 3.13 (s, 3H), 3.08 (m, 2H), 2.66 (m, 2H), 2.43 (m, 1H), 1.79 (br m, 4H), 1.22 (m, 3H), 0.96 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2015		[B4]	LCMS : Purity: 95%, RT: min, MI: 476.21 (M+H)	(dmso-d6) 9.91 (br s, 1H), 9.13 (br s, 1H), 9.10 (s, 2H), 8.38-8.32 (m, 2H), 8.24 (s, 1H), 8.15 (s, 1H), 7.90 (dd, J = 5.8; 1.1 Hz, 1H), 5.25 (br s, exch. H's), 4.19 (q, J = 7.2 Hz, 2H), 3.96 (br s, 4H), 3.67 (br s, 4H), 2.90-2.60 (m, 1H), 1.47 (t, J = 7.2 Hz, 3H), 1.34-1.25 (m, 2H), 1.41-1.08 (m, 2H)	(4-Chloro-1-ethyl-1H-pyrazol-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

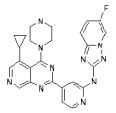
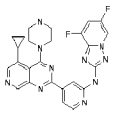
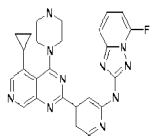
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2016		[B4]	LCMS: Purity: 96%, RT: min, MI: 496.20 (M+H)	(dmso-d6) 10.68 (br s, 1H), 9.09 (br s, 3H), 8.44 (s, 1H), 8.38 (d, J = 5.8 Hz, 1H), 8.22 (s, 1H), 7.87 (d, J = 5.5 Hz, 2H), 6.50 (d, J = 2.4 Hz, 1H), 5.86 (br s, exch. H's), 5.12 (q, J (CH2-CF3) = 9.0 Hz, 2H), 3.96 (br s, 4H), 3.35 (br s, 4H), 2.73-2.65 (m, 1H), 1.32-1.23 (m, 2H), 1.14-1.06 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-amine
2017		[B4]	LCMS: Purity: 95%, RT: min, MI: 524.24 (M+H)	(dmso-d6) 10.79 (br s, 1H), 9.32 (br s, 2H), 9.10 (s, 1H), 8.42-8.36 (m, 2H), 8.26 (s, 1H), 7.93-7.87 (m, 2H), 6.58 (d, J = 2.3 Hz, 1H), 5.56 (br s, exch. H's), 5.14 (q, J(CH2CF3) = 9.0 Hz, 2H), 3.99 (br s, 4H), 3.38 (br s, 2H), 2.58-2.50 (m overlapping solvent signal, 1H), 1.70-1.00 (m, 10H)	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-amine
2018		[B4]	LCMS: Purity: 97%, RT: min, MI: 484.28 (M+H)	(dmso-d6) 11.37 (br s, 1H), 9.34 (br s, 2H), 9.10 (s, 1H), 8.44 (d, J = 6.3 Hz, 1H), 8.42 (s, 1H), 8.28 (s, 1H), 7.97 (d, J = 6.3 Hz, 1H), 7.88 (d, J = 2.2 Hz, 1H), 6.32 (d, J = 2.3 Hz, 1H), 4.94 (br s, exch. H's), 4.59 (hept, J = 6.6 Hz, 1H), 3.99 (br s, 4H), 3.38 (br s, 2H), 2.55-2.48 (m, partially overlaped by solvent peak, 1H), 1.53 (d, J = 6.6 Hz, 6H), 1.52-1.00 (m, 10H)	{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-isopropyl-1H-pyrazol-3-yl)-amine

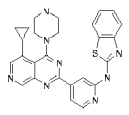
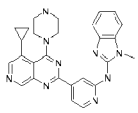
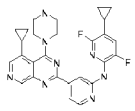
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2019		[B4]	LCMS: Purity: 92%, RT: min, MI: 507 (M+H)	1H-NMR: DMSO 10.03 (br s, 1H), 8.93 (s, 1H), 8.73 (s, 1H), 8.45 (m, 1H), 8.12 (s, 1H), 7.97 (m, 1H), 7.01 (m, 1H), 4.59 (br m, 1H), 3.12 (s, 3H), 3.00 (m, 2H), 2.67 (m, 2H), 2.42 (m, 1H), 1.72 (br m, 4H), 1.23 (m, 3H), 0.96 (m, 2H)	{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2020		[B4]	LCMS: Purity: 95%, RT: min, MI: 479 (M+H):	1H-NMR: DMSO 9.66 (br s, 1H), 9.02 (s, 1H), 8.75 (s, 1H), 8.45 (s, 1H), 8.39 (m, 1H), 8.26 (m, 1H), 7.95 (m, 2H), 4.85 (m, 1H), 3.20 (m, 1H), 3.04 (m, 1H), 2.95 (m, 1H), 2.87 (m, 1H), 2.56 (m, 1H), 2.26 (m, 1H), 1.85 (m, 1H), 1.19 (m, 3H), 1.08 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine
2021		[B4]	LCMS: Purity: >95%, RT: min, MI: 479 (M+H)	1H-NMR: DMSO 10.07 (s, 1H), 9.08 (s, 1H), 9.03 (br s, 1H), 8.95 (br s, 1H), 8.82 (s, 1H), 8.48 (m, 2H), 8.03 (m, 1H), 7.89 (m, 1H), 7.00 (m, 1H), 5.03 (m, 1H), 3.69 (m, 1H), 3.48 (m, 2H), 3.34 (m, 1H), 2.62 (m, 1H), 2.52 (m, 2H), 2.26 (m, 1H), 1.22 (m, 2H), 1.07 (m, 2H)	{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine
2022		[B4]	LCMS: Purity: 95%, RT: min, MI: 479.25 (MH)+	(400 MHz, d6-DMSO,δ): 10.50 (br s, 1H), 9.22 (s, 1H), 9.18 (s, 1H), 8.95-8.75 (m, 4H), 8.44 (d, J=5.3 Hz, 1H), 7.91 (dd, J=5.4, 1.4 Hz, 1H), 7.71-7.63 (m, 2H), 7.14 (dt, J=6.5, 2.0 Hz, 1H), 4.32-4.23 (m, 1H), 3.87 (br s, 4H), 3.41-3.23 (m, 4H), 2.51-2.43 (m, 2H), 2.29-2.05 (m, 3H), 1.98-1.88 (m, 1H).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl-amine

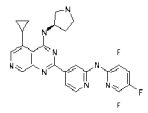
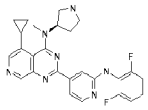
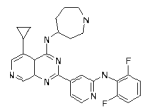
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2023		[B4]	LCMS: Purity: 93%, RT: min, MI: 509.3 (M+H)	(dmso-d6) 9.93 (br s, 1H), 9.50-8.5 (broad signal -in the noise), 9.12 (br s, 1H), 9.11 (s, 1H), 8.29 (d, J = 5.8 Hz, 1H), 8.24 (s, 1H), 8.09 (s, 1H), 7.80 (dd, J = 5.8; 1.3 Hz, 1H), 7.33 (br s, 1H), 7.28 (app t, J = 8.1 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 6.75 (d, J = 8.1 Hz, 1H), 3.97 (br s, 4H), 3.82-3.78 (m, 4H), 3.37 (br s, 4H), 3.21-3.16 (m, 4H), 2.75-2.68 (m, 1H), 1.33-1.26 (m, 2H), 1.16-1.10 (m, 2H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-morpholin-4-yl-phenyl)-amine
2024		[D4],[D3]	Method 5: RT: 3.93 min, MI: 455.38 [M+H]	1H NMR (500MHz, DMSO) 13.20 (1H, s), 8.99 (1H, s, br), 8.88 (1H, s, br), 8.81 (1H, s), 8.69 (1H, d), 8.25 (1H, d), 7.95 (1H, s), 4.30-4.24 (1H, 3.86-3.81 (4H, m), 3.35-3.29 (4H, m), 2.50.2.45 (2H, m), 2.26-2.08 (3H, m), 1.96-1.90 (1H, m).	5-Cyclobutyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
2025		[B4]	LCMS: Purity: >95%, RT: min, MI: 474 (M+H)	1H-NMR: DMSO 9.02 (s, 1H), 8.93 (br m, 2H), 8.89 (s, 1H), 8.21 (m, 2H), 7.84 (s, 1H), 7.71 (m, 1H), 7.29 (m, 1H), 7.16 (m, 2H), 5.13 (br m, 1H),3.79 (m, 1H), 3.45 (m, 1H), 3.29 (br m, 2H), 3.12 (s, 3H), 2.54 (m, 1H), 2.40 (m, 1H), 2.25 (br m, 1H), 1.26 (br m, 2H), 1.01 (m, 2H)	{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-pyrrolidin-3-yl-amine

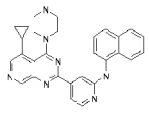
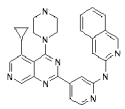
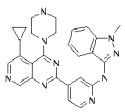
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2026		[B4]	LCMS: Purity: >95%, RT: min, MI: 446 (M+H)	1H-NMR: DMSO 9.07 (s, 1H), 8.90 (br s, 3H), 8.51 (s, 1H), 8.25 (d, 1H, J = 4.6 Hz), 8.17 (d, 1H, J = 5.6 Hz), 7.78 (s, 1H), 7.66 (m, 1H), 7.30 (m, 1H), 7.18 (m, 2H), 5.11 (m, 1H), 4.44 (m, 2H), 4.25 (m, 2H), 2.64 (m, 1H), 2.54 (m, 1H), 1.27 (m, 2H), 1.05 (m, 2H)	Azetidin-3-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine
2027		[D3]	LCMS: Purity: 95%, RT: min, MI: 458 (M+H)+	1H-NMR (DMSO-d6, 400 MHz): 9.05 (s, 1H), 8.85 (br s, 2H), 8.69 (d, 1H, J = 4.1 Hz), 8.24 (s, 1H), 7.53 (d, 1H, J = 4.9 Hz), 7.34 (m, 1H), 6.78 (m, 1H), 3.73 (m, 4H), 3.25 (m, 4H), 2.77 (m, 1H), 1.29 (m, 2H), 1.14 (m, 2H)	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5,8-difluoro-9H-pyrido[2,3-b]indole
2028		[D4],[D3]	Method 5: RT: 4.03 min, MI: 470.45 [M+H]	1H NMR (d6-DMSO, 500MHz) 11.71 (1H, s), 9.07 (1H, s), 8.65 (1H, s), 8.26 (1H, d), 8.04 (1H, d), 7.17 (1H, s), 4.24 (1H, m), 3.84 (1H, m), 3.56 (1H, m), 3.38 (1H, m), 3.36 (1H, m), 2.94 (2H, s), 2.41 (2H, m), 2.15 (2H, m), 2.12 (1H, m), 2.04 (1H, m), 1.41 (9H, s), 1.10 (3H, s), 0.75 (3H, s).	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine
2029		[B4]	LCMS: Purity: >90%, RT: min, MI: 460 (M+H)	1H-NMR: DMSO 9.04 (s, 1H), 8.88 (s, 1H), 8.85 (br s, 2H), 8.24 (s, 1H), 8.19 (d, 1H, J = 5.3 Hz), 7.73 (s, 1H), 7.61 (m, 1H), 7.29 (m, 1H), 7.18 (m, 2H), 4.74 (m, 1H), 4.24-4.35 (br m, 4H), 3.11 (s, 3H), 2.70 (m, 1H), 1.30 (br m, 2H), 1.07 (m, 2H)	Azetidin-3-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine

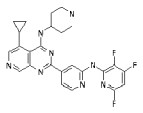
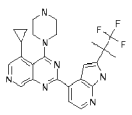
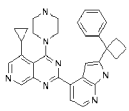
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2030		[B4]	LCMS: Purity: 96%, RT: min, MI: 530.15 (M+H)	(dmso-d6) 9.36 (br s, 1H), 9.09 (s, 1H), 9.02 (br s, 2H), 8.35 (d, J = 5.4 Hz, 1H), 8.27 (s, 1H), 8.22 (s, 1H), 8.20 (s, 1H), 7.85 (d, J = 5.4 Hz, 1H), 5.16 (q, J(H,F) = 9.0 Hz, 2H), 3.94 (br s, 4H), 3.36 (br s, 4H), 2.77-2.66 (m, 1H), 1.33-1.25 (m, 2H), 1.15-1.07 (m, 2H)	[4-Chloro-1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2031		[D3]	LCMS: Purity: 95%, RT: min, MI: 440 (M+H)+	1H-NMR (DMSO-d6, 400 MHz): 12.60 (s, 1H), 9.18 (s, 1H), 8.88 (br s, 2H), 8.66 (d, 1H, J = 5.1 Hz), 8.53 (d, 1H, J = 8.1 Hz), 8.27 (s, 1H), 7.95 (d, 1H, J = 5.1 Hz), 7.38 (m, 1H), 7.16 (ddd, 1H, J = 5.1, 8.1, 8.1 Hz), 3.92 (br s, 4H), 3.34 (br s, 4H), 2.76 (m, 1H), 1.30 (m, 2H), 1.14 (m, 2H)	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-8-fluoro-9H-pyrido[2,3-b]indole
2032		[B4]	LCMS: Purity: 99%, RT: min, MI: 483.21 (MH)+	(400 MHz, d6-DMSO,δ): 10.62 (s, 1H), 9.27 (s, 1H), 9.13 (s, 1H), 8.90 (br s, 2H), 8.76 (dd, J=6.7, 0.7 Hz, 1H), 8.46 (dd, J=5.2, 0.4 Hz, 1H), 8.20 (s, 1H), 7.94 (dd, J=5.2, 1.4 Hz, 1H), 7.65-7.59 (m, 1H), 7.14-7.08 (m, 1H), 3.97 (br s, 4H), 3.36 (br s, 4H), 2.75-2.68 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine

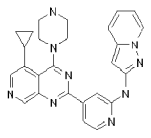
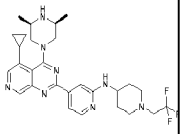
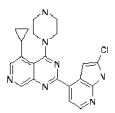
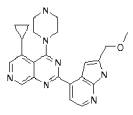
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2039		[B4]	LCMS : Purity: 97%, RT:2.76 min, MI: 507 (MH)+	(400 MHz, d6-DMSO,δ): 10.51 (br s, 1H), 9.23-9.20 (m, 1H), 9.18 (s, 1H), 9.16 (s, 1H), 8.86 (br s, 2H), 8.45 (d, J=5.2 Hz, 1H), 8.21 (s, 1H), 7.92 (d, J=5.2 Hz, 1H), 7.80-7.70 (m, 2H), 3.96 (br s, 4H), 3.36 (br s, 4H), 2.76-2.67 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine
2040		[B4]	LCMS : Purity: 97%, RT:2.76 min, MI: 507 (MH)+	(400 MHz, d6-DMSO,δ): 10.61 (s, 1H), 9.24 (s, 1H), 9.20-9.17 (m, 1H), 9.14 (s, 1H), 8.87 (br s, 2H), 8.46 (dd, J=5.1, 0.6 Hz, 1H), 8.20 (s, 1H), 8.04-7.97 (m, 1H), 7.93 (dd, J=5.2, 1.4 Hz, 1H), 3.96 (br s, 4H), 3.35 (br s, 4H), 2.75-2.67 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6,8-difluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine
2041		[B4]	LCMS : Purity: 97%, RT:2.76 min, MI: 507 (MH)+	(400 MHz, d6-DMSO,δ): 10.61 (s, 1H), 9.31 (s, 1H), 9.10 (s, 1H), 8.90 (br s, 2H), 8.46 (d, J=5.3 Hz, 1H), 8.20 (s, 1H), 7.95 (dd, J=5.2, 1.3 Hz, 1H), 7.77-7.70 (m, 1H), 7.56 (dd, J=8.8, 06 Hz, 1H), 7.10-7.05 (m, 1H), 3.97 (br s, 4H), 3.36 (br s, 4H), 2.76-2.67 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine

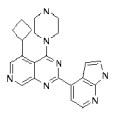
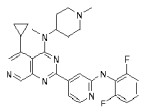
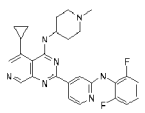
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2045		[B4]	LCMS: Purity: 97%, RT:2.76 min, MI: 507 (MH)+	(400 MHz, d6-DMSO,δ): 11.75 (br s, 1H), 9.10 (s, 1H), 8.86 (br s, 2H), 8.55 (d, J=5.8 Hz, 1H), 8.31 (s, 1H), 8.20 (s, 1H), 7.97 (dd, J=5.3, 1.4 Hz, 1H), 7.92 (d, J=7.5 Hz, 1H), 7.66 (d, J=8.1 Hz, 1H), 7.42-7.37 (m, 1H), 7.25-7.20 (m, 1H), 3.95 (br s, 4H), 3.34 (br s, 4H), 2.73-2.65 (m, 1H), 1.29-1.24 (m, 2H), 1.12-1.06 (m, 2H).	Benzothiazol-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2046		[B4]	LCMS: Purity: 97%, RT:2.76 min, MI: 507 (MH)+	(400 MHz, d6-DMSO,δ): 13.68 (br s, 1H), 11.71 (br s, 1H), 9.10 (s, 1H), 8.93 (br s, 2H), 8.75-8.62 (m, 1H), 8.60-8.45 (m, 1H), 8.27-8.20 (m, 2H), 7.85-7.65 (m, 2H), 4.15-3.80 (m, 7H), 3.35 (m, 4H), 2.73-2.65 (m, 1H), 1.30-1.24 (m, 2H), 1.13-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-benzoimidazol-2-yl)-amine
2047		[B4]	Method 5: RT: 2.77 min, MI: 501 [M+H]	1H NMR (DMSO, 400MHz, 90°C, 1IGO667) 8.98 (1H, s), 8.85 (1H, s), 8.38(1H, d), 8.13(1H, s), 7.91(1H, dd), 7.46 (1H, m), 3.77 (4H, t), 2.91 (4H, t), 2.66 (1H, m), 1.96 (1h, m), 1.27 (2H, m), 0.98 (4H, m), 0.79 (2H, m).	(5-Cyclopropyl-3,6-difluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

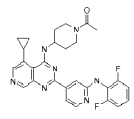
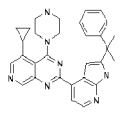
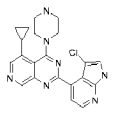
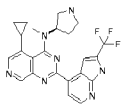
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2056		[B4]	LCMS : Purity: 98%, RT: min, MI: 465.19 (MH)+	1H-NMR: DMSO 9.78 (s, 1H), 9.08 (br s, 2H), 8.97 (br s, 1H), 8.73 (s, 1H), 8.51 (s, 1H), 8.43 (d, 1H, J = 5.2 Hz), 8.29 (m, 1H), 7.98 (m, 1H), 7.90 (m, 1H), 5.04 (m, 1H), 3.72 (m, 1H), 3.48 (m, 2H), 3.37 (m, 1H), 2.62 (m, 1H), 2.52 (m, 1H), 2.26 (m, 1H), 1.24 (m, 2H), 1.06 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine
2057		[B4]	LCMS : Purity: 95%, RT: min, MI: 474 (MH)+	1H-NMR: DMSO 9.02 (s, 1H), 8.88 (br s, 2H), 8.84 (s, 1H), 8.20 (m, 2H), 7.83 (s, 1H), 7.70 (d, 1H, J = 5.2 Hz), 7.29 (m, 1H), 7.17 (m, 2H), 5.12 (br m, 1H), 3.78 (m, 1H), 3.45 (m, 1H), 3.29 (m, 2H), 3.11 (s, 3H), 2.54 (m, 1H), 2.40 (m, 1H), 2.25 (m, 1H), 1.26 (m, 2H), 1.01 (m, 2H)	{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(R)-pyrrolidin-3-yl-amine
2058		[B4]	LCMS : Purity: 100%, RT: min, MI: 465.19 (MH)+	1H-NMR: DMSO 9.03 (s, 1H), 8.90 (s, 1H), 8.69 (br s, 2H), 8.48 (s, 1H), 8.19 (d, 1H, J = 5.2 Hz), 7.86 (m, 1H), 7.80 (s, 1H), 7.72 (m, 1H), 7.33 (m, 1H), 7.19 (m, 2H), 4.58 (m, 1H), 3.35 (m, 4H), 2.60 (m, 1H), 2.32 (m, 2H), 2.14 (m, 1H), 1.94 (m, 3H), 1.22 (m, 2H), 1.11 (m, 1H), 1.05 (m, 1H)	Azepan-4-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine

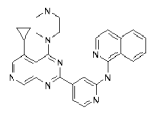
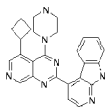
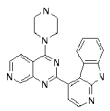
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2059		[B4]	LCMS: Purity: 101%, RT: min, MI: 465.19 (MH)+	(400 MHz, d6-DMSO,δ): 9.72 (br s, 1H), 9.06 (s, 1H), 8.89 (br s, 2H), 8.23-8.16 (m, 3H), 8.08 (s, 1H), 8.02-7.98 (m, 1H), 7.90 (d, J=7.3 Hz, 1H), 7.80 (d, J=7.5 Hz, 1H), 7.76 (d, J=5.5 Hz, 1H), 7.61-7.53 (m, 3H), 3.88 (br s, 4H), 3.30 (br s, 4H), 2.71-2.63 (m, 1H), 1.28-1.23 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-naphthalen-1-yl-amine
2060		[B4]	LCMS: Purity: 102%, RT: min, MI: 465.19 (MH)+	(400 MHz, d6-DMSO,δ): 10.69 (br s, 1H), 9.19 (s, 1H), 9.10 (s, 1H), 8.89 (br s, 2H), 8.49 (d, J=5.6 Hz, 1H), 8.46 (s, 1H), 8.32 (br s, 1H), 8.21 (s, 1H), 8.09 (d, J=8.1 Hz, 1H), 7.94-7.87 (m, 2H), 7.71 (t, J=7.5 Hz, 1H), 7.49 (t, J=7.4 Hz, 1H), 3.97 (br s, 4H), 3.34 (br s, 4H), 2.73-2.65 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-iso[D4],[D3]uinolin-3-yl-amine
2061		[B4]	LCMS: Purity: 103%, RT: min, MI: 465.19 (MH)+	(400 MHz, d6-DMSO,δ): 10.60 (br s, 1H), 9.11 (s, 1H), 9.05-8.80 (m, 3H), 8.41 (d, J=5.5 Hz, 1H), 8.21 (s, 1H), 8.07 (d, J=8.1 Hz, 1H), 7.91 (d, J=5.4 Hz, 1H), 7.61 (d, J=8.6 Hz, 1H), 7.49-7.44 (m, 1H), 7.13 (t, J=7.5 Hz, 1H), 4.05 (s, 3H), 3.95 (br s, 4H), 3.36 (br s, 4H), 2.75-2.67 (m, 1H), 1.30-1.24 (m, 2H), 1.12-1.07 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-indazol-3-yl)-amine

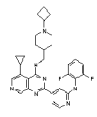
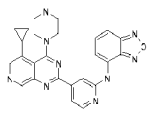
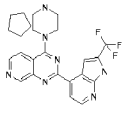
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2062		[B4]	LCMS : Purity: 104%, RT: min, MI: 465.19 (MH)+	1H-NMR: DMSO 10.06 (s, 1H), 9.06 (s, 1H), 8.73 (s, 1H), 8.70 (br s, 1H), 8.50 (s, 1H), 8.45 (m, 1H), 8.37 (br m, 1H), 8.02 (m, 1H), 7.82 (m, 1H), 6.99 (m, 1H), 4.59 (m, 1H), 3.40 (m, 2H), 3.13 (m, 2H), 2.66 (m, 1H), 2.34 (m, 2H), 1.90 (m, 2H), 1.19 (m, 2H), 1.07 (m, 2H)	{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine
2063		[D4],[D3]	Method 5: RT: 2.75 min, MI:482 [M+H]	1H NMR (500 MHz, d6-DMSO) 12.09 (brs, 1H), 9.15 (s, 1H), 8.42 (d, 1H), 8.17 (s, 1H), 8.13 (d, 1H), 7.48 (d, 1H), 4.10-3.71 (m, 4H), 3.41-3.31 (m, 4H), 2.77-2.71 (m, 1H), 1.69 (s, 6H), 1.28-1.21 (m, 2H), 1.10-1.05 (m, 2H).	5-Cyclopropyl-4-piperazin-1-yl-2-[2-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine
2064		[D4],[D3]	Method 5: RT: 3.05 min, MI:502 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.88 (brs, 1H), 9.12 (s, 1H), 8.29 (d, 1H), 8.16 (s, 1H), 8.07 (d, 1H), 7.44 (dd, 2H), 7.33 (t, 2H), 7.23 (d, 1H), 7.19 (t, 1H), 4.08-3.66 (m, 4H), 3.36-3.27 (m, 4H), 2.94-2.86 (m, 2H), 2.75-2.68 (m, 3H), 2.10-2.00 (m, 1H), 1.96-1.86 (m, 1H), 1.28-1.21 (m, 2H), 1.11-1.03 (m, 2H).	5-Cyclopropyl-2-[2-(1-phenyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

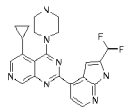
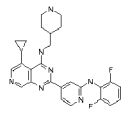
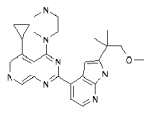
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2072		[B4]	LCMS: Purity: >90%, RT: min, MI: 464 (M+H)+	1H NMR (400 MHz, DMSO-d6) δ ppm 10.48 (br. s, 1 H) 9.11 (s, 1 H) 8.94 (br. s, 2 H) 8.54 (dd, J=6.8, 0.8 Hz, 1 H) 8.46 (s, 1 H) 8.41 (d, J=5.5 Hz, 1 H) 8.20 (s, 1 H) 7.84 (d, J=5.5 Hz, 1 H) 7.58 (d, J=8.8 Hz, 1 H) 7.12 - 7.30 (m, 1 H) 6.68 - 6.85 (m, 2 H) 3.95 (br. s., 4 H) 3.35 (br. s., 4 H) 2.60 - 2.79 (m, 1 H) 1.21 - 1.32 (m, 2 H) 0.98 - 1.16 (m, 2 H)	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-2-yl-amine
2073		[B4]	Method 5: RT: 1.7 min, MI: 541 [M+H]	1H NMR (DMSO, 400MHz, 90°C) 8.96 (1H, s), 8.12 (2H, m), 7.51(1H, s), 7.43 (1H, dd), 4.26 (2H, m), 3.76 (1H, m), 3.16 (3H, m), 2.92 (2H, m), 2.71 (1H, m), 2.46 (1H, m), 1.90 (2H, m), 1.49 (3H, m), 1.08 (9H, m).	{4-[5-Cyclopropyl-4-((cis)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine
2074		[D4],[D3], [D5]	Method 5: RT: 3.29 min, MI: 406 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 9.06 (1H, s), 8.37 (1H, d, J = 4.9 Hz), 8.13 - 8.11 (2H, m), 7.42 (1H, s), 3.74 - 3.71 (4H, m), 2.94 - 2.91 (4H, m), 2.72 - 2.66 (1H, m), 1.28 - 1.24 (2H, m), 1.01 - 0.97 (2H, m).	2-(2-Chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2075		[D4],[D3]	LCMS: Purity: 93%, RT: min, MI: 416.22 (M+H)	(dmso-d6) 12.00 (br s, 1H), 9.17 (s, 1H), 8.92 (br s, 2H), 8.40 (d, J = 5.1 Hz, 1H), 8.20 (s, 1H), 8.15 (d, J = 5.1 Hz, 1H), 7.44 (br s, 1H), 4.66 (s, 2H), 3.92 (br s, 4H), 3.39 (br s, 7H), 2.80-2.70 (m, 1H), 1.30-1.25 (m, 2H), 1.12-1.10 (m, 2H)	5-Cyclopropyl-2-(2-methoxymethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

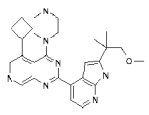
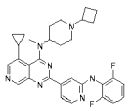
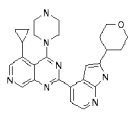
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2082		[D4],[D3]	Method 5: RT: 3.10 min, MI: 386 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.88 (brs, 1H), 9.22 (s, 1H), 8.99 (brs, 1H), 8.86 (brs, 1H), 8.78 (s, 1H), 8.38 (s, 1H), 8.12 (s, 1H), 7.65 (d, 1H), 7.46 (d, 1H), 4.32-4.24 (m, 1H), 3.93-3.84 (m, 2H), 3.78-3.69 (m, 2H), 3.41-3.34 (m, 2H), 3.32-3.24 (m, 2H), 2.27-2.18 (m, 2H), 2.15-2.06 (m, 1H), 1.96-1.87 (m, 1H).	5-Cyclobutyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
2083		[B4]	LCMS: Purity: >95%, RT: min, MI: 454 (M+H)	1H-NMR: DMSO 9.47 (br m, 1H), 8.98 (s, 1H), 8.87 (s, 1H), 8.18 (d, 2H, J = 4.8 Hz), 7.81 (s, 1H), 7.69 (m, 1H), 7.30 (m, 1H), 7.18 (m, 2H), 4.79 (m, 1H), 3.56 (m, 2H), 3.24 (m, 2H), 3.09 (s, 3H), 2.84 (d, 3H, J = 4.4 Hz), 2.44 (m, 1H), 2.10 (br m, 4H), 1.23 (m, 2H), 0.98 (m, 2H)	{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(1-methyl-piperidin-4-yl)-amine
2084		[B4]	LCMS: Purity: >95%, RT: min, MI: 488 (M+H)	1H-NMR: DMSO 9.45 (br m, 1H), 9.04 (s, 1H), 8.81 (s, 1H), 8.48 (s, 1H), 8.18 (d, 1H, J = 5.3 Hz), 7.78 (m, 2H), 7.71 (m, 1H), 7.30 (m, 1H), 7.18 (m, 2H), 4.49 (m, 1H), 3.59 (m, 2H), 3.21 (m, 2H), 2.85 (s, 3H), 2.32 (br m, 3H), 1.90 (m, 2H), 1.17 (m, 2H), 1.04 (m, 2H)	{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(1-methyl-piperidin-4-yl)-amine

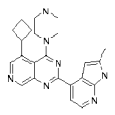
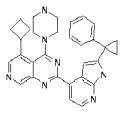
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2085		[B4]	LCMS: Purity: >95%, RT: min, MI: 516 (M+H)	1H-NMR: DMSO 9.03 (br s, 2H), 8.46 (s, 1H), 8.19 (d, 1H, J = 5.4 Hz), 7.85 (m, 1H), 7.80 (s, 1H), 7.73 (m, 1H), 7.32 (m, 1H), 7.21 (m, 2H), 4.52 (m, 1H), 4.35 (m, 1H), 3.87 (m, 1H), 3.26 (m, 1H), 2.84 (m, 1H), 2.58 (m, 1H), 2.13 (m, 2H), 2.05 (s, 3H), 1.78 (br m, 2H), 1.18 (br m, 2H), 1.04 (m, 2H)	1-(4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ylamino}-piperidin-1-yl)-ethanone
2086		[D4],[D3]	Method 5: RT: 4.06 min, MI: 490 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.72 (s, 1H), 9.10 (s, 1H), 8.30 (d, 1H), 8.16 (s, 1H), 8.09 (d, 1H), 7.34-7.28 (m, 4H), 7.25-7.19 (m, 2H), 4.12-3.67 (m, 4H), 3.38-3.28 (m, 4H), 2.78-2.70 (m, 1H), 1.81 (s, 6H), 1.28-1.20 (m, 2H), 1.10-1.05 (m, 2H).	5-Cyclopropyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2087		[D3], [D7]			2-(3-Chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2088		[D4],[D3]	LCMS: Purity: >95%, RT: min, MI: 454 (M+H)	1H-NMR: DMSO 13.17 (s, 1H), 9.18 (s, 1H), 8.92 (br m, 2H), 8.64 (d, 1H, J = 4.9 Hz), 8.23 (m, 2H), 8.00 (s, 1H), 5.20 (m, 1H), 3.78 (m, 1H), 3.27-3.45 (br m, 3H), 3.14 (s, 3H), 2.42 (m, 1H), 2.26 (br m, 2H), 1.26 (m, 2H), 1.02 (m, 2H)	[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-(R)-pyrrolidin-3-yl-amine

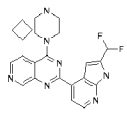
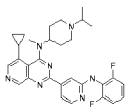
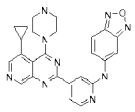
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2089		[B4]	LCMS: Purity: 96%, RT: min, MI: 475.21 (MH)+	(400 MHz, d6-DMSO,δ): 9.13 (s, 1H), 9.05-8.85 (m, 4H), 8.71 (d, J=4.9 Hz, 1H), 8.35-8.29 (m, 1H), 8.24 (s, 1H), 8.22-8.05 (m, 3H), 8.01-7.94 (m, 1H), 7.74-7.68 (m, 1H), 3.95 (br s, 4H), 3.36 (br s, 4H), 2.72-2.65 (m, 1H), 1.31-1.25 (m, 2H), 1.12-1.08 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-iso[D4],[D3]uinolin-1-yl-amine
2090		[D3]	LCMS: Purity: >95%, RT: min, MI: 436 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 12.09 (s, 1H), 9.26 (s, 1H), 8.8-9.0 (m, 3H), 8.69 (d, 1H, J = 8.2 Hz), 8.59 (d, 1H, J = 5.1 Hz), 7.89 (d, 1H, J = 5.1 Hz), 7.55 (d, 1H, J = 7.9 Hz), 7.49 (m, 1H), 7.19 (m, 1H), 4.32 (m, 1H), 3.83 (m, 4H), 3.30 (m, 4H), 2.57 (m, 2H), 2.28 (m, 2H), 2.13 (m, 1H), 1.95 (m, 1H).	4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole
2091		[B01]	LCMS: Purity: >95%, RT: min, MI: 382 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 12.07 (s, 1H), 9.43 (s, 1H), 8.89 (br s, 2H), 8.73 (d, 1H, J = 5.7 Hz), 8.58 (d, 1H, J = 5.1 Hz), 8.55 (d, 1H, J = 8.0 Hz), 8.11 (d, 1H, J = 5.2 Hz), 7.81 (d, 1H, J = 5.1 Hz), 7.55 (d, 1H, J = 8.0 Hz), 7.49 (m, 1H), 7.17 (m, 1H), 4.14 (m, 4H), 3.38 (m, 4H).	4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole

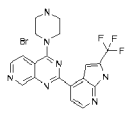
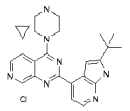
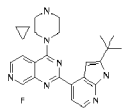
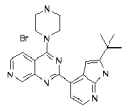
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2103		[B4]	LCMS: Purity: >95%, RT: min, MI: 542 (M+H)	1H-NMR: DMSO 9.23 (br m, 1H), 9.02 (s, 1H), 8.87 (s, 1H), 8.46 (s, 1H), 8.18 (d, 1H, J = 5.3 Hz), 8.12 (m, 1H), 7.84 (m, 1H), 7.71 (m, 1H), 7.30 (m, 1H), 7.18 (m, 2H), 3.73 (m, 2H), 3.58 (m, 1H), 3.36 (m, 2H), 2.74 (m, 2H), 2.17 (m, 5H), 1.98 (m, 2H), 1.73 (m, 3H), 1.48 (m, 2H), 1.25 (m, 2H), 1.00 (m, 2H)	(1-Cyclobutyl-piperidin-4-ylmethyl)-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine
2104		[B4]	LCMS: Purity: 98%, RT: min, MI: 466.19 (MH)+	(400 MHz, d6-DMSO,δ): 10.18 (s, 1H), 9.08 (s, 1H), 8.87 (br s, 2H), 8.54-8.46 (m, 3H), 8.19 (s, 1H), 7.92 (dd, J=5.2, 1.3 Hz, 1H), 7.59 (dd, J=8.9, 7.5 Hz, 1H), 7.47 (d, J=8.8 Hz, 1H), 3.94 (br s, 4H), 3.34 (br s, 4H), 2.73-2.65 (m, 1H), 1.29-1.24 (m, 2H), 1.12-1.07 (m, 2H).	Benzo[1,2,5]oxadiazol-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2105		[D4],[D3]	Method 5: RT: 4.08 min, MI: 468.53 [M+H]	1H NMR (500MHz, DMSO) 13.18 (1H, s), 9.27 (1H, s), 8.99 (1H, s, br), 8.88 (1H, s, br), 8.74 (1H, s), 8.63 (1H, d), 8.25 (1H, d), 7.96 (1H, s), 4.31 (4H, s, br), 3.96-3.93 (2H, m, br), 3.89-3.84 (1H, m), 3.77-3.74 (2H, m), 3.61-3.56 (1H, m), 2.13-2.12 (2H, m), 1.89-1.67 (6H, m).	5-Cyclopentyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine

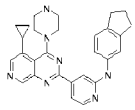
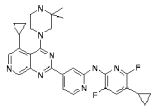
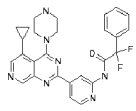
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2106		[D4],[D3], [D8]	Method 5: RT: 3.19 min, MI: 422 [M+H]	1H NMR (400 MHz, d6-DMSO 90 °C) 12.58 (1H, s), 9.06 (1H, s), 8.53 (1H, d, J = 4.9 Hz), 8.18 (1H, d, J = 4.9 Hz), 8.11 (1H, s), 7.78 (1H, br m), 7.33 (1H, t, J = 54.2 Hz), 3.93 - 3.47 (4H, br m), 2.89 (4H, br s), 2.70 - 2.65 (1H, m), 1.29 - 1.25 (2H, m), 1.06 - 1.03 (2H, m).	5-Cyclopropyl-2-(2-difluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2107		[B4]	LCMS: Purity: >95%, RT: min, MI: 488 (M+H)	1H-NMR: DMSO 9.02 (s, 1H), 8.91 (s, 1H), 8.55 (m, 1H), 8.46 (s, 1H), 8.26 (m, 1H), 8.18 (d, 1H, J = 5.3 Hz), 8.09 (m, 1H), 7.81 (s, 1H), 7.71 (m, 1H), 7.31 (m, 1H), 7.19 (m, 2H), 3.72 (m, 2H), 3.32 (m, 2H), 2.88 (m, 2H), 2.54 (m, 1H), 2.14 (m, 1H), 1.90 (m, 2H), 1.47 (m, 2H), 1.25 (m, 2H), 1.01 (m, 2H)	{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ylmethyl-amine
2108		[D4],[D3]	LCMS: Purity: 93%, RT: min, MI: 458.27 (M+H)	(dmso-d6) 11.74 (s, 1H), 9.14 (s, 1H), 8.93 (br s, 2H), 8.32 (d, J = 5.2 Hz, 1H), 8.18 (s, 1H), 8.09 (d, J = 5.2 Hz, 1H), 7.21 (d, J = 2.2 Hz, 1H), 3.93 (br s, 4H), 3.55 (s, 2H), 3.37 (br s, 4H), 3.26 (s, 3H), 2.80-2.71 (m, 1H), 1.40 (s, 6H), 1.30-1.20 (m, 2H), 1.12-1.05 (m, 2H)	5-Cyclopropyl-2-[2-(2-methoxy-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

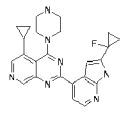
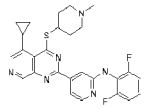
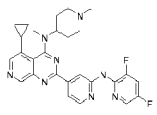
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2109		[D4],[D3]	LCMS: Purity: 97%, RT: min, MI: 472.29 (M+H)	(dmso-d6) 11.74 (br s, 1H), 9.21 (s, 1H), 8.99 (br s, 1H), 8.85 (br s, 1H), 8.79 (s, 1H), 8.31 (d, J = 5.2 Hz, 1H), 8.07 (d, J = 5.2 Hz, 1H), 7.19 (d, J = 2.2 Hz, 1H), 4.29 (quint, 1H), 3.90-3.70 (m, 4H), 3.54 (s, 2H), 3.40-3.25 (m, 4H), 3.26 (s, 3H), 2.47 (m, 2H),2.30-2.15 (m, 2H), 2.15-2.05 (m, 1H), 1.95-1.85 (m, 1H), 1.40 (s, 6H)	5-Cyclobutyl-2-[2-(2-methoxy-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2110		[B4]	LCMS: Purity: >95%, RT: min, MI: 461 (M+H)+	1H-NMR: DMSO 9.60 (br m, 1H), 8.98 (s, 1H), 8.90 (s, 1H), 8.18 (m, 2H), 7.81 (s, 1H), 7.69 (m, 1H), 7.28 (m, 1H), 7.19 (m, 2H), 4.84 (m, 1H), 3.64 (m, 1H), 3.48 (m, 2H), 3.09 (s, 3H), 3.05 (m, 2H), 2.45 (m, 1H), 2.07-2.25 (br m, 8H), 1.77 (m, 2H), 1.24 (m, 2H), 0.99 (m, 2H)	(1-Cyclobutyl-piperidin-4-yl)-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine
2111		[D4],[D3]	Method 5: RT: 3.20 min, MI: 456 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.87 (brs, 1H), 9.16 (s, 1H), 8.31 (d, 1H), 8.16 (s, 1H), 8.08 (d, 1H), 7.21 (s, 1H), 4.11-3.73 (m, 4H), 4.00 (dd, 2H), 3.49 (t, 2H), 3.41-3.32 (m, 4H), 3.12-3.04 (m, 1H), 2.78-2.70 (m, 1H), 2.02-1.97 (m, 2H), 1.87-1.76 (m, 2H), 1.29-1.23 (m, 2H), 1.10-1.05 (m, 2H).	5-Cyclopropyl-4-piperazin-1-yl-2-[2-(tetrahydro-pyran-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine

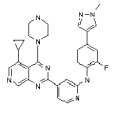
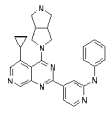
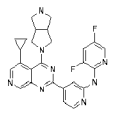
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2112		[D4],[D3]	Method 5: RT: 3.25 min, MI: 400 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.99 (1H, s), 9.25 (1H, s), 9.11 (1H, brs), 8.96 (1H, brs), 8.79 (1H, s), 8.31 (1H, d), 8.13-8.12 (1H, m), 7.22 (1H, s), 4.31-4.24 (1H, m), 3.93-3.85 (2H, m), 3.83-3.72 (2H, m), 3.43-3.34 (2H, m), 3.32-3.21 (2H, m), 2.51 (3H, s), 2.47-2.42 (1H, m), 2.26-2.17 (2H, m), 2.15-2.06 (1H, m), 1.94-1.87 (1H, m).	5-Cyclobutyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2113		[D4],[D3]	Method 5: RT: 3.18 min, MI:502 [M+H]	1H NMR (400 MHz, d6-DMSO 90 °C) 11.25 (1H, s), 9.02 (1H, s), 8.63 (1H, s), 8.26 (1H, d, J = 5.0 Hz), 8.03 (1H, d, J = 5.0 Hz), 7.45 - 7.42 (2H, m), 7.37 - 7.34 (2H, m), 7.29 - 7.25 (1H, m), 7.01 (1H, s), 4.34 - 4.30 (1H, m), 3.48 (4H, br s), 2.88 - 2.85 (4H, br. m), 2.55 - 2.50 (2H, m largely obscured by DMSO peak - visible but broad at lower T), 2.20 - 2.05 (3H, m), 1.97 - 1.92 (1H, m), 1.59 - 1.56 (2H, m), 1.39 - 1.36 (2H, m).	5-Cyclobutyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

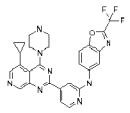
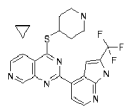
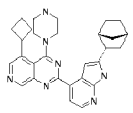
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2114		[D4],[D3], [D8]	Method 5: RT: 2.55 min, MI:436 [M+H]	1H NMR (400 MHz, d6-DMSO, 90 °C) 9.13 (1H, s), 8.68 (1H, s), 8.51 (1H, d, J = 5.0 Hz), 8.16 (1H, d, J = 5.0 Hz), 7.75 (1H, s), 7.23 (1H, t, J = 54.7 Hz), 4.36 - 4.32 (1H, m), 3.64 - 3.61 (4H, br m), 2.95 - 2.93 (4H, br. m), 2.56 - 2.49 (2H, m overlapping with DMSO signal), 2.22 - 2.07 (3H, m), 1.99 - 1.94 (1H, m).	5-Cyclobutyl-2-(2-difluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2115		[B4]	LCMS: Purity: >95%, RT: min, MI: 542 (M+H)	1H-NMR: DMSO 9.20 (br m, 1H), 8.98 (s, 1H), 8.92 (s, 1H), 8.19 (d, 2H, J = 4.5 Hz), 7.83 (s, 1H), 7.73 (m, 1H), 7.32 (m, 1H), 7.18 (m, 2H), 4.87 (m, 1H), 3.54 (m, 3H), 3.25 (m, 2H), 3.10 (s, 3H), 2.45 (m, 1H), 2.15 (br m, 4H), 1.31 (d, 6H, J = 6.6 Hz), 1.26 (m, 2H), 0.99 (m, 2H)	{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(1-isopropyl-piperidin-4-yl)-methyl-amine
2116		[B4]	LCMS: Purity: >95%, RT: min, MI: 530 (M+H)	(400 MHz, d6-DMSO,δ): 10.19 (s, 1H), 9.08 (s, 1H), 8.85 (br s, 2H), 8.76 (s, 1H), 8.57 (d, J=5.3 Hz, 1H), 8.20 (s, 1H), 8.13 (s, 1H), 7.99 (d, J=9.6 Hz, 1H), 7.94 (dd, J=5.4, 1.2 Hz, 1H), 7.56 (dd, J=9.6, 1.8 Hz, 1H), 3.93 (br s, 4H), 3.34 (br s, 4H), 2.72-2.65 (m, 1H), 1.29-1.23 (m, 2H), 1.12-1.06 (m, 2H).	Benzo[1,2,5]oxadiazol-5-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

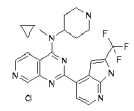
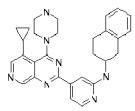
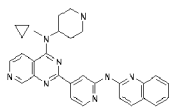
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2117		[B1]	LCMS : Purity: >95%, RT: min, MI: 478 (M+H)+	1H-NMR (DMSO-d6, 400 MHz): 13.23 (s, 1H), 9.44 (s, 1H), 8.97 (br s, 1H), 8.85 (s, 1H), 8.77 (br s, 1H), 8.66 (d, 1H, J = 5.0 Hz), 8.28 (d, 1H, J = 5.0 Hz), 7.97 (s, 1H), 3.7-4.0 (m, 8H)	5-Bromo-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
2118		[D4],[D3]	LCMS : Purity: >95%, RT: min, MI: 462 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 11.80 (s, 1H), 8.96 (br s, 1H), 8.77 (br s, 1H), 8.32 (d, 1H, J = 5.1 Hz), 8.11 (d, 1H, J = 5.1 Hz), 7.95 (s, 1H), 7.49 (d, 1H, J = 2.3 Hz), 3.9-4.0 (m, 4H), 3.33 (m, 4H), 2.67 (m, 1H), 1.43 (s, 9H), 1.25 (m, 2H), 1.06 (m, 2H)	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-8-chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2119		[D4],[D3]	LCMS : Purity: >95%, RT: min, MI: 446 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 11.80 (s, 1H), 8.88 (br s, 2H), 8.32 (d, 1H, J = 5.1 Hz), 8.08 (d, 1H, J = 5.1 Hz), 7.73 (s, 1H), 7.21 (d, 1H, J = 2.3 Hz), 3.9-4.0 (m, 4H), 3.34 (m, 4H), 2.67 (m, 1H), 1.43 (s, 9H), 1.21 (m, 2H), 1.01 (m, 2H)	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-8-fluoro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2120		[D4],[D3]	LCMS : Purity: >95%, RT: min, MI: 466 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 11.82 (s, 1H), 9.35 (s, 1H), 9.01 (br s, 1H), 8.81 (s, 1H), 8.79 (br s, 1H), 8.32 (d, 1H, J = 5.2 Hz), 8.08 (d, 1H, J = 5.2 Hz), 7.16 (d, 1H, J = 2.2 Hz), 3.7-4.0 (m, 4H), 3.37 (m, 4H), 1.44 (s, 9H)	5-Bromo-2-(2-tert-butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

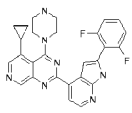
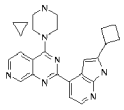
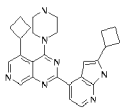
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2124		[B4]	LCMS: Purity: 96%, RT: min, MI: 464.28 (MH)+	(400 MHz, d6-DMSO,δ): 9.35 (s, 1H), 9.06 (s, 1H), 8.86 (br s, 2H), 8.26 (d, J=5.6 Hz, 1H), 8.18 (s, 1H), 7.94 (s, 1H), 7.68 (dd, J=5.4, 1.3 Hz, 1H), 7.66 (s, 1H), 7.39 (dd, J=8.0, 1.7 Hz, 1H), 7.16 (d, J=8.0 Hz, 1H), 3.92 (br s, 4H), 3.33 (br s, 4H), 2.89-2.79 (m, 4H), 2.73-2.65 (m, 1H), 2.07-1.98 (m, 2H), 1.28-1.23 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-indan-5-yl-amine
2125		[B4]	Method 5: RT: 2.88 min, MI: 529 [M+H]	1H NMR (500MH, d6-DMSO) 9.69 (1H, s), 9.06 (1H, s), 8.82 (1H, s), 8.43 (1H, d), 8.21 (1H, s), 7.98 (1H, dd), 7.56 (1H, m), 3.93 (4H, s), 3.36 (2H, s,), 1.95 (1H, m), 1.39 (3H, m), 1.28 (3H, m), 1.06 (2H, m), 0.98 (2H, m), 0.79 (2H, m).	(5-Cyclopropyl-3,6-difluoro-pyridin-2-yl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine
2126		[B4]	LCMS: Purity: 98%, RT: min, MI: 502.1 (MH)+	(400 MHz, d6-DMSO,δ): 11.53 (s, 1H), 9.09 (s, 1H), 9.00 (s, 1H), 8.89 (br s, 2H), 8.61 (dd, J=5.2, 0.5 Hz, 1H), 8.21-8.18 (m, 2H), 7.79-7.75 (m, 2H), 7.64-7.55 (m, 3H), 3.92 (br s, 4H), 3.37-3.28 (m, 4H), 2.72-2.64 (m, 1H), 1.28-1.22 (m, 2H), 1.11-1.05 (m, 2H).	N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2,2-difluoro-2-phenyl-acetamide

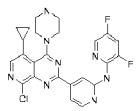
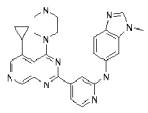
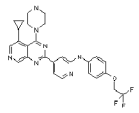
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2127		[D4],[D3]	Method 5: RT: 3.40 min, MI: 430 [M+H]	1H NMR (600 MHz, d6-DMSO) 12.06 (1H, s), 9.08 (1H, s), 8.37 (1H, d, J = 5.0 Hz), 9.11 - 8.10 (2H, m), 7.45 (1H, br d, J = 1.6 Hz), 3.96 - 3.51 (4H, very broad m), 2.94 (4H, br s), 2.70 - 2.66 (1H, m), 1.58 - 1.542H, m), 1.36 - 1.34 (2H, m), 1.27 - 1.24 (2H, m), 1.05 - 1.04 (2H, m).	5-Cyclopropyl-2-[2-(1-fluoro-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2128		[B4]	LCMS: Purity: >95%, RT: min, MI: 505 (MH)+	1H-NMR: DMSO 9.65 (br s, 1H), 9.27 (s, 1H), 8.86 (s, 1H), 8.57 (s, 1H), 8.25 (d, 1H, J = 5.3 Hz), 7.85 (s, 1H), 7.72 (m, 1H), 7.30 (m, 1H), 7.19 (m, 2H), 4.35 (m, 1H), 3.61 (m, 2H), 3.30 (m, 2H), 2.88 (s, 3H), 2.46 (m, 1H), 2.27 (m, 2H), 1.93 (m, 2H), 1.22 (m, 2H), 1.07 (m, 2H)	{4-[5-Cyclopropyl-4-(1-methyl-piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine
2129		[B4]	LCMS: Purity: >95%, RT: min, MI: 503 (MH)+	1H-NMR: DMSO 10.33 (br s, 1H), 9.62 (br s, 1H), 9.01 (s, 1H), 8.61 (s, 1H), 8.41 (d, 1H, J = 5.7 Hz), 8.31 (m, 1H), 8.20 (s, 1H), 8.07 (m, 1H), 7.99 (m, 1H), 4.80 (m, 1H), 3.57 (m, 2H), 3.20 (m, 2H), 3.12 (s, 3H), 2.82 (m, 3H), 2.44 (m, 1H), 2.07 (br m, 4H), 1.25 (m, 2H), 0.99 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(1-methyl-piperidin-4-yl)-amine

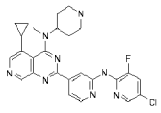
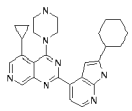
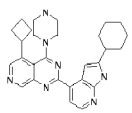
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2130		[B4]	LCMS : Purity: 90.012 %, RT: min, MI: 522		[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)-phenyl]-amine
2131		[B4]	LCMS : Purity: 98%, RT: min, MI: 450.0 (MH)+	(400 MHz, d6-DMSO,δ): 9.52 (s, 1H), 8.96 (s, 1H), 8.83 (br s, 2H), 8.31 (d, J=5.5 Hz, 1H), 8.18 (s, 1H), 7.95 (s, 1H), 7.75-7.70 (m, 3H), 7.34-7.29 (m, 2H), 6.96 (t, J=8.0 Hz, 1H), 4.12-4.06 (m, 2H), 3.88-3.82 (m, 2H), 3.45-3.35 (m, 2H), 3.15-2.95 (m, 4H), 2.45-2.37 (m, 1H), 1.31-1.25 (m, 2H), 1.04-0.98 (m, 2H).	{4-[5-Cyclopropyl-4-(hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine
2132		[B4]	LCMS : Purity: 97%, RT: min, MI: 487.0 (MH)+	(400 MHz, d6-DMSO,δ): 10.27 (s, 1H), 8.99 (s, 1H), 8.86 (br s, 2H), 8.72 (s, 1H), 8.41 (d, J=5.5 Hz, 1H), 8.29 (d, J=2.6 Hz, 1H), 8.20 (s, 1H), 8.10-8.04 (m, 1H), 7.99 (dd, J=5.7, 1.4 Hz, 1H), 4.14-4.08 (m, 2H), 3.89-3.83 (m, 2H), 3.45-3.35 (m, 2H), 3.15-2.95 (m, 4H), 2.44-2.36 (m, 1H), 1.31-1.26 (m, 2H), 1.04-0.99 (m, 2H).	{4-[5-Cyclopropyl-4-(hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine

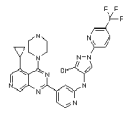
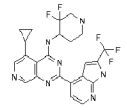
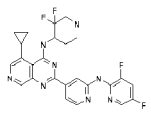
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2133		[B4]	LCMS: Purity: 96%, RT: min, MI: 533.18 (MH)+	(400 MHz, d6-DMSO,δ): 9.76 (s, 1H), 9.07 (s, 1H), 8.87 (br s, 2H), 8.67 (d, J=2.1 Hz, 1H), 8.42 (d, J=5.3 Hz, 1H), 8.19 (s, 1H), 8.00 (s, 1H), 7.88 (d, J=9.1 Hz, 1H), 7.80-7.76 (m, 2H), 3.92 (br s, 4H), 3.34 (br s, 4H), 2.74-2.65 (m, 1H), 1.29-1.23 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-benzooxazol-5-yl)-amine
2134		[D4],[D3]	LCMS: Purity: 95%, RT: min, MI: 471 (MH)+	1H-NMR: DMSO 13.25 (s, 1H), 9.46 (s, 1H), 8.70 (m, 2H), 8.59 (s, 1H), 8.49 (m, 1H), 8.32 (m, 1H), 8.05 (s, 1H), 4.58 (m, 1H), 3.40 (m, 2H), 3.28 (m, 2H), 2.56 (m, 1H), 2.40 (m, 2H), 1.97 (m, 2H), 1.24 (m, 2H), 1.08 (m, 2H)	5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
2135		[D4],[D3]	LCMS: Purity: 97%, RT: min, MI: 480.1 (M+H)	(dmso-d6) 1H-NMR (dmso-d6): 11.76 (s, 1H), 9.24 (s, 1H), 9.03 (br s, 1H), 8.92 (br s, 1H), 8.79 (s, 1H), 8.29 (d, J = 5.2 Hz, 1H), 8.07 (d, J = 5.2 Hz, 1H), 7.25 (s, 1H), 4.29 (quint, J = 8.8 Hz, 1H), 3.88 (br s, 2H), 3.79 (br s, 2H), 3.40-3.20 (m, 5H), 2.69 (br s, 1H), 2.50-2.40 (m, 2H), 2.36 (br s, 1H), 2.30-1.80 (m, 5H), 1.70-1.40 (m, 4H), 1.30-1.20 (m, 2H), 1.15-1.05 (m, 1H)	(±)-endo-2-(2-Bicyclo[2.2.1]hept-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

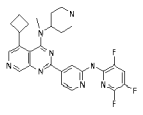
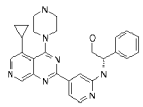
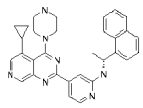
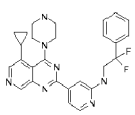
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2136		[D4],[D3]	LCMS: Purity: 95%, RT: min, MI: 502 (M+H)	1H-NMR: DMSO 13.16 (s, 1H), 8.75 (m, 1H), 8.65 (d, 1H, J = 4.9 Hz), 8.37 (m, 1H), 8.32 (m, 1H), 8.21 (s, 1H), 7.98 (s, 1H), 4.95 (m, 1H), 3.47 (m, 2H), 3.21 (m, 2H), 3.11 (s, 3H), 2.40 (m, 1H), 1.91-2.18 (br m, 4H), 1.14-1.33 (br m, 2H), 0.96 (m, 2H)	[8-Chloro-5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine
2137		[B4]	LCMS: Purity: 95%, RT: min, MI: 478.27 (MH)+	(400 MHz, d6-DMSO,δ): 9.07 (s, 1H), 8.94 (br s, 2H), 8.22 (s, 1H), 8.10 (d, J=6.2 Hz, 1H), 8.02 (br s, 1H), 7.69-7.64 (m, 1H), 7.17-7.11 (m, 4H), 4.21-4.13 (m, 1H), 3.93 (br s, 4H), 3.32 (br s, 4H), 3.20 (dd, J=16.5, 5.2 Hz, 1H), 2.94 (t, J=6.3 Hz, 2H), 2.80 (dd, J=16.4, 8.4 Hz, 1H), 2.70-2.63 (m, 1H), 2.20-2.13 (m, 1H), 1.89-1.77 (m, 1H), 1.29-1.23 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1,2,3,4-tetrahydro-naphthalen-2-yl)-amine
2138		[B4]	LCMS: Purity: 95%, RT: min, MI: 503 (M+H)	1H-NMR: DMSO 12.20 (br s, 1H), 9.03 (s, 1H), 8.84 (m, 1H), 8.69 (d, 2H, J = 5.7 Hz), 8.57 (m, 1H), 8.45 (m, 1H), 8.22 (m, 3H), 8.04 (m, 1H), 7.88 (m, 1H), 7.61 (m, 1H), 7.56 (m, 1H), 4.89 (m, 1H), 3.45 (m, 2H), 3.19 (m, 2H), 3.15 (s, 3H), 2.45 (m, 1H), 2.07 (br m, 4H), 1.26 (m, 2H), 1.00 (m, 2H)	{5-Cyclopropyl-2-[2-([D4],[D3]uinolin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

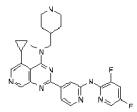
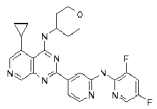
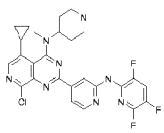
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2145		[D4],[D3]	LCMS: Purity: 95%, RT: min, MI: 484.2 (M+H)	(dmso-d6) 12.23 (d, J = 1.3 Hz, 1H), 9.14 (s, 1H), 8.91 (br s, 2H), 8.49 (d, J = 5.0 Hz, 1H), 8.19 (d, J = 5.0 Hz, 1H), 8.18 (s, 1H), 7.78 (br s, 1H), 7.56 (m, 1H), 7.33 (m, 2H), 3.93 (br s, 4H), 3.36 (br s, 4H), 2.75 (m, 1H), 1.30-1.23 (m, 2H), 1.12-1.06 (m, 2H)	5-Cyclopropyl-2-[2-(2,6-difluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2146		[D4],[D3]	LCMS: Purity: 96%, RT: min, MI: 426.1 (M+H)	(dmso-d6) 11.82 (br s, 1H), 9.16 (s, 1H), 8.93 (br s, 2H), 8.30 (d, J = 5.2 Hz, 1H), 8.17 (s, 1H), 8.09 (d, J = 5.2 Hz, 1H), 7.24 (d, J = 1.7 Hz, 1H), 3.91 (br s, 4H), 3.74 (quint, J = 8.4 Hz, 1H), 3.37 (br s, 4H), 2.75 (m, 1H), 2.45-2.75 (m, 4H), 2.35-1.98 (m, 1H), 1.96-1.85 (m, 1H), 1.30-1.22 (m, 2H), 1.12-1.08 (m, 2H)	2-(2-Cyclobutyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2147		[D4],[D3]	LCMS: Purity: 92%, RT: min, MI: 440.28 (M+H)	(dmso-d6) 11.89 (br s, 1H), 9.25 (s, 1H), 9.10 (br s, 1H), 8.94 (br s, 1H), 8.79 (s, 1H), 8.30 (d, J = 5.2 Hz, 1H), 8.09 (d, J = 5.2 Hz, 1H), 7.23 (d, J = 1.6 Hz, 1H), 4.29 (quint, 1H), 3.88 (br s, 2H), 3.79 (br s, 2H), 3.75 (quint, J = 8.8 Hz, 1H), 3.50-3.20 (m, 4H), 2.50-2.43 (m, 2H), 2.43-2.31 (m, 4H), 2.31-2.16 (m, 2H), 2.16-1.97 (m, 2H), 1.97-1.07 (m, 2H)	5-Cyclobutyl-2-(2-cyclobutyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

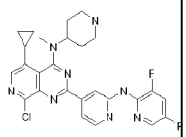
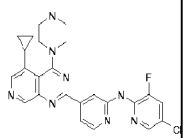
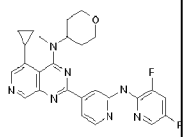
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2148		[B4]	LCMS : Purity: 98%, RT: min, MI: 495 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.80 - 10.03 (1 H, m), 8.83 - 9.14 (2 H, m), 8.81 (1 H, s), 8.43 (1 H, d, J=5.5 Hz), 8.26 (1 H, d, J=2.5 Hz), 7.90 - 8.08 (3 H, m), 3.97 (4 H, br. s.), 3.32 (4 H, br. s.), 2.57 - 2.64 (1 H, m), 1.18 - 1.30 (2 H, m), 1.01 - 1.11 (2 H, m)	[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine
2149		[B4]	LCMS : Purity: 98%, RT: min, MI: 478.24 (MH)+	(400 MHz, d6-DMSO,δ): 9.91 (s, 1H), 9.34 (s, 1H), 9.07 (s, 1H), 8.97 (br s, 2H), 8.68 (d, J=1.4 Hz, 1H), 8.45 (d, J=5.3 Hz, 1H), 8.20 (s, 1H), 8.04 (s, 1H), 7.82 (dd, J=5.4, 1.4 Hz, 1H), 7.78 (d, J=8.9 Hz, 1H), 7.65 (dd, J=9.0, 1.8 Hz, 1H), 4.03 (s, 3H), 3.93 (br s, 4H), 3.35 (br s, 4H), 2.74-2.65 (m, 1H), 1.29-1.23 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-3H-benzoimidazol-5-yl)-amine
2150		[B4]	Method 5: RT: 2.34 min, MI:522 [M+H]	1H NMR (500MH, DMSO) 9.43 (1H, s), 9.06 (1H, s), 8.29 (1H, d), 8.18 (1H, s), 7.91 (1H, s), 7.68 (3H, m), 7.05 (2H, d), 4.72 (2H, m), 3.91 (4H, s, broad), 3.33 (4H, s,), 2.69 (1H, m), 1.26 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-amine

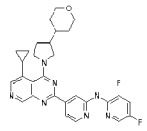
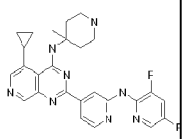
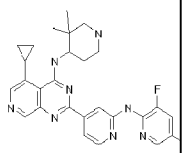
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2151		[B4]	LCMS: Purity: >95%, RT: min, MI: 506 (MH)+	1H-NMR: DMSO 10.29 (br s, 1H), 9.01 (s, 1H), 8.80 (br m, 1H), 8.73 (s, 1H), 8.45 (d, 1H, J = 5.5 Hz), 8.38 (br m, 1H), 8.27 (m, 1H), 8.20 (s, 1H), 8.10 (m, 1H), 8.03 (m, 1H), 4.84 (m, 1H), 3.44 (m, 2H), 3.15 (m, 2H), 3.12 (s, 3H), 2.44 (m, 1H), 2.07 (br m, 4H), 1.25 (m, 2H), 0.98 (m, 2H)	{2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2152		[D4],[D3]	LCMS: Purity: 95%, RT: min, MI: 454.23 (M+H)	(dmso-d6) 11.71 (d, J = 1.3 Hz, 1H), 9.09 (s, 1H), 8.89 (br s, 2H), 8.23 (d, J = 5.2 Hz, 1H), 8.10 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.11 (d, J = 1.7 Hz, 1H), 3.84 (br s, 4H), 3.30 (br s, 4H), 2.76 (m, 1H), 2.68 (m, 1H), 2.15 (m, 2H), 1.77 (m, 2H), 1.67 (m, 1H), 1.51 (m, 2H), 1.36 (m, 2H), 1.28-1.13 (m, 3H), 1.06-0.80 (m, 2H)	5-Cyclopropyl-2-(2-cyclohexyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2153		[D4],[D3]	LCMS: Purity: 94%, RT: min, MI: 468.28	(dmso-d6) 11.72 (s, 1H), 9.17 (s, 1H), 8.99 (br s, 1H), 8.84 (br s, 1H), 8.72 (s, 1H), 8.22 (d, J = 5.3 Hz, 1H), 8.01 (d, J = 5.3 Hz, 1H), 7.1 (d, J = 1.8 Hz, 1H), 6.28 (br s, exch. protons), 4.11 (m, 1H), 3.76 (m, 4H), 3.17 (m, 4H), 2.75 (m, 1H), 2.42 (m, 2H), 2.15 (m, 2H), 2.58-1.95 (m, 3H), 1.77 (m, 4H), 1.50 (m, 2H), 1.35 (m, 2H), 1.24 (m, 1H)	5-Cyclobutyl-2-(2-cyclohexyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

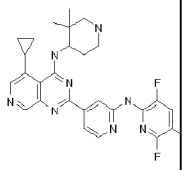
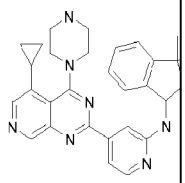
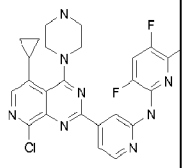
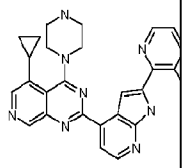
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2154		[B4]	LCMS: Purity: 94%, RT: min, MI: 593.17 (M+H)	(dmso-d6) 9.10 (s, 1H), 9.05 (br s, 1H), 9.02 (br s, 1H), 8.92 (br s, 2H), 8.53 (s, 1H), 8.49 (dd, J = 8.3, 2.3 Hz, 1H), 8.36 (d, J = 5.2 Hz, 1H), 8.22 (s, 1H), 8.10 (d, J = 8.3 Hz, 1H), 8.06 (s, 1H), 7.77 (dd, J = 5.3, 1.3 Hz, 1H), 3. 88 (br s, 4H), 3.37 (br s, 4H), 2.71 (m, 1H), 1.28 (m, 2H), 1.12 (m, 2H)	[3-Chloro-1-(5-trifluoromethyl-pyridin-2-yl)-1H-pyrazol-4-yl]-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2155		[D4],[D3]	LCMS: Purity: >95%, RT: min, MI: 490 (M+H)	1H-NMR: DMSO 13.14 (s, 1H), 9.73 (br m, 1H), 9.35 (br m, 1H), 9.26 (s, 1H), 8.64 (d, 1H, J = 4.9 Hz), 8.56 (s, 1H), 8.34 (d, 1H, J = 4.9 Hz), 7.97 (m, 2H), 5.50 (m, 1H), 4.02 (m, 1H), 3.82-3.90 (br m, 1H), 3.45 (m, 2H), 2.61 (m, 1H), 2.54 (m, 1H), 2.08 (m, 1H), 1.21 (m, 3H), 1.05 (m, 1H)	[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-difluoro-piperidin-4-yl)-amine
2156		[B4]	LCMS: Purity: >95%, RT: min, MI: 511 (M+H)	1H-NMR: DMSO 10.06 (br s, 1H), 9.84 (br m, 1H), 9.37 (br m, 1H), 9.14 (s, 1H), 8.65 (s, 1H), 8.56 (s, 1H), 8.41 (d, 1H, J = 5.5 Hz), 8.28 (m, 1H), 8.06 (m, 3H), 5.50 (m, 1H), 4.01 (m, 1H), 3.76-3.87 (br m, 1H), 3.45 (m, 1H), 3.35 (m, 1H), 2.60 (m, 1H), 2.46 (m, 1H), 2.07 (m, 1H), 1.20 (m, 3H), 1.03 (m, 1H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-difluoro-piperidin-4-yl)-amine

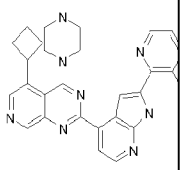
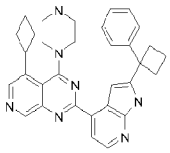
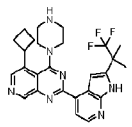
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2163		[B4]	LCMS : Purity: 95%, RT: min, MI: 521 (M+H)	1H-NMR: 9.80 (s, 1H), 9.05 (s, 1H), 8.73 (m, 1H), 8.65 (s, 1H), 8.56 (s, 1H), 8.41 (d, 1H, J = 5.2 Hz), 8.30 (m, 2H), 7.95 (m, 1H), 4.79 (m, 1H), 4.16 (m, 1H), 3,50 (m, 1H), 3.37 (m, 1H), 3.15 (m, 2H), 2.98 (s, 3H), 2.62 (m, 1H), 2.23-2.37 (br m, 4H), 1.84-2.10 (br m, 5H)	{5-Cyclobutyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2164		[B4]	LCMS : Purity: 90%, RT: min, MI: 468.24 (MH)+	(400 MHz, d6-DMSO,δ): 9.06 (s, 1H), 8.99 (br s, 2H), 8.21 (s, 1H), 8.12-7.95 (m, 2H), 7.67 (d, J=6.3 Hz, 1H), 7.49-7.27 (m, 5H), 5.08-5.00 (m, 1H), 4.10-3.65 (m, 6H), 3.33 (br s, 4H), 2.70-2.61 (m, 1H), 1.29-1.23 (m, 2H), 1.11-1.05 (m, 2H).	(S)-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-phenyl-ethanol
2165		[B4]	LCMS : Purity: 95%, RT: min, MI: 502.24 (MH)+	(400 MHz, d6-DMSO,δ): 9.00 (s, 1H), 8.86 (br s, 2H), 8.27-8.22 (m, 1H), 8.18 (s, 1H), 8.07 (d, J=6.0 Hz, 1H), 7.85 (d, J=8.0 Hz, 1H), 7.66-7.47 (m, 4H), 5.91-5.85 (m, 1H), 3.80 (br s, 4H), 3.24 (br s, 4H), 2.66-2.59 (m, 1H), 1.67 (d, J=6.4 Hz, 3H), 1.27-1.21 (m, 2H), 1.09-1.04 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-naphthalen-1-yl-ethyl)-amine
2166		[B4]	LCMS : Purity: 96%, RT: min, MI: 488.23 (MH)+	(400 MHz, d6-DMSO,δ): 9.05 (d, J=2.2 Hz, 1H), 8.89 (br s, 2H), 8.19 (s, 1H), 8.12 (d, J=5.8 Hz, 1H), 7.85 (br s, 1H), 7.64-7.49 (m, 6H), 4.30-4.19 (m, 2H), 3.92 (br s, 4H), 3.31 (br s, 4H), 2.74-2.64 (m, 1H), 1.28-1.22 (m, 2H), 1.10-1.05 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2-difluoro-2-phenyl-ethyl)-amine

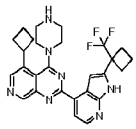
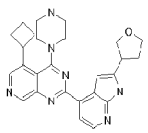
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2167		[B4]	LCMS: Purity: 95%, RT: min, MI: 503 (M+H)	1H-NMR: DMSO 10.33 (br s, 1H), 9.00 (s, 1H), 8.71 (s, 1H), 8.50 (m, 1H), 8.41 (d, 1H, J = 5.7 Hz), 8.28 (d, 1H, J = 2.5 Hz), 8.17 (s, 1H), 8.08 (m, 2H), 7.99 (m, 1H), 3.30 (s, 3H), 3.16 (m, 2H), 2.80 (m, 2H), 2.38 (m, 1H), 2.19 (m, 1H), 1.57 (br m, 2H), 1.29 (m, 2H), 1.03 (m, 6H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-ylmethyl-amine
2168		[B4]	LCMS: Purity: >95%, RT: min, MI: 477 (M+H)	1H-NMR: DMSO 10.17 (br s, 1H), 9.05 (s, 1H), 8.64 (s, 1H), 8.48 (s, 1H), 8.40 (d, 1H, J = 5.6 Hz), 8.28 (d, 1H, J = 2.5 Hz), 8.06 (m, 1H), 7.98 (m, 1H), 7.87 (m, 1H), 4.53 (m, 1H), 3.95 (m, 2H), 3.53 (m, 2H), 2.61 (m, 1H), 2.13 (m, 2H), 1.79 (m, 2H), 1.22 (m, 2H), 1.06 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(tetrahydro-pyran-4-yl)-amine
2169		[B4]	LCMS: Purity: 95%, RT: min, MI: 541 (M+H)	1H-NMR: DMSO 9.76 (s, 1H), 8.73 (s, 1H), 8.71 (m, 1H), 8.43 (d, 1H, J = 5.2 Hz), 8.29 (m, 2H), 7.95 (m, 2H), 4.87 (m, 1H), 3.45 (m, 2H), 3.10 (s, 3H), 2.98 (m, 2H), 2.38 (m, 1H), 1.90-2.28 (br m, 4H), 1.14-1.29 (br m, 2H), 0.95 (m, 2H)	{8-Chloro-5-cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

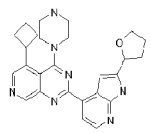
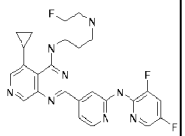
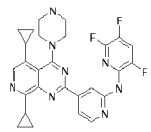
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2170		[B4]	LCMS : Purity: 95%, RT: min, MI: 523 (M+H)	1H-NMR: DMSO 10.02 (br s, 1H), 8.79 (m, 1H), 8.66 (s, 1H), 8.39 (m, 2H), 8.26 (d, 1H, J = 2.5 Hz), 8.03 (m, 1H), 7.96 (2H), 4.89 (m, 1H), 3.45 (m, 2H), 3.12 (m, 2H), 3.10 (s, 3H), 2.37 (m, 1H), 1.90-2.15 (br m, 4H), 1.14-1.29 (br m, 2H), 0.95 (m, 2H)	{8-Chloro-5-cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2171		[B4]	LCMS : Purity: 95%, RT: min, MI: 477 (M+H)	1H-NMR: DMSO 10.16 (s, 1H), 9.05-9.10 (m, 3H), 8.88 (s, 1H), 8.45 (m, 1H), 8.26 (d, 1H, J = 2.1 Hz), 8.20 (s, 1H), 8.10 (m, 1H), 8.02 (m, 1H), 3.94 (m, 4H), 3.34 (m 4H), 2.69 (m, 1H), 1.27 (m, 2H), 1.09 (m, 2H)	(5-Chloro-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2172		[B4]	LCMS : Purity: 95%, RT: min, MI: 490 (M+H)	1H-NMR: DMSO 10.48 (br s, 1H), 8.99 (s, 1H), 8.65 (s, 1H), 8.41 (d, 1H, J = 5.8 Hz), 8.30 (d, 1H, J = 2.4 Hz), 8.18 (s, 1H), 8.09 (m, 1H), 7.98 (m, 1H), 4.81 (m, 1H), 3.97 (m, 2H), 3.48 (m, 2H), 3.15 (s, 3H), 2.40 (m, 1H), 1.75-2.07 (br m, 4H), 1.23 (m, 2H), 0.98 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(tetrahydro-pyran-4-yl)-amine

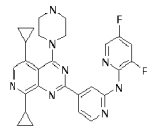
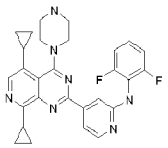
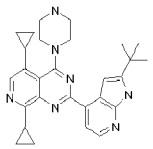
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2173		[B4]	LCMS : Purity: 95%, RT: min, MI: 530 (M+H)	1H-NMR: DMSO 10.73 (br s, 1H), 8.94 (s, 1H), 8.71 (s, 1H), 8.42 (d, 1H, J = 5.9 Hz), 8.29 (d, 1H, J = 2.5 Hz), 8.19 (s, 1H), 8.13 (m, 1H), 8.04 (m, 1H), 4.03 (m, 1H), 3.84 (m, 4H), 3.67 (m, 1H), 3.29 (m, 2H), 2.28 (m, 1H), 2.11 (m, 1H), 1.98 (m, 1H), 1.53 (m, 4H), 1.16-1.37 (br m, 4H), 1.03 (m, 1H), 0.94 (m, 1H)	(4-{5-Cyclopropyl-4-[3-(tetrahydro-pyran-4-yl)-pyrrolidin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(3,5-difluoro-pyridin-2-yl)-amine
2174		[B4]	LCMS : Purity: 95%, RT: min, MI: 489 (M+H)	1H-NMR: DMSO 10.09 (s, 1H), 9.08 (s, 1H), 8.73 (s, 1H), 8.59 (m, 1H), 8.53 (s, 1H), 8.50 (m, 1H), 8.41 (d, 1H, J = 5.5 Hz), 8.24 (d, 1H, J = 2.5 Hz), 8.05 (m, 1H), 7.95 (m, 1H), 7.69 (s, 1H), 3.24 (m, 2H), 3.17 (m, 2H), 2.74 (m, 2H), 2.64 (m, 1H), 2.06 (m, 2H), 1.75 (s, 3H), 1.22 (m, 2H), 1.16 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine
2175		[B4]	LCMS : Purity: 95%, RT: min, MI: 503 (M+H)	1H-NMR: DMSO 10.15 (br s, 1H), 9.09 (s, 1H), 9.07 (m, 1H), 8.63 (s, 1H), 8.52 (s, 1H), 8.41 (d, 1H, J = 5.6 Hz), 8.35 (m, 1H), 8.27 (d, 1H, J = 2.5 Hz), 8.05 (m, 2H), 7.67 (d, 1H, J = 8.7 Hz), 4.82 (m, 1H), 3.37 (m, 1H), 3.20 (m, 2H), 3.06 (m, 1H), 2.60 (m, 1H), 2.12 (m, 1H), 1.96 (m, 1H), 1.26 (m, 1H), 1.19 (s, 3H), 1.16 (m, 3H), 1.11 (s, 3H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

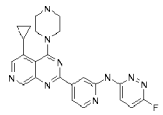
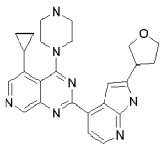
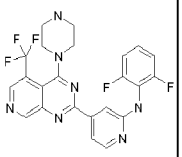
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2176		[B4]	LCMS: Purity: 95%, RT: min, MI: 521 (M+H)	1H-NMR: DMSO 9.72 (s, 1H), 9.06 (s, 1H), 8.99 (m, 1H), 8.58 (s, 1H), 8.51 (s, 1H), 8.40 (m, 1H), 8.27 (m, 2H), 8.00 (m, 1H), 7.64 (d, 1H, J = 8.8 Hz), 4.81 (m, 1H), 3.32 (m, 1H), 3.22 (m, 1H), 3.19 (m, 1H), 3.01 (m, 1H), 2.59 (m, 1H), 2.14 (m, 1H), 1.95 (m, 1H), 1.25 (m, 1H), 1.19 (s, 3H), 1.14 (m, 3H), 1.09 (s, 3H)	{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine
2177		[B4]	LCMS: Purity: 92%, RT: min, MI: 492.26 (MH)+	(400 MHz, d6-DMSO,δ): 9.06 (s, 1H), 8.85 (br s, 2H), 8.20 (s, 1H), 8.16 (d, J=6.0 Hz, 1H), 7.61 (br s, 1H), 7.34-7.20 (m, 4H), 5.62-5.55 (m, 1H), 3.88 (br s, 4H), 3.31 (br s, 4H), 2.70-2.63 (m, 1H), 1.85-1.79 (m, 1H), 1.40 (s, 3H), 1.28-1.23 (m, 6H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-dimethyl-indan-1-yl)-amine
2178		[B4]	LCMS: Purity: 99%, RT: min, MI: 513 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.79 (1 H, s), 8.65 - 9.06 (3 H, m), 8.41 - 8.51 (1 H, m), 8.20 - 8.36 (1 H, m), 7.90 - 8.04 (2 H, m), 3.98 (4 H, br. s.), 3.30 (4 H, br. s.), 2.56 - 2.65 (1 H, m), 1.19 - 1.28 (2 H, m), 1.00 - 1.10 (2 H, m)	[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine
2179		[D4],[D3]	LCMS: Purity: 96%, RT: min, MI: 467.21	(dmso-d6) 12.45 (d, J = 1.4 Hz, 1H), 9.13 (s, 1H), 8.96 (br s, 2H), 8.62 (m, 1H), 8.51 (d, J = 5.0 Hz, 1H), 8.20 (m, 3H), 7.93 (m, 1H), 7.53 (m, 1H), 3.98 (br s, 4H), 3.38 (br s, 4H), 2.76 (m, 1H), 1.28 (m, 2H), 1.11 (m, 2H)	5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

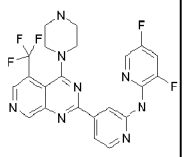
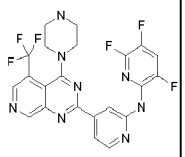
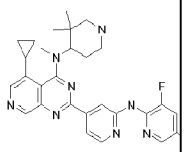
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2180		[D4],[D3]	LCMS: Purity: 96%, RT: min, MI: 481.22 (M+H)	(dmso-d6) 12.45 (d, J = 1.5 Hz, 1H), 9.20 (s, 1H), 8.99 (br s, 1H), 8.89 (br s, 1H), 8.81 (s, 1H), 8.61 (m, 1H), 8.51 (d, J = 5.0 Hz, 1H), 8.19 (d, J = 5.0 Hz, 1H), 8.17 (m, 1H), 7.93 (m, 1H), 7.53 (m, 1H), 4.30 (m, 1H), 3.87 (m, 4H), 3.35 (m, 4H), 2.47 (m, 2H), 2.24 (m, 2H), 2.12 (m, 1H), 1.93 (m, 1H)	5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2181		[D4],[D3]	Method 5: RT: 3.27 min, MI: 516 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.86 (brs, 1H), 9.19 (s, 1H), 8.97 (brs, 1H), 8.82 (brs, 1H), 8.77 (s, 1H), 8.28 (d, 1H), 8.06 (d, 1H), 7.53-7.40 (m, 2H), 7.38-7.30 (m, 2H), 7.25-7.15 (m, 2H), 4.27 (q, 1H), 3.90-3.56 (m, 5H), 3.40-3.20 (m, 4H), 3.08 (m, 1H), 2.97-2.85 (m, 2H), 2.78-2.67 (m, 2H), 2.27-2.16 (m, 2H), 2.14-2.03 (m, 2H), 1.95-1.87 (m, 2H).	5-Cyclobutyl-2-[2-(1-phenyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2182		[D4],[D3]	Method 5: RT: 2.98 min, MI:496 [M+H]	1H NMR (500 MHz, d6-DMSO) 12.11 (brs, 1H), 9.25 (s, 1H), 9.07 (brs, 1H), 8.92 (brs, 1H), 8.79 (s, 1H), 8.43 (d, 1H), 8.12 (d, 1H), 7.46 (d, 1H), 4.28 (q, 1H), 3.99-3.70 (m, 4H), 3.45-3.20 (m, 4H), 2.52-2.42 (m, 2H), 2.28-2.16 (m, 2H), 2.10 (m, 1H), 1.92 (m, 1H), 1.69 (s, 6H).	5-Cyclobutyl-4-piperazin-1-yl-2-[2-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine

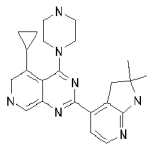
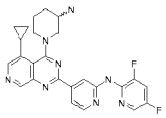
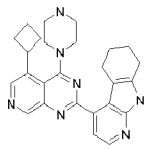
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2183		[D4],[D3]	Method 5: RT: 3.06min, MI: 508 [M+H]	1H NMR (d6-DMSO, 600MHz) 12.20 (brs, 1H), 9.25 (s, 1H), 8.98 (brs, 1H), 8.84 (brs, 1H), 8.80 (s, 1H), 8.43 (d, 1H), 8.14 (d, 1H), 7.49 (d, 1H), 4.29 (q, 1H), 3.98-3.71 (m, 4H), 3.46-3.21 (m, 4H), 2.84-2.59 (m, 4H), 2.50-2.41 (m, 2H), 2.30-2.18 (m, 2H), 2.18-2.00 (m, 3H), 1.93 (m, 1H).	5-Cyclobutyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine
2184		[D4],[D3]	Method 5: RT: 5.02min, MI: 456 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.80 (1H, s), 9.05 (1H, s), 8.29 (1H, d, J = 5.0 Hz), 8.08 (1H, s), 8.06 (1H, d, J = 5.0 Hz), 7.28 (1H, d, J = 1.3 Hz), 4.13 (1H, t, J = 7.6 Hz), 3.98 - 3.93 (1H, m), 8.89 - 8.84 (1H, m), 3.80 - 3.77 (1H, t, J = 7.7 Hz), 3.68 - 3.61 (1H, m), 3.92 - 3.50 (4H very broad s), 2.89 (4H, s), 2.71 - 2.65 (1H, m), 2.42 - 2.35 (1H, m), 2.21 - 2.14 (1H, m), 1.28 - 1.24 (2H, m), 1.05 - 1.02 (2H, m).	5-Cyclobutyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine

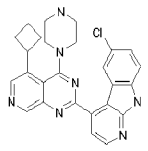
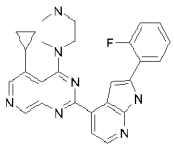
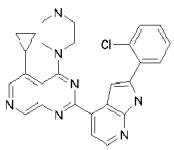
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2185		[D4],[D3]	Method 5: RT: 2.51min, MI: 456 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.82 (1H, s), 9.13 (1H, s), 8.70 (1H, s), 8.32 (1H, d, J = 4.9 Hz), 8.06 (1H, d, J = 4.9 Hz), 7.33 (1H, d, J = 1.7 Hz), 5.09 (1H, t, J = 6.8 Hz), 4.32 - 4.25 (1H, m), 4.03 - 3.98 (1H, m) 3.87 - 3.82 (1H, m), 3.68 (2H, br s), 3.51 (2H, br s), 2.94 (2H, br s), 2.87 (2H, br s), 2.38 - 2.28 (1H, m), 2.23 - 2.15 (2H, m), 2.12 - 1.96 (5H, m), 1.93 - 1.89 (1H, m).	5-Cyclobutyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine
2186		[B4]	LCMS: Purity: 95%, RT: min, MI: 493 (M+H)	1H-NMR: DMSO 9.97 (br s, 1H), 9.21 (m, 1H), 9.12 (s, 1H), 8.79 (m, 1H), 8.62 (s, 1H), 8.54 (s, 1H), 8.39 (d, 1H, J = 5.5 Hz), 8.28 (d, 1H, J = 2.5 Hz), 8.02 (m, 3H), 5.37-5.44 (br m, 1H), 4.85-4.96 (br m, 1H), 3.77 (m, 1H), 3.40-3.63 (br m, 2H), 3.27 (m, 1H), 2.59 (m, 1H), 2.33 (m, 1H), 2.07 (m, 1H), 1.21 (m, 2H), 1.13 (m, 2H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3-fluoro-piperidin-4-yl)-amine
2187		[B4]	LCMS: Purity: 95%, RT: min, MI: 519 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.76 (1 H, s), 9.05 (1 H, s), 8.86 (2 H, br. s.), 8.46 (1 H, d, J=5.0 Hz), 8.20 - 8.35 (1 H, m), 7.95 - 8.05 (2 H, m), 3.74 - 4.06 (4 H, m), 3.49 - 3.63 (1 H, m), 3.31 (4 H, br. s.), 2.57 - 2.70 (1 H, m), 1.05 - 1.25 (6 H, m), 0.90 - 1.03 (2 H, m)	[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine

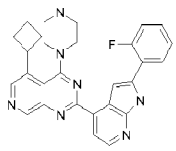
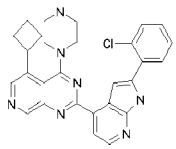
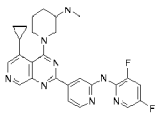
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2188		[B4]	LCMS : Purity: 90%, RT: min, MI: 501 (M+H)	1H NMR (400 MHz, DMSO-d6) 9.84 (1 H, br. s.), 8.63 - 9.04 (3 H, m), 8.41 (1 H, d, J=5.0 Hz), 8.25 (1 H, d, J=2.5 Hz), 7.92 - 8.09 (3 H, m), 3.90 (4 H, br. s.), 3.47 - 3.58 (1 H, m), 3.32 (4 H, br. s.), 2.57 - 2.65 (1 H, m), 1.05 - 1.26 (6 H, m), 0.90 - 1.00 (2 H, m)	[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine
2189		[B4]	LCMS : Purity: 90%, RT: min, MI: 500 (M+H)	1H NMR (400 MHz, DMSO-d6) 8.83 (2 H, s), 8.19 (1 H, d, J=5.3 Hz), 8.00 (1 H, s), 7.88 (1 H, s), 7.73 (1 H, dd, J=5.4, 1.4 Hz), 7.23 - 7.34 (1 H, m), 7.11 - 7.21 (2 H, m), 3.85 - 3.96 (4 H, m), 3.46 - 3.49 (1 H, m), 3.30 (4 H, br. s.), 2.57 - 2.65 (1 H, m), 1.05 - 1.23 (6 H, m), 0.96 (2 H, m)	[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine
2190		[D4],[D3]	LCMS : Purity: 95%, RT: min, MI: 468 (M+H)	1H NMR (400 MHz, DMSO-d6) 11.80 (1 H, d, J=1.8 Hz), 8.48 - 9.20 (2 H, m), 8.32 (1 H, d, J=5.0 Hz), 8.12 (1 H, d, J=5.0 Hz), 8.00 (1 H, s), 7.24 (1 H, d, J=2.3 Hz), 3.71 - 4.20 (4 H, m), 3.47 - 3.59 (1 H, m), 3.34 (4 H, br. s.), 2.63 - 2.76 (1 H, m), 1.41 (9 H, s), 1.10 - 1.28 (6 H, m), 0.89 - 1.00 (2 H, m)	2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5,8-dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

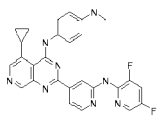
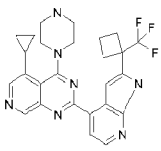
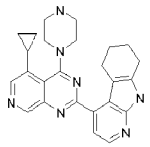
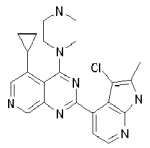
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2191		[B4]	Method 5: RT: 1.86 min, MI: 444 [M+H]	1H NMR (500MHz, DMSO) 9.08 (1H, s), 9.07 (1H, s), 8.76 (1H, s), 8.46 (1H, d), 8.35 (1H, m), 8.19 (1H, s), 7.93 (1H, dd), 7.63 (1H, dd), 7.43 (2H, dd), 7.17 (2H, m), 3.95 (4H, br s), 3.33 (4H, s), 2.69 (1H, m), 1.25 (2H, m), 1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridazin-3-yl)-amine
2192		[D4],[D3]	Method 5: RT: 3.08 min, MI: 442 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.80 (1H, s), 9.05 (1H, s), 8.29 (1H, d, J = 5.0 Hz), 8.08 (1H, s), 8.06 (1H, d, J = 5.0 Hz), 7.28 (1H, d, J = 1.3 Hz), 4.13 (1H, t, J = 7.6 Hz), 3.98 - 3.93 (1H, m), 8.89 - 8.84 (1H, m), 3.80 - 3.77 (1H, t, J = 7.7 Hz), 3.68 - 3.61 (1H, m), 3.92 - 3.50 (4H very broad s), 2.89 (4H, s), 2.71 - 2.65 (1H, m), 2.42 - 2.35 (1H, m), 2.21 - 2.14 (1H, m), 1.28 - 1.24 (2H, m), 1.05 - 1.02 (2H, m).	5-Cyclopropyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine
2193		[B1]	LCMS: Purity: 90%, RT: min, MI: 488 (M+H)+	TFA Salt 1H NMR (400 MHz, DMSO-d6) δ ppm 9.55 (br. s, 1 H) 9.05 (br. s, 1 H) 8.79 - 8.87 (m, 2 H) 8.21 (d, J=5.3 Hz, 1 H) 7.82 (s, 1 H) 7.69 (dd, J=5.3, 1.3 Hz, 1 H) 7.23 - 7.35 (m, 1 H) 7.10 - 7.22 (m, 2 H) 3.51 - 4.03 (m, 9 H)	(2,6-Difluoro-phenyl)-[4-(4-piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine

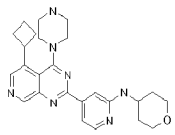
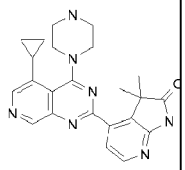
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2194		[B1]	LCMS : Purity: 90%, RT: min, MI: 489 (M+H) +	TFA Salt 1H NMR (400 MHz, DMSO-d6) δ ppm 9.65 - 9.72 (m, 1 H) 9.58 (s, 1 H) 9.06 (s, 1 H) 8.80 - 8.98 (m, 2 H) 8.76 (br. s., 1 H) 8.38 - 8.47 (m, 1 H) 8.27 (br. s., 1 H) 7.99 (t, J=8.4 Hz, 1 H) 7.87 - 7.94 (m, 1 H) 3.70 - 4.04 (m, 8 H)	(3,5-Difluoro-pyridin-2-yl)-[4-(4-piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine
2195		[B1]	LCMS : Purity: 90%, RT: min, MI: 507 (M+H) +	TFA Salt 1H NMR (400 MHz, DMSO-d6) δ ppm 9.79 - 9.83 (m, 1 H) 9.56 (s, 1 H) 9.04 - 9.07 (m, 1 H) 8.82 - 8.93 (m, 2 H) 8.78 - 8.81 (m, 1 H) 8.47 (d, J=5.0 Hz, 1 H) 8.23 - 8.33 (m, 1 H) 7.96 (dd, J=5.3, 1.5 Hz, 1 H) 3.70 - 4.12 (m, 9 H)	[4-(4-Piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine
2196		[B4]	LCMS : Purity: 95%, RT: min, MI: 517 (M+H)	1H-NMR: DMSO 10.42 (br s, 1H), 9.14 (br m, 1H), 9.01 (s, 1H), 8.61 (br m, 1H), 8.41 (d, 1H, J = 5.7 Hz), 8.30 (br m, 1H), 8.28 (d, 1H, J = 2.4 Hz), 8.16 (s, 1H), 8.07 (m, 2H), 5.56 (m, 1H), 3.45 (m, 1H), 3.30 (m, 2H), 3.16 (s, 3H), 2.78 (m, 1H), 2.41 (m, 1H), 2.22 (m, 1H), 1.91 (m, 1H), 0.98-1.47 (br m, 10H)	{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2197		[D3]	LCMS: Purity: 90%, RT: min, MI: 402 (M+H)+	NH protons coalesced with water. 1H NMR (400 MHz, CHLOROFORM-d) δ ppm 9.10 (s, 1 H) 8.04 (s, 1 H) 7.95 (d, J=4.5 Hz, 1 H) 7.53 (d, J=5.5 Hz, 1 H) 7.27 (s, 1 H) 4.83 (br. s., 1 H) 3.54 - 3.92 (m, 4 H) 3.48 (s, 2 H) 3.04 (t, J=4.8 Hz, 4 H) 2.73 (tt, J=8.5, 5.2 Hz, 1 H) 1.40 (s, 6 H) 0.98 - 1.05 (m, 2 H) 0.85 - 0.91 (m, 2 H)	5-Cyclopropyl-2-(2,2-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2198		[B4]	LCMS: Purity: 95%, RT: min, MI: 475 (M+H)	1H-NMR: DMSO 10.23 (br s, 1H), 9.05 (s, 1H), 8.73 (s, 1H), 8.42 (d, 1H, J = 5.6 Hz), 8.29 (d, 1H, J = 2.4 Hz), 8.19 (s, 1H), 8.08 (br m, 4H), 4.44 (m, 1H), 4.07-4.23 (br m, 2H), 3.22-3.47 (br m, 3H), 2.67 (m, 1H), 2.07 (m, 1H), 1.84 (m, 1H), 1.61 (m, 1H), 1.26 (m, 2H), 1.05 (m, 2H)	{4-[4-(3-Amino-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine
2199		[D3], [D9]	Method 5: RT: 3.31 min, MI:440 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.59 (brs, 1H), 9.15 (s, 1H), 9.04 (brs, 1H), 8.91 (brs, 1H), 8.79 (s, 1H), 8.11 (d, 1H), 7.58 (d, 1H), 4.32-4.21 (m, 1H), 3.89-3.63 (m, 4H), 3.39-3.19 (m, 4H), 2.78-2.70 (m, 2H), 2.64-2.52 (m, 2H), 2.28-2.16 (m, 2H), 2.15-2.02 (m, 1H), 1.97-1.87 (m, 1H), 1.85-1.72 (m, 2H), 1.70-1.54 (m, 2H).	4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole

Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2200		[D3]	LCMS : Purity: 98%, RT: min, MI: 470 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 12.30 (s, 1H), 9.22 (s, 1H), 9.06 (d, 1H, J = 2.1 Hz), 8.90 (br s, 2H), 8.86 (s, 1H), 8.65 (d, 1H, J = 5.1 Hz), 8.03 (5.1 Hz), 7.58 (d, 1H, J = 8.6 Hz), 7.54 (dd, 1H, J = 2.1, 8.6 Hz), 4.30 (pent, 1H, J = 8.6 Hz), 3.86 (m, 4H), 3.2-3.4 (m, 4H), 2.28 (m, 2H), 2.14 (m, 1H), 1.94 (m, 1H)	6-Chloro-4-(5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole
2201		[D4],[D3]	LCMS : Purity: 95%, RT: min, MI: 410.0 (MH)+	(dmso-d6) 12.40 (d, J = 1.7 Hz, 1H), 9.14 (s, 1H), 8.95 (br s, 2H), 8.46 (d, J = 5.0 Hz, 1H), 8.18 (m, 2H), 8.10 (m, 1H), 7.98 (m, 1H), 7.52-7.35 (m, 3H), 3.98 (br s, 4H), 3.38 (br s, 4H), 2.76 (m, 1H), 1.27 (m, 2H), 1.10 (m, 2H)	5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2202		[D4],[D3]	LCMS : Purity: 95%, RT: min, MI: 466.22 (M+H)	(dmso-d6) 12.32 (d, J = 1.7 Hz, 1H), 9.14 (s, 1H), 8.94 (br s, 2H), 8.47 (d, J = 5.0 Hz, 1H), 8.19 (d, J = 5.0 Hz, 1H), 8.19 (s, 1H), 7.94 (d, J = 2.2 Hz, 1H), 7.85 (dd, J = 7.7, 1.7 Hz, 1H), 7.67 (dd, J = 7.8, 1.4 Hz, 1H), 7.55-7.45 (m, 2H), 3.96 (br s, 4H), 3.37 (br s, 4H), 2.76 (m, 1H), 1.27 (m, 2H), 1.10 (m, 2H)	2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2203		[D4],[D3]	LCMS: Purity: 97%, RT: min, MI: 482.18 (M+H)	(dmso-d6) 12.40 (s, 1H), 9.22 (s, 1H), 9.00 (br s, 1H), 8.89 (br s, 1H), 8.80 (s, 1H), 8.46 (d, J = 5.0 Hz, 1H), 8.17 (d, J = 5.0 Hz, 1H), 8.10 (m, 1H), 7.96 (m, 1H), 7.52-7.36 (m, 3H), 4.30 (m, 1H), 3.87 (m, 4H), 3.35 (m, 4H), 2.48 (m, 2H), 2.24 (m, 2H), 2.11 (m, 1H), 1.93 (m, 1H)	5-Cyclobutyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2204		[D4],[D3]	LCMS: Purity: 97%, RT: min, MI: 480.22 (M+H)	(dmso-d6) 12.32 (d, J = 1.7 Hz, 1H), 9.22 (s, 1H), 8.98 (br s, 1H), 8.85 (br s, 1H), 8.80 (s, 1H), 8.46 (d, J = 5.0 Hz, 1H), 8.18 (d, J = 5.0 Hz, 1H), 7.92 (d, J = 2.2 Hz, 1H), 7.84 (dd, J = 7.6, 1.8 Hz, 1H), 7.67 (dd, J = 7.9, 1.6 Hz, 1H), 7.56-7.44 (m, 2H), 4.30 (m, 1H), 3.84 (m, 4H), 3.34 (m, 4H), 2.47 (m, 2H), 2.24 (m , 2H), 2.11 (m, 1H), 1.93 (m, 1H)	2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2205		[B4]	LCMS: Purity: 95%, RT: min, MI: 489 (M+H)	1H-NMR: DMSO 10.08 (br s, 1H), 9.05 (s, 1H), 8.70 (br m, 3H), 8.40 (d, 1H, J = 5.5 Hz), 8.29 (d, 1H, J = 2.2 Hz), 8.18 (s, 1H), 8.00 (m, 2H), 4.56 (br m, 1H), 4.18 (br m, 1H), 3.50 (m, 2H), 3.16 (m, 1H), 2.63 (s, 3H), 2.54 (m, 1H), 2.12 (m, 1H), 1.82 (m, 1H), 1.64 (m, 2H), 1.25 (m, 2H), 1.05 (m, 2H)	{4-[5-Cyclopropyl-4-(3-methylamino-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine

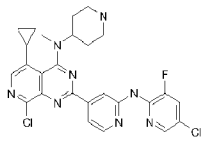
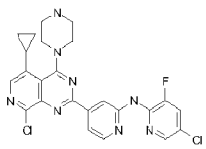
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2206		[B4]	LCMS : Purity: 95%, RT: min, MI: 497 (M+H)	1H-NMR: DMSO 10.38 (br s, 1H), 9.66 (s, 1H), 9.09 (s, 1H), 8.67 (s, 1H), 8.55 (s, 1H), 8.43 (d, 1H, J = 5.7 Hz), 8.22 (d, 1H, J = 2.5 Hz), 8.10 (m, 1H), 7.94 (m, 1H), 7.76 (m, 2H), 6.77 (m, 2H), 2.79 (m, 1H), 2.76 (s, 3H), 1.30 (m, 2H), 1.14 (m, 2H)	N-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N'-methyl-benzene-1,4-diamine
2207		[D4],[D3]	Method 5: RT: 2.87 min, MI: 494 [M+H]	1H NMR (500 MHz, d6-DMSO) 12.17 (brs, 1H), 9.17 (s, 1H), 8.89 (brs, 2H), 8.42 (t, 1H), 8.17 (d, 1H), 8.14 (t, 1H), 7.49 (s, 1H), 4.21-3.56 (m, 6H), 2.82-2.64 (m, 6H), 2.17-1.98 (m, 3H), 1.34-1.20 (m, 2H), 1.14-1.03 (m, 2H).	5-Cyclopropyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine
2208		[D3], [D9]	Method 5: RT: 2.88 min, MI:426 [M+H]	1H NMR (500 MHz, d6-DMSO) 11.53 (s, 1H), 9.06 (s, 1H), 8.21 (d, 1H), 8.17 (s, 1H), 7.56 (d, 1H), 4.09-3.61 (m, 4H), 3.35-3.28 (m, 4H), 2.78-2.68 (m, 3H), 2.64-2.58 (m, 2H), 1.85-1.77 (m, 2H), 1.69-1.61 (m, 2H), 1.30-1.23 (m, 2H), 1.12-1.07 (m, 2H).	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole
2209		[D4],[D3], [D7]	Method 5: RT: 3.45 min, MI: 474 [M+H]	1H NMR (500 MHz, d6-DMSO) 8.96 (1H, s), 8.59 (1H, d), 8.13 (1H, s), 7.57 (1H, d), 3.89-3.46 (4H, m), 2.84 (4H, s), 2.71-2.59 (1H, m), 1.29-1.24 (2H, m), 1.06-1.01 (2H, m).	2-(3-Chloro-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

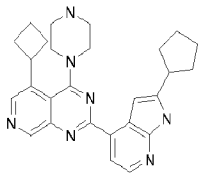
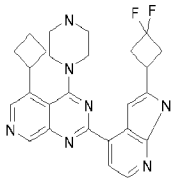
Ex	Structure	Scheme	Analysis		Name
			LCMS	1H-NMR	
2210		[B4]	Method 5: RT: 1.44 min, MI:446 [M+H]	1H NMR (500MHz, DMSO) 9.07 (1H, s), 8.74 (1H, s), 8.12 (1H, d), 7.54 (1H, s), 7.42 (1H, dd), 6.79 (1H, d), 4.24 (1H, m), 3.98 (1H, m), 3.89 (2H, m), 3.78-3.67 (4H, m), 3.42 (2H, m), 3.19 (2H, m), 3.09 (2H, m), 2.46 (2H, m). 2.19 (2H, m), 2.09 (1H, m), 1.90 (3H, m), 1.46 (2H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(tetrahydro-pyran-4-yl)-amine
2211		[D3], [D10]	Method 5: RT: 2.71 min, MI:416 [M+H]	1H NMR (300 MHz, DMSO-d6) d 11.20 (s, 1H), 9.08 (s, 1H), 8.94 (bs, 2H), 8.25 (d, J = 5.5 Hz, 1H), 8.21 (s, 1H), 7.80 (d, J = 5.5 Hz, 1H), 3.86 (bs, 4H), 3.32 (bs, 4H), 2.73–2.64 (m, 1H), 1.55 (s, 6H), 1.31–1.19 (m, 2H), 1.14 – 1.04 (m, 2H)	4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-3,3-dimethyl-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one

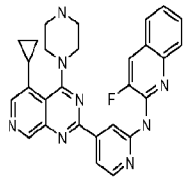
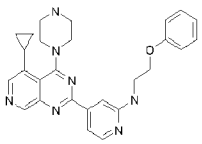
General synthesis of 2-substituted-azaindole derivatives of general formula [I-034] Scheme D5

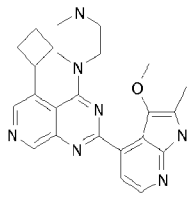
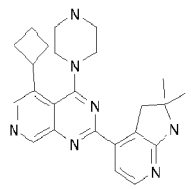
The 2-substituted azaindole derivatives of general formula [I-034] were prepared by the reaction of a 1-benzenesulfonyl-4-bromo-1H-pyrrolo[2,3-b]pyridine derivative of general formula [I-030] in a palladium catalysed cross coupling reaction with a palladium catalyst such as $PdCl_2dppf:CH_2Cl_2$, a cyanide reagent such as $Zn(CN)_2$, zinc dust, in a polar aprotic solvent such as DMF at high temperature either by heating thermally or using a microwave reactor. The crude product was purified by column chromatography. The 1-benzenesulfonyl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile derivative of general formula [I-031] was then reacted with a strong base such as LDA in a polar aprotic solvent such as THF at a low reaction temperature such as -78 °C with an electrophile such as a ketone, a disulfide or a halogenating agent such as NIS or NCS of general formula [I-035] to yield the 2-substituted 1-benzenesulfonyl-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile derivative of general formula [I-032] following reaction work up, typically by a liquid-liquid extraction and purification by column chromatography. The intermediate of general formula [I-032] was deprotected by reaction with fluoride reagent such as TBAF in a polar aprotic solvent such as THF to yield the reaction intermediate of general formula [I-033]. The reaction intermediate of general formula [I-033] was then reacted with hydroxylamine (50% wt/wt in water) and a polar protic solvent such as EtOH at elevated temperature. The intermediate N-Hydroxy-1H-pyrazolo[3,4-b]pyridine-4-carboxamidine was then subjected

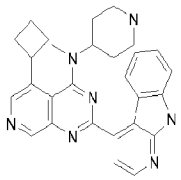
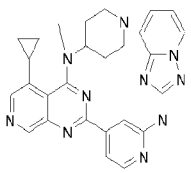
5

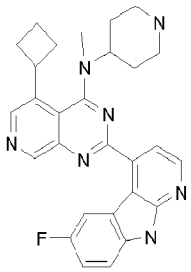
Ex	Structure	Scheme	Analysis		Name
2301		[B4]	540 (M+H)	1H-NMR: DMSO 9.98 (br s, 1H), 8.77 (s, 1H), 8.74 (m, 1H), 8.44 (d, 1H, J = 5.3 Hz), 8.33 (m, 1H), 8.22 (d, 1H, J = 2.1 Hz), 8.05 (m, 1H), 7.99 (m, 1H), 7.96 (s, 1H), 4.88 (m, 1H), 3.45 (m, 2H), 3.12 (m, 2H), 3.10 (s, 3H), 2.37 (m, 1H), 1.90-2.14 (br m, 4H), 1.09-1.30 (br m, 2H), 0.94 (m, 2H)	4-({8-Chloro-2-[2-(5-chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidine di-trifluoroacetate
2302		[B4]	512 (M+H)	1H-NMR: DMSO 9.88 (s, 1H), 9.00 (br m, 1H), 8.92 (s, 1H), 8.89 (br m, 1H), 8.47 (m, 1H), 8.22 (d, 1H, J = 2.2 Hz), 8.04 (m, 1H), 7.98 (m, 1H), 7.96 (s, 1H), 3.96 (m, 4H), 3.31 (m, 4H), 2.61 (m, 1H), 1.23 (m, 2H), 1.05 (m, 2H)	4-{8-Chloro-2-[2-(5-chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-piperazine di-trifluoroacetate

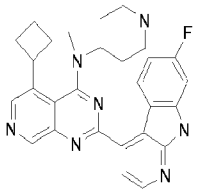
2305		[D3], [D4]	454.28 (M+H)	(dmso-d6) 11.84 (s, 1H), 9.24 (s, 1H), 9.11 (br s, 1H), 8.96 (br s, 1H), 8.79 (s, 1H), 8.30 (d, J = 5.2 Hz, 1H), 8.08 (d, J = 5.2 Hz, 1H), 7.20 (d, J = 1.6 Hz, 1H), 4.29 (m, 1H), 3.84 (m, 4H), 3.33 (m, 4H), 3.28 (m, 1H), 2.48 (m, 2H), 2.22 (m, 2H), 2.19-2.05 (m, 3H), 1.98-1.87 (m, 1H), 1.87-1.62 (m, 6H))	5-Cyclobutyl-2-(2-cyclopentyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2306		[D3], [D4]	Method 6: RT: 2.78 min, MI: 476.19 [M+H]	^{1}H NMR (500MHz, DMSO) 11.96 (1H, brs), 9.26 (1H, s), 9.00 (1H, brs), 8.87 (1H, brs), 8.78 (1H, s), 8.33 (1H, d), 8.10 (1H, d), 7.33 (1H, d), 4.28 (1H, q), 3.97-3.69 (4H, m), 3.65 (1H, m), 3.44-3.23 (4H, m), 3.15-3.00 (2H, m), 3.00-2.86 (2H, m), 2.28-2.16 (2H, m), 2.11 (1H, m), 1.90 (1H, m)	5-Cyclobutyl-2-[2-(3,3-difluoro-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

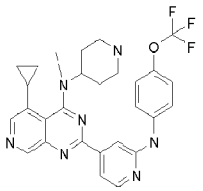
2311		[B4]	493.22 (MH)+	(400 MHz, d6-DMSO,δ): 10.22 (br s, 1H), 9.49 (s, 1H), 9.14 (s, 1H), 8.91 (br s, 2H), 8.59 (d, J=5.4 Hz, 1H), 8.26 (d, J=11.6 Hz, 1H), 8.23 (s, 1H), 8.13 (d, J=5.5 Hz, 1H), 7.99 (d, J=7.7 Hz, 1H), 7.91 (d, J=8.1 Hz, 1H), 7.77-7.73 (m, 1H), 7.53 (t, J=7.6 Hz, 1H), 4.30-3.60 (m, 4H), 3.36 (br s, 4H), 2.76-2.68 (m, 1H), 1.30-1.25 (m, 2H), 1.13-1.08 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-quinolin-2-yl)-amine
2312		[B4]	468.24 (MH)+	(400 MHz, d6-DMSO,δ): 9.07 (s, 1H), 8.96 (br s, 2H), 8.21 (s, 1H), 8.12 (d, J=6.3 Hz, 1H), 8.02 (s, 1H), 7.67 (d, J=5.9 Hz, 1H), 7.34-7.28 (m, 2H), 7.00-6.93 (m, 3H), 4.22 (t, J=5.2 Hz, 2H), 3.92 (br s, 4H), 3.81 (br s, 2H), 3.32 (br s, 4H), 2.70-2.62 (m, 1H), 1.29-1.23 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-phenoxy-ethyl)-amine

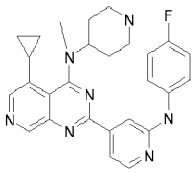
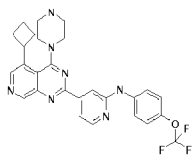
2315		[D3], [D9]	Method 5: RT: 2.86 min, MI: 430 [M+H]	^{1}H NMR (500MHz, DMSO) 11.46 (s, 1H), 9.14 (s, 1H), 8.90 (brs, 1H), 8.82 (brs, 1H), 8.74 (s, 1H), 8.23 (d, 1H), 7.56 (d, 1H), 4.30-4.23 (m, 1H), 3.86-3.63 (m, 4H), 3.29 (s, 3H), 3.3.-3.18 (m, 4H), 2.25 (s, 3H), 2.25-2.06 (m, 4H), 1.95-1.85 (m, 2H).	5-Cyclobutyl-2-(3-methoxy-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2316		[D3],	416 (M+H)+	1H NMR (400 MHz, DMSO-d6) δ ppm 7.77 (s, 1 H) 6.57 (d, J=5.5 Hz, 1 H) 6.13 (d, J=5.8 Hz, 1 H) 5.87 (s, 1 H) 3.27 (br. s., 1 H) 2.91 (quin, J=8.7 Hz, 1 H) 2.29 (d, J=2.5 Hz, 2 H) 2.09 (d, J=4.8 Hz, 5 H) 1.65 (d, J=17.8 Hz, 5 H) 1.05 - 1.20 (m, 2 H) 0.53 - 0.89 (m, 6 H) 0.39 - 0.51 (m, 3 H)	5-Cyclobutyl-2-(2,2-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

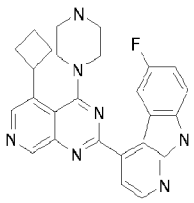
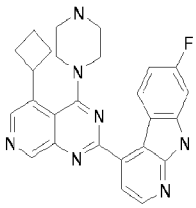
2317		[D3],	464 (M+ H)	1H-NMR: DMSO 12.07 (s, 1H), 9.15 (s, 1H), 8.74 (m, 2H), 8.62 (m, 1H), 8.58 (d, 1H, J = 5.0 Hz), 8.29 (m, 1H), 7.90 (d, 1H, J = 5.0 Hz), 7.53 (m, 1H), 7.48 (m, 1H), 7.18 (m, 1H), 4.80 (m, 1H), 4.23 (m, 1H), 3.46 (m, 1H), 3.34 (m, 1H), 3.12 (m, 1H), 3.01 (s, 3H), 2.98 (m, 1H), 2.67 (m, 1H), 2.22-2.42 (br m, 4H), 2.09 (m, 2H), 1.92 (m, 3H)	4-{[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin- 4-yl]-methyl-amino)-piperidine
2318		[B4]	493.27 (MH)+	(400 MHz, d6-DMSO,δ): 10.75 (br s, 1H), 9.06 (s, 1H), 9.01 (s, 1H), 8.91 (d, J=6.7 Hz, 1H), 8.70-8.63 (m, 1H), 8.45 (d, J=5.6 Hz, 1H), 8.35-8.19 (m, 2H), 7.95 (d, J=5.4 Hz, 1H), 7.74-7.65 (m, 2H), 7.16 (t, J=6.6 Hz, 1H), 4.90-4.82 (m, 1H), 3.48-3.40 (m, 2H), 3.18-3.05 (m, 5H), 2.51-2.43 (m, 1H), 2.09 (br s, 4H), 1.25 (br s, 2H), 0.99 (br s, 2H).	{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

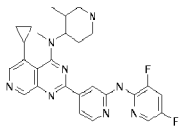
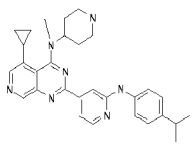
2319		[D3],	482 (M+ H)	1H-NMR (DMSO-d6, 400 MHz): 12.15 (s, 1H), 9.14 (s, 1H), 8.74 (s, 1H), 8.60-8.75 (m, 3H), 8.28 (m, 1H), 7.98 (d, 1H, J = 5.1 Hz), 7.56 (dd, 1H, J = 4.8, 8.8 Hz), 7.38 (ddd, 1H, J = 2.7, 9.0, 9.0 Hz), 4.81 (m, 1H), 4.23 (m, 1H), 3.47 (m, 1H), 3.38 (m, 1H), 3.16 (m, 1H), 3.05 (m, 1H), 3.02 (s, 3H), 2.67 (m, 1H), 2.42 (m, 1H), 2.15-2.30 (m, 3H), 2.09 (m, 2H), 1.91 (m, 3H)	5-cyclobutyl-2-(6-fluoro-9H-pyrido[2,3-b]indol-4-yl)-N-methyl-N-(4-piperidyl)pyrido[3,4-d]pyrimidin-4-amine

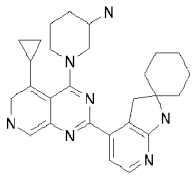
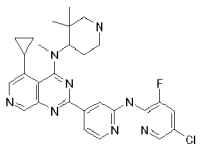
2321		[D3],	482 (M+H)	1H-NMR (DMSO-d6, 400 MHz): 12.20 (s, 1H), 9.18 (s, 1H), 8.96 (dd, 1H, J = 5.9, 8.9 Hz), 8.74 (s, 1H), 8.62 (br m, 1H), 8.57 (d, 1H, J = 5.1 Hz), 8.26 (br m, 1H), 7.99 (d, 1H, J = 5.1 Hz), 7.28 (dd, 1H, J = 2.5, 9.6 Hz)) 7.08 (ddd, 1H, J = 2.5, 9.5, 9.5 Hz), 4.81 (m, 1H), 4.23 (m, 1H), 3.47 (m, 1H), 3.38 (m, 1H), 3.16 (m, 1H), 3.05 (m, 1H), 3.00 (s, 3H), 2.67 (m, 1H), 2.42 (m, 1H), 2.15-2.30 (m, 3H), 2.09 (m, 2H), 1.91 (m, 3H)	[5-Cyclobutyl-2-(7-fluoro-9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine

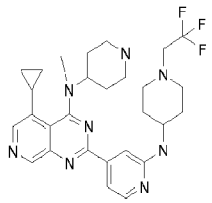
2322		[B4]	536.20 (MH)+	(400 MHz, d6-DMSO,δ): 9.60 (s, 1H), 8.98 (s, 1H), 8.76-8.69 (m, 1H), 8.35 (d, J=5.3 Hz, 1H), 8.31 (br s, 1H), 8.18 (s, 1H), 7.93 (s, 1H), 7.88-7.83 (m, 2H), 7.76 (dd, J=5.4, 1.3 Hz, 1H), 7.30 (d, J=8.5 Hz, 2H), 4.89-4.80 (m, 1H), 3.50-3.42 (m, 2H), 3.25-3.12 (m, 2H), 3.11 (s, 3H), 2.49-2.41 (m, 1H), 2.06 (br s, 4H), 1.24 (br s, 2H), 0.98 (br s, 2H).	{5-Cyclopropyl-2-[2-(4-trifluoromethoxy-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

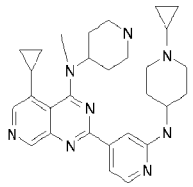
2327		[B4]	470.25 (MH)+	(400 MHz, d6-DMSO,δ): 9.57 (br s, 1H), 8.98 (s, 1H), 8.80-8.72 (m, 1H), 8.40-8.27 (m, 2H), 8.18 (s, 1H), 7.91 (s, 1H), 7.76-7.70 (m, 3H), 7.21-7.14 (m, 2H), 4.89-4.79 (m, 1H), 3.50-3.42 (m, 2H), 3.24-3.09 (m, 5H), 2.48-2.40 (m, 1H), 2.05 (br s, 4H), 1.24 (br s, 2H), 0.98 (br s, 2H).	{5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2328		[B4]	Method 6: RT: 3.33 min, MI: 522 [M+H]	^{1}H NMR (500MHz, DMSO) 9.67 (1H, s), 9.14 (1H, s), 8.80 (1H, s), 8.35 (1H, d), 7.96 (1H, s), 7.85 (2H, d), 7.76 (1H, dd), 7.31 (2H, d), 4.25 (1H, m), 3.86 (4H, m), 3.35-3.25 (4H, m), 2.45 (2H, m), 2.21 (2H, m), 2.11 (1H, m), 1.93 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethoxy-phenyl)-amine

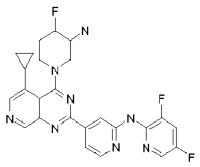
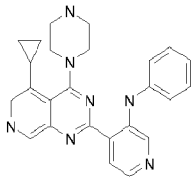
2329		[D3],	454 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.18 (1 H, s), 9.23 (1 H, s), 8.71 - 9.02 (3 H, m), 8.53 - 8.69 (2 H, m), 7.95 (1 H, d, J=5.0 Hz), 7.56 (1 H, dd, J=8.8, 4.8 Hz), 7.28 - 7.49 (1 H, m), 4.27 - 4.34 (1 H, m), 3.76 - 3.92 (4 H, m), 3.19 - 3.41 (4 H, m), 2.52 - 2.57 (2 H, m), 2.21 - 2.32 (2 H, m), 2.05 - 2.20 (1 H, m), 1.88 - 2.03 (1 H, m)	4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6-fluoro-9H-pyrido[2,3-b]indole
2330		[D3]	454 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.23 (1 H, s), 9.28 (1 H, s), 8.73 - 9.02 (4 H, m), 8.57 (1 H, d, J=5.0 Hz), 7.96 (1 H, d, J=5.0 Hz), 7.29 (1 H, dd, J=9.8, 2.5 Hz), 7.07 (1 H, td, J=9.3, 2.5 Hz), 4.31 (1 H, quin, J=8.7 Hz), 3.69 - 3.94 (4 H, m), 3.19 - 3.46 (4 H, m), 2.51 - 2.56 (2 H, m), 2.21 - 2.36 (2 H, m), 2.07 - 2.19 (1 H, m), 1.89 - 2.02 (1 H, m)	4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-7-fluoro-9H-pyrido[2,3-b]indole

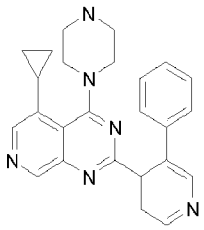
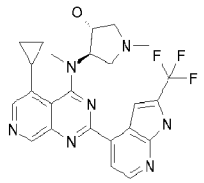
2333		[B4]	503 (M+ H)	1H-NMR: DMSO 10.43 (br s, 1H), 9.00 (s, 1H), 8.93 (m, 1H), 8.65 (s, 1H), 8.58 (m, 1H), 8.42 (d, 1H, J = 5.7 Hz), 8.30 (d, 1H, J = 2.5 Hz), 8.16 (s, 1H), 8.05 (m, 2H), 4.72 (m, 1H), 3.49 (m, 1H), 3.39 (m, 1H), 3.15 (m, 1H), 3.11 (s, 3H), 2.87 (m, 1H), 2.33 (m, 2H), 2.14 (m, 1H), 2.07 (m, 1H), 1.39 (m, 1H), 1.09-1.22 (br m, 4H), 0.99 (m, 2H)	4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3, 4-d]pyrimidin-4-yl}-methyl-amino)-3-methyl-piperidine
2334		[B4]	494.30 (MH)+	(400 MHz, d6-DMSO,δ): 9.35 (br s, 1H), 8.97 (s, 1H), 8.72-8.65 (m, 1H), 8.29-8.20 (m, 2H), 8.17 (s, 1H), 7.91 (s, 1H), 7.69 (dd, J=5.3, 1.3 Hz, 1H), 7.61 (d, J=8.5 Hz, 2H), 7.18 (d, J=8.4 Hz, 2H), 4.87-4.78 (m, 1H), 3.50-3.42 (m, 2H), 3.24-3.12 (m, 2H), 3.10 (s, 3H), 2.86 (pent, J=6.9 Hz, 1H), 2.49-2.41 (m, 1H), 2.05 (br s, 4H), 1.30-1.16 (m, 7H), 1.01-0.95 (m, 2H).	{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

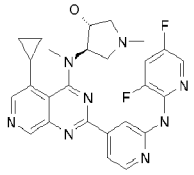
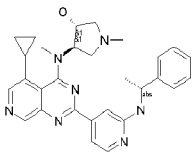
2335		[D3]	456 (M+ H)+	1H NMR (400 MHz, CHLOROFORM-d) δ ppm 9.12 (s, 1 H) 8.07 (s, 1 H) 7.98 (d, J=5.5 Hz, 1 H) 7.56 (d, J=5.5 Hz, 1 H) 5.04 (br. s., 1 H) 4.31 (br. s., 2 H) 3.52 (s, 2 H) 2.50 - 3.34 (m, 4 H) 2.08 (br. s., 1 H) 1.49 - 1.77 (complex series of m, 15 H) 1.25 - 1.32 (m, 2 H) 0.99 - 1.07 (m, 2 H)	1-(5-cyclopropyl-2-spiro[1,3-dihydropyrrolo[2,3-b]pyridine-2,1'-cyclohexane]-4-yl-pyrido[3,4-d]pyrimidin-4-yl)piperidin-3-amine
2336		[B4]	534 (M+ H)	1H-NMR: DMSO 10.24 (br s, 1H), 9.08 (m, 1H), 9.01 (s, 1H), 8.69 (m, 1H), 8.45 (d, 1H, J = 5.5 Hz), 8.28 (m, 1H), 8.24 (d, 1H, J = 2.0 Hz), 8.15 (s, 1H), 8.12 (m, 1H), 8.05 (m, 1H), 5.55 (m, 1H), 3.43 (m, 1H), 3.25 (m, 2H), 3.15 (s, 3H), 2.78 (m, 1H), 2.41 (m, 1H), 2.22 (m, 1H), 1.91 (m, 1H), 1.46 (m, 1H), 1.09-1.21 (br m, 7H), 0.98 (m, 2H)	4-({2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3,3-dimethyl-piperidine

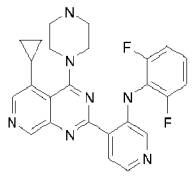
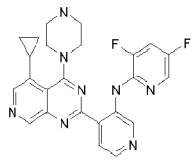
2337		[B4]	541.30 (MH)+	(400 MHz, d6-DMSO,δ): 8.99 (s, 1H), 8.85-8.79 (m, 1H), 8.45-8.33 (m, 1H), 8.22 (s, 1H), 8.05 (d, J=6.7 Hz, 1H), 8.03 (s, 1H), 7.71 (d, J=6.6 Hz, 1H), 4.86-4.78 (m, 1H), 3.79-3.70 (m, 1H), 3.51-3.40 (m, 2H), 3.33-3.23 (m, 2H), 3.20-3.08 (m, 5H), 3.04-2.97 (m, 2H), 2.59-2.51 (m, 2H), 2.46-2.38 (m, 1H), 2.25-1.80 (m, 6H), 1.63-1.52 (m, 2H), 1.25 (br s, 2H), 0.98 (br s, 2H).	(5-Cyclopropyl-2-{2-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-methyl-piperidin-4-yl-amine

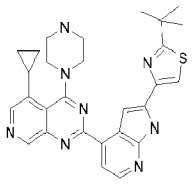
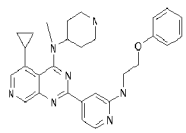
2338		[B4]	499.35 (MH)+	(400 MHz, d6-DMSO,δ): 9.02 (br s, 1H), 8.95 (s, 1H), 8.80-8.72 (m, 1H), 8.38-8.28 (m, 1H), 8.18 (s, 1H), 8.14 (d, J=5.9 Hz, 1H), 7.85-7.70 (m, 1H), 7.62.-7.58 (m, 1H), 4.85-4.75 (m, 1H), 4.06-3.96 (m, 2H), 3.65-3.58 (m, 2H), 3.50-3.40 (m, 3H), 3.33-3.11 (m, 4H), 3.10 (s, 3H), 2.95-2.82 (m, 1H), 2.47-2.40 (m, 1H), 2.26-2.20 (m, 2H), 2.15-1.90 (m, 4H), 1.72-1.60 (m, 2H), 1.30-1.15 (m, 2H), 1.00-0.93 (m, 4H), 0.88-0.82 (m, 2H).	{5-Cyclopropyl-2-[2-(1-cyclopropyl-piperidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

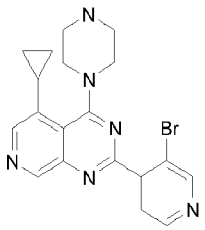
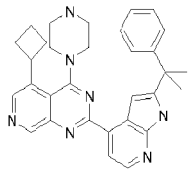
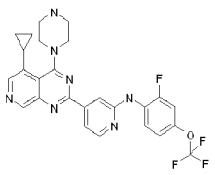
2339		[B4]	493 (M+ H)	1H-NMR: DMSO 10.45 (br s, 1H), 9.08 (s, 1H), 8.75 (s, 1H), 8.55 (m, 2H), 8.44 (d, 1H, J = 5.7 Hz), 8.31 (m, 1H), 8.21 (m, 1H), 8.09 (m, 2H), 4.80-5.15 (br m, 1H), 4.37-4.56 (br m, 1H), 3.94-4.26 (br m, 1H), 3.14-3.76 (br m, 3H), 2.67 (m, 1H), 2.07-2.33 (br m, 1H), 1.75-1.95 (br m, 1H), 1.27 (m, 2H), 1.07 (m, 2H)	(1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3, 4-d]pyrimidin-4-yl}-4-fluoro-piperidin-3-yl)
2340		[D16]	424.28 (MH)+	(400 MHz, d6-DMSO,δ): 11.18 (br s, 1H), 9.23 (s, 1H), 8.93 (br s, 2H), 8.73 (s, 1H), 8.49 (d, J=5.4 Hz, 1H), 8.22 (s, 1H), 8.20 (d, J=5.5 Hz, 1H), 7.46-7.39 (m, 4H), 7.16-7.11 (m, 1H), 3.95 (br s, 4H), 3.33 (br s, 4H), 2.70-2.62 (m, 1H), 1.29-1.24 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-phenyl-amine

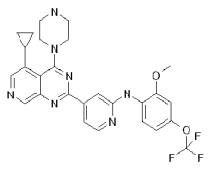
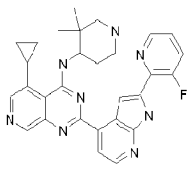
2341		[D16]	409.25 (MH)+	(400 MHz, d6-DMSO,δ): 8.99 (s, 1H), 8.82-8.60 (m, 4H), 8.18 (s, 1H), 8.09 (d, J=5.1 Hz, 1H), 7.36-7.30 (m, 3H), 7.22-7.17 (m, 2H), 3.33 (br s, 4H), 2.99 (br s, 4H), 2.57-2.50 (m, 1H), 1.22-1.17 (m, 2H), 1.04-0.99 (m, 2H).	5-Cyclopropyl-2-(3-phenyl-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2342		[D3], [D4]	484.21 (M+H)	(dmso-d6) 13.17 (s, 1H), 10.51 (br s, 1H), 10.39 (br s, 1H), 9.20 (s, 1H), 8.65 (d, J = 4.9 Hz, 1H), 8.30 (d, J = 4.9 Hz, 1H), 8.23 (br s, 1H), 8.02 (br s, 1H), 5.12 (br s, 1H), 4.80 (m, 1H), 4.18 (br s, 1H), 3.83 (m, 1H), 3.50 (m, 1H), 3.22 (s, 3H), 3.19 (br s, 1H), 2.94 (m, 3H), 2.61 (m, 1H), 1.36 (br s, 1H), 1.23 (br s, 1H), 1.10 (br s, 1H), 0.99 (m, 1H)	(±)-3,4-trans-4-{[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-1-methyl-pyrrolidin-3-ol

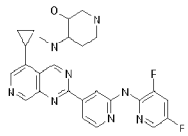
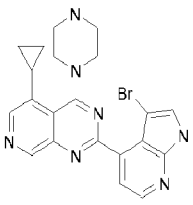
2343		[B4]	505.24 (M+H)	(dmso-d6) 10.45 (br m, 2H), 9.07 (s, 1H), 8.70 (m, 1H), 8.43 (d, J = 5.7 Hz, 1H), 8.30 (d, J = 2.5 Hz, 1H), 8.24 (br s, 1H), 8.07 (m, 2H), 6.73 (br s, exch. protons), 5.12 (br s, 1H), 4.80 (m, 1H), 4.20 (br s, 1H), 3.82 (m, 1H), 3.48 (m, 1H), 3.21 (br s, 4H), 2.93 (br s, 3H), 2.58 (br s, 1H), 1.35 (br s, 1H), 1.23 (br s, 1H), 1.10 (br s, 1H), 0.98 (m, 1H)	(±)-3,4-trans-4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-1-methyl-pyrrolidin-3-ol
2344		[B4]	496.29 (M+H)	(dmso-d6) 10.60 (m, 1H), 9.15 (br s, 1H), 9.03 (s, 1H), 8.25 (s, 1H), 8.06 (m, 2H), 7.72 (br s, 1H), 7.47 (m, 2H), 7.38 (m, 2H), 7.28 (m, 1H), 6.20 (br s, exch. protons), 5.13 (br s, 1H), 4.75 (m, 1H), 4.15 (br s, 1H), 3.80 (m, 1H), 3.47 (m, 1H), 3.18 (m, 4H), 2.93 (br s, 3H), 2.53 (m, 2H), 1.57 (d, J = 6.5 Hz, 3H), 1.35 (br s, 1H), 1.21 (br s, 1H), 1.08 (br s, 1H), 0.96 (br s, 1H)	(±)-3,4-trans-4-({5-Cyclopropyl-2-[2-((R)-1-phenyl-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-1-methyl-pyrrolidin-3-ol (mixture of two diastereoisomers)

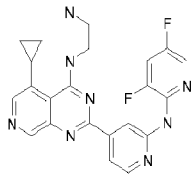
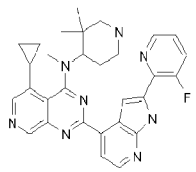
2345		[D16]	460.21 (MH)+	(400 MHz, d6-DMSO,δ): 10.97 (s, 1H), 9.17 (s, 1H), 8.92 (br s, 2H), 8.47 (d, J=5.3 Hz, 1H), 8.21 (s, 1H), 8.20 (d, J=5.4 Hz, 1H), 8.06 (t, J=2.4 Hz, 1H), 7.34-7.27 (m, 3H), 3.96 (br s, 4H), 3.33 (br s, 4H), 2.70-2.62 (m, 1H), 1.30-1.24 (m, 2H), 1.11-1.06 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-(2,6-difluoro-phenyl)-amine
2346		[D16]	461.18 (MH)+	(400 MHz, d6-DMSO,δ): 13.10 (s, 1H), 10.20 (s, 1H), 9.02 (d, J=0.9 Hz, 1H), 8.91 (br s, 2H), 8.56 (d, J=5.2 Hz, 1H), 8.39 (d, J=5.2 Hz, 1H), 8.26 (d, J=2.5 Hz, 1H), 8.25 (s, 1H), 8.11-8.05 (m, 1H), 3.98 (br s, 4H), 3.32 (br s, 4H), 2.68-2.60 (m, 1H), 1.30-1.25 (m, 2H), 1.13-1.08 (m, 2H).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-(3,5-difluoro-pyridin-2-yl)-amine

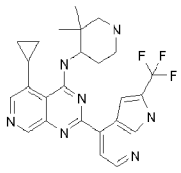
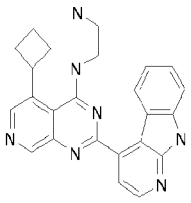
2347		[D3], [D4]	511.23 (M+H)	(dmso-d6) 12.39 (d, J = 1.7 Hz, 1H), 9.17 (s, 1H), 8.97 (br s, 1H), 8.42 (d, J = 5.1 Hz, 1H), 8.19 (s, 1H), 8.17 (d, J = 5.1 Hz, 1H), 8.11 (s, 1H), 7.91 (d, J = 2.1 Hz, 1H), 3.82 (br s, 4H, overalpped on exch. protons), 3.38 (br s, 4H), 2.76 (m, 1H), 1.50 (s, 9H), 1.27 (m, 2H), 1.11 (m, 2H)	2-[2-(2-tert-Butyl-thiazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2348		[B4]	496.26 (MH)+	(400 MHz, d6-DMSO,δ): 8.98 (s, 1H), 8.75-8.66 (m, 1H), 8.35-8.20 (m, 2H), 8.11 (d, J=6.3 Hz, 1H), 8.00-7.90 (m, 1H), 7.70-7.65 (m, 1H), 7.33-7.27 (m, 2H), 6.99-6.93 (m, 3H), 4.85-4.77 (m, 1H), 4.24-4.19 (m, 1H), 3.84-3.78 (m, 4H), 3.50-3.40 (m, 2H), 3.20-3.07 (m, 5H), 2.48-2.38 (m, 1H), 2.15-1.90 (m, 4H), 1.30-1.15 (m, 2H), 1.00-0.95 (m, 2H).	{5-Cyclopropyl-2-[2-(2-phenoxy-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

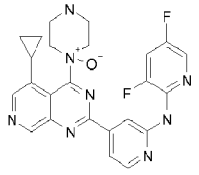
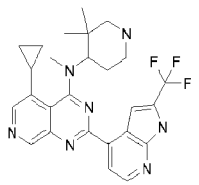
2349		[D16]	413.08 (MH)+	(400 MHz, d6-DMSO,δ): 9.06 (s, 1H), 8.92 (s, 1H), 8.83 (br s, 2H), 8.73 (d, J=4.9 Hz, 1H), 8.22 (s, 1H), 7.98 (d, J=4.8 Hz, 1H), 4.25-3.70 (m, 4H), 3.30 (br s, 4H), 2.71-2.64 (m, 1H), 1.30-1.25 (m, 2H), 1.13-1.08 (m, 2H).	2-(3-Bromo-pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2350		[D3], [D4]	Method 5: RT: 4.35 min, MI: 504 [M+H]	^{1}H NMR (500MHz, DMSO) 11.64 (brs, 1H), 9.07 (s, 1H), 8.65 (s, 1H), 8.25 (d, 1H), 8.03 (d, 1H), 7.37-7.16 (m, 7H), 4.31-4.22 (m, 1H), 3.67-3.55 (m, 2H), 3.50-3.37 (m, 2H), 2.95-2.75 (m, 4H), 2.47-2.38 (m, 2H), 2.22-2.11 (m, 2H), 2.09-2.00 (m, 1H), 1.78 (s, 6H).	5-Cyclobutyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2351		[B4]	Method 6: RT: 3.14 min, MI: 526 [M+H]	^{1}H NMR (500MHz, DMSO) 9.18 (1H, s), 9.06 (1H, s), 8.40 (1H, t), 8.33 (1H, d), 8.18 (1H, s), 8.13 (1H, s), 7.80 (1H, dd), 7.45 (1H, dd), 7.23 (1H, d), 3.94 (8H, broad s), 2.69 (1H, m), 1.26 (2H, m),1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-trifluoromethoxy-phenyl)-amine

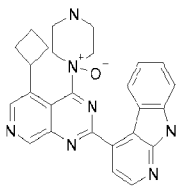
2352		[B4]	Method 6: RT: 2.80 min, MI: 538 [M+H]	^{1}H NMR (500MHz, DMSO) 9.07 (1H, s), 8.26 (2H, d), 8.19 (2H, d), 7.78 (1H, dd), 7.10 (1H, d), 6.98 (1H, d), 3.91 (7H, m), 3.33 (4H, s), 2.69 (1H, m), 1.27 (2H, m), 1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-4-trifluoromethoxy-phenyl)-amine
2353		[D3], [D4]	509.24 (M+H)	(dmso-d6) 12.38 (d, J = 5.6 Hz, 1H), 9.12 (s, 1H), 9.03 (m, 1H), 8.62 (m, 1H), 8.52 (s, 1H), 8.50 (d, J = 5.0 Hz, 1H), 8.30 m, 1H), 8.20 (d, J = 5.0 Hz, 1H), 8.19 (M, 1H), 7.92(m, 1H), 7.63 (d, J = 8.9 Hz, 1H), 7.54 (m, 1H), 4.89 (m, 1H), 3.38 (m, 1H), 3.23 (m, 1H), 3.13 (m, 2H), 2.63 (m, 1H), 2.18 (m, 1H), 1.98 (m, 1H), 1.27 (m, 1H), 1.22 (s, 3H), 1.20 (m, 1H), 1.15 (m, 2H), 1.13 (s, 3H)	(±)-{5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

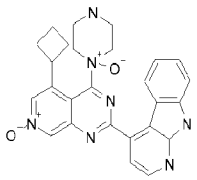
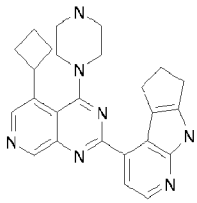
2354		[B4]	519 (M+ H)	1H-NMR: DMSO 10.31 (br m, 1H), 9.10 (br m, 1H), 9.01 (s, 1H), 8.65 (br m, 1H), 8.60 (s, 1H), 8.41 (m, 1H), 8.29 (m, 1H), 8.00-8.19 (br m, 3H), 4.95 (m, 1H), 3.65-3.85 (br m, 1H), 3.12-3.49 (br m, 7H), 2.89 (br m, 1H), 2.07-2.33 (br m, 4H), 1.21-1.39 (br m, 1H), 1.17 (m, 2H), 0.99 (m, 2H)	4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3, 4-d]pyrimidin-4-yl}-methyl-amino)-3-methoxy-cyclohexane
2355		[D3], [D6]	Method 5: RT: 2.65 min, MI: 452.08 [M+ H]	^{1}H NMR (500 MHz, d6-DMSO) 12.36 (1h, s), 9.06 (1H, s), 8.43 (1H, d), 8.21 (1H, s), 7.79 (1H, d), 7.50 (1H, d), 4.03-3.68 (4H, m), 3.30 (4H, s), 2.76-2.69 (1H, m), 1.31-1.21 (2H, m), 1.12-1.05 (2H, m).	2-(3-Bromo-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

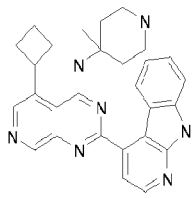
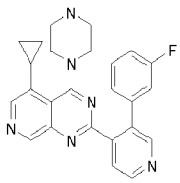
2356		[B4]	435 (M+ H)+	1H NMR (400 MHz, CHLOROFOR M-d) δ ppm 9.39 (s, 1 H) 9.19 (s, 1 H) 8.44 (d, J=0.8 Hz, 1 H) 8.40 (d, J=5.0 Hz, 1 H) 8.24 - 8.29 (m, 1 H) 8.09 (d, J=2.5 Hz, 1 H) 8.02 (dd, J=5.1, 1.4 Hz, 1 H) 7.50 - 7.55 (m, 1 H) 7.22 - 7.28 (m, 1 H) 3.88 - 3.94 (m, 2 H) 3.19 (t, J=5.8 Hz, 2 H) 2.31 - 2.40 (m, 1 H) 1.33 - 1.40 (m, 2 H) 1.05 - 1.12 (m, 2 H). NH2 coalesced with water	N*1*-{5-Cyclopropyl-2-[2-(3,5-diflu oro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-ethane-1,2-diamine
2357		[D3], [D4]	523.25 (M+ H)	(dmso-d6) 12.40 (s, 1H), 9.05 (s, 1H), 8.98 (br s, 1H), 8.62 (m, 1H), 8.50 (d, J = 5.0 Hz, 1H), 8.20 (br s, 2H), 8.18 (d, J = 5.0 Hz, 1H), 8.14 (s, 1H), 7.93 (m, 1H), 7.53 (m, 1H), 5.62 (m, 1H), 3.16 (br s, 6H), 2.78 (m, 1H), 2.23 (m, 2H), 1.92 (m, 1H), 1.45 (m, 1H), 1.22 (m, 7H), 1.00 (m, 2H)	(±)-{5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

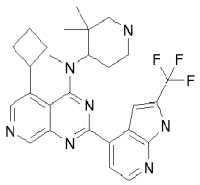
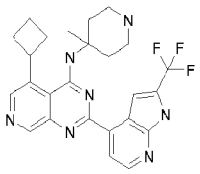
2358		[D3], [D4]	482.22 (M+H)	(dmso-d6) 13.13 (s, 1H), 9.20 (s, 1H), 9.08 (m, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.52 (s, 1H), 8.36 (m, 1H), 8.32 (d, J = 5.0 Hz, 1H), 7.99 (s, 1H), 7.63 (d, J = 8.8 Hz, 1H), 4.86 (m, 1H), 3.38 (m, 1H), 3.22 (m, 1H), 3.12 (m, 2H), 2.61 (m, 1H), 2.15 (m, 1H), 1.97 (m, 1H), 1.27 (m, 1H), 1.21 (s, 3H), 1.8 (m, 2H), 1.13 (m, 1H), 1.12 (s, 3H)	(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine
2359		[D3]	410 (M+H)	1H NMR (400 MHz, DMSO-d6) 12.04 (1 H, s), 9.14 (1 H, s), 8.62 (1 H, d, J=8.0 Hz), 8.54 - 8.59 (2 H, m), 7.85 (1 H, d, J=5.0 Hz), 7.73 (3 H, br. s.), 7.52 - 7.57 (1 H, m), 7.44 - 7.51 (1 H, m), 7.39 (1 H, t, J=5.9 Hz), 7.17 (1 H, ddd, J=8.2, 7.0, 1.1 Hz), 4.47 (1 H, quin, J=8.3 Hz), 3.97 (2 H, q, J=5.9 Hz), 3.19 (2 H, q, J=5.9 Hz), 2.59 (2 H, q, J=8.2 Hz), 2.26 - 2.40 (2 H, m), 2.06 - 2.19 (1 H, m), 1.82 - 1.94 (1 H, m)	N(1)-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3, 4-d]pyrimidin-4-yl]-ethane-1,2-diamine

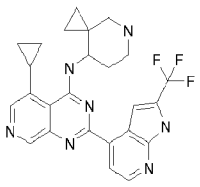
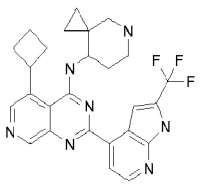
2360		[B4], [D14]	477 (M+ H)+	TFA Salt 1H NMR (400 MHz, DMSO-d6) δ ppm 9.78 - 9.88 (m, 1 H) 8.76 - 9.07 (m, 2 H) 8.73 (s, 1 H) 8.61 (d, J=1.8 Hz, 1 H) 8.40 (d, J=5.3 Hz, 1 H) 8.27 (d, J=2.3 Hz, 1 H) 7.96 - 8.04 (m, 1 H) 7.86 - 7.91 (m, 1 H) 7.79 (d, J=1.8 Hz, 1 H) 3.84 - 4.01 (m, 4 H) 3.25 - 3.40 (m, 4 H) 2.57 - 2.69 (m, 2 H) 1.20 - 1.31 (m, 2 H) 1.04 - 1.12 (m, 2 H)	{4-[5-Cyclopropyl-4-(1-oxy-piperazi n-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine
2361		[D3], [D4]	496.19 (M+ H)	(dmso-d6) 13.15 (s, 1H), 9.12 (s, 1H), 9.09 (br s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.29 (br s, 1H), 8.28 (d, J = 4.9 Hz, 1H), 8.15 (s, 1H), 7.96 (s, 1H), 5.58 (br s, 1H), 3.33 (m, 2H), 3.16 (br s, 4H), 2.78 (m, 1H), 2.23 (m, 1H), 1.94 (m, 1H), 1.48 (br s, 1H), 1.35-1.05 (m, 7H), 1.00 (br s, 2H)	(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

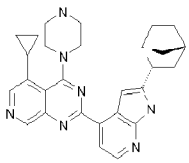
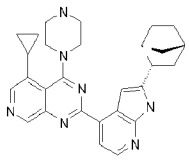
2364		[D3], [B14]	452 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.84 (1 H, s), 9.28 (1 H, s), 9.13 (1 H, d, J=8.0 Hz), 8.73 - 9.01 (3 H, m), 8.53 (1 H, d, J=6.8 Hz), 8.11 (1 H, d, J=6.8 Hz), 7.61 - 7.67 (1 H, m), 7.55 - 7.61 (1 H, m), 7.33 (1 H, ddd, J=8.2, 7.0, 1.4 Hz), 4.25 - 4.36 (1 H, m), 3.72 - 3.94 (4 H, m), 3.14 - 3.42 (4 H, m), 2.47 (2 H, br. s.), 2.21 - 2.31 (2 H, m), 2.06 - 2.19 (1 H, m), 1.86 - 2.01 (1 H, m)	4-[5-Cyclobutyl-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H- pyrido[2,3-b]indole

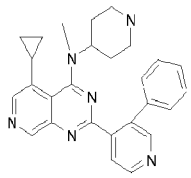
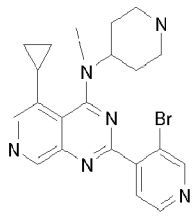
2365		[D3], [B14]	468 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.83 (1 H, s), 8.95 (1 H, d, J=8.3 Hz), 8.85 (2 H, d, J=17.1 Hz), 8.77 (1 H, d, J=1.8 Hz), 8.52 (1 H, d, J=6.8 Hz), 8.38 (1 H, d, J=1.3 Hz), 8.06 (1 H, d, J=6.8 Hz), 7.51 - 7.68 (2 H, m), 7.33 (1 H, ddd, J=8.2, 6.9, 1.3 Hz), 4.16 - 4.22 (1 H, m), 3.80 - 3.85 (4 H, m), 3.23 - 3.39 (4 H, m), 2.37 - 2.48 (2 H, m), 2.15 - 2.30 (2 H, m), 2.00 - 2.14 (1 H, m), 1.81 - 1.94 (1 H, m)	4-[5-Cyclobutyl-7-oxy-4-(1-oxy-piperazin-1-yl)-pyrido[3, 4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole
2366		[D3], [D9]	Method 5: RT: 3.44 min, MI: 426 [M+ H]	^{1}H NMR (500 MHz, d6-DMSO) 11.69 (brs, 1H), 9.17 (s, 1H), 8.97 (brs, 1H), 8.86 (brs, 1H), 8.77 (s, 1H), 8.19 (d, 1H), 7.95 (d, 1H), 4.27 (qt, 1H), 3.91-3.66 (m, 4H), 3.40-3.22 (m, 6H), 2.96-2.89 (m, 2H), 2.49-2.33 (m, 4H), 2.28-2.17 (m, 2H), 2.15-2.06 (m, 1H), 1.95-1.87 (m, 1H).	4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5,6,7,8-tetrahydro-cyclopenta[4,5]pyrrolo[2,3-b]pyridine

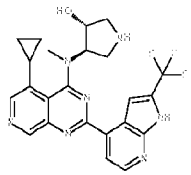
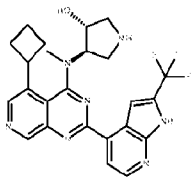
2371		[D3]	464 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.06 (1 H, s), 9.14 (1 H, s), 8.53 - 8.65 (3 H, m), 8.46 (2 H, br. s.), 7.74 (1 H, d, J=5.0 Hz), 7.51 - 7.58 (1 H, m), 7.43 - 7.51 (1 H, m), 7.15 (1 H, td, J=7.5, 1.3 Hz), 6.64 (1 H, s), 4.48 (1 H, d, J=8.5 Hz), 3.21 (4 H, br. s.), 2.54 - 2.63 (4 H, m), 2.28 - 2.44 (2 H, m), 2.05 - 2.20 (3 H, m), 1.84 - 1.98 (1 H, m), 1.65 (3 H, s)	[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine
2372		[D16]	427.21 (MH)+	(400 MHz, d6-DMSO,δ): 8.87 (s, 1H), 8.76 (d, J=5.0 Hz, 1H), 8.68 (s, 1H), 8.09 (s, 1H), 7.99 (d, J=5.0 Hz, 1H), 7.37-7.31 (m, 1H), 7.19-7.13 (m, 1H), 7.11-7.06 (m, 1H), 7.02-6.98 (m, 1H), 3.40-3.00 (m, 4H), 2.56 (br s, 4H), 2.50-2.43 (m, 1H), 1.23-1.17 (m, 2H), 0.98-0.93 (m, 2H).	5-Cyclopropyl-2-[3-(3-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

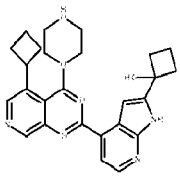
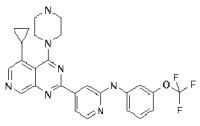
2376		[D3], [D4]	510.23 (M+H)	(dmso-d6) 13.16 (s, 1H), 9.23 (s, 1H), 9.17 (m, 1H), 9.01 (s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.40 (m, 1H), 8.27 (d, J = 4.9 Hz, 1H), 7.94 (s, 1H), 5.58 (m, 1H), 4.33 (m, 1H), 3.50 (m, 1H), 3.40-3.09 (m, 4H), 2.97 (s, 3H), 2.69 (m, 2H), 2.25 (m, 2H), 2.04 (br s, 2H), 1.91 (m, 1H), 1.43 (s, 3H), 1.19 (s, 3H), 1.06 (br s, 1H)	(±)-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine
2377		[D3], [D4]	482.20 (M+H)	(dmso-d6) 13.14 (s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.63 (br s, 2H), 8.54 (s, 1H), 8.11 (d, J = 4.9 Hz, 1H), 8.03 (s, 1H), 6.62 (s, 1H), 4.43 (m, 1H), 3.26 (br s, 4H), 2.64-2.50 (m, 4H), 2.36-2.17 (m, 4H), 2.09 (m, 1H), 1.87 (m, 1H), 1.74 (s, 3H)	[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine

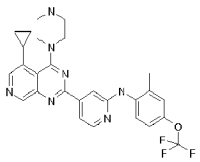
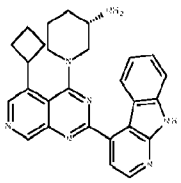
2378		[D3], [D4]	480.18 (M+H)	(dmso-d6) 13.14 (s, 1H), 9.18 (s, 1H), 8.83 (br s, 2H), 8.62 (d, J = 4.9 Hz, 1H), 8.53 (s, 1H), 8.25 (d, J = 4.9 Hz, 1H), 7.97 (s, 1H), 7.81 (d, J = 5.8 Hz, 1H), 4.33 (br s, 1H), 3.33 (br s, 3H), 3.03 (m, 1H), 2.73 (m, 1H), 2.46 (m, 1H), 2.24 (m, 1H), 1.24 (m, 3H), 1.05 (m, 1H), 0.85 (m, 2H), 0.75 (m, 1H), 0.71 (m, 1H)	(±)-(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine
2379		[D3], [D4]	494.20 (M+H)	(dmso-d6) 13.15 (s, 1H), 9.18 (s, 1H), 8.84 (br s, 2H), 8.62 (d, J = 4.9 Hz, 1H), 8.55 (s, 1H), 8.24 (d, J = 4.9 Hz, 1H), 7.96 (s, 1H), 6.79 (d, J = 6.5 Hz, 1H), 4.55 (m, 1H), 4.44 (br s, 1H), 3.39 (m, 2H), 3.30 (br s, 1H), 3.05 (m, 1H), 2.57 (m, 1H), 2.46-2.30 (m, 2H), 2.20 (m, 2H), 2.09 (m, 1H), 1.90 (m, 1H), 0.89 (m, 1H), 0.80-0.64 (m, 3H)	(±)-(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine

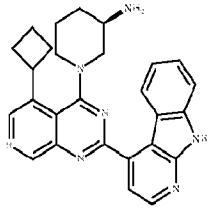
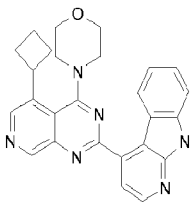
2380		[D3], [D4]	466.27 (M+H)	(dmso-d6) 11.76 (s, 1H), 9.19 (s, 1H), 8.93 (br s, 2H), 8.33 (d, J = 5.1 Hz, 1H), 8.22 (s, 1H), 8.11 (d, J = 5.1 Hz, 1H), 7.29 (br s, 1H), 6.29 (very br signal, water exch. H's), 3.97 (br s, 4H), 3.40 (br s, 5H), 2.84-2.75 (m, 1H), 2.72 (br s, 1H), 2.40 (br s, 1H), 2.11-2.04 (m, 1H), 1.66-1.46 (m, 4H), 1.33-1.27 (m, 4H), 1.15-1.11 (m, 3H)	5-cyclopropyl-2-[2-[(1R,2S,4S)-norbornan-2-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2381		[D3], [D4]	466.27 (M+H)	(dmso-d6) 11.76 (s, 1H), 9.19 (s, 1H), 8.93 (br s, 2H), 8.33 (d, J = 5.1 Hz, 1H), 8.22 (s, 1H), 8.11 (d, J = 5.1 Hz, 1H), 7.29 (br s, 1H), 5.74 (very br signal, water exch. H's), 3.97 (br s, 4H), 3.40 (br s, 5H), 2.84-2.75 (m, 1H), 2.72 (br s, 1H), 2.40 (br s, 1H), 2.11-2.04 (m, 1H), 1.66-1.46 (m, 4H), 1.33-1.27 (m, 4H), 1.15-1.11 (m, 3H)	5-cyclopropyl-2-[2-[(1S,2R,4R)-norbornan-2-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

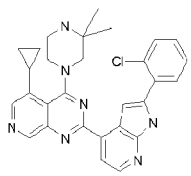
2382		[D16]	437.24 (MH)+	(400 MHz, d6-DMSO,δ): 8.88 (s, 1H), 8.71 (d, J=5.0 Hz, 1H), 8.67 (s, 1H), 8.13 (s, 1H), 7.90 (d, J=5.0 Hz, 1H), 7.34-7.29 (m, 3H), 7.19-7.13 (m, 2H), 3.79-3.70 (m, 1H), 2.86 (br s, 2H), 2.71 (s, 3H), 2.44-2.00 (m, 4H), 1.74-0.75 (m, 8H).	[5-Cyclopropyl-2-(3-phenyl-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine
2383		[D16]	439.11 (MH)+	(400 MHz, d6-DMSO,δ): 8.91 (s, 1H), 8.88 (s, 1H), 8.68 (d, J=4.9 Hz, 1H), 8.15 (s, 1H), 7.87 (d, J=4.8 Hz, 1H), 4.60-4.51 (m, 1H), 3.11 (s, 3H), 3.06-2.96 (m, 2H), 2.60-2.48 (m, 2H), 2.45-2.37 (m, 1H), 2.00-0.95 (m, 9H).	[2-(3-Bromo-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine

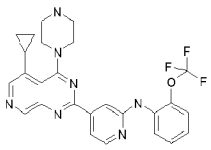
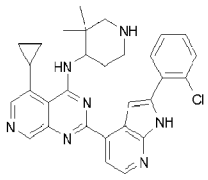
2384		[D3], [D4]	470.17 (M+H)	(dmso-d6) 13.17 (s, 1H), 9.29 (br s, 1H), 9.20 (s, 1H), 9.17 (br s, 1H), 8.65 (d, J = 4.9 Hz, 1H), 8.31 (d, J = 4.9 Hz, 1H), 8.22 (s, 1H), 8.03 (s, 1H), 4.80 (br s, exch. protons), 4.73 (br s, 2H), 3.92 (br s, 1H), 3.50 (br s, 1H), 3.42 (br s, 1H), 3.18 (s, 3H), 3.16 (m, 1H), 2.61 (b, 1H), 1.36 (br s, 1H), 1.23 (br s, 1H), 1.11 (m, 1H), 0.99 (m, 1H)	(±)-3,4-trans-4-{[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-pyrrolidin-3-ol
2385		[D3], [D4]	484.20 (M+H)	(dmso-d6) 13.18 (s, 1H), 9.33 (br s, 1H), 9.26 (br s, 1H), 9.19 (br s, 1H), 8.72 (br s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.31 (m, 1H), 8.03 (s, 1H), 5.07 (m, 1H), 4.82 (m, 1H), 4.29 (m, 1H), 3.89 (m, 1H), 3.53 (br s, 1H), 3.20 (m, 2H), 3.13 (br s, 1H), 3.04 (s, 3H), 2.67 (m, 1H), 2.55 (m, 1H), 2.39 (m, 1H), 2.10 (m, 2H), 1.89 (m, 2H)	(±)-(3,4-trans)-4-{[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-pyrrolidin-3-ol

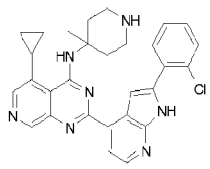
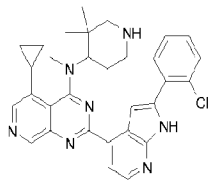
2386		[D3], [D5]	Method 5: RT: 3.47 min, MI: 456 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 11.70 (1H, s),9.19 (1H, s), 8.75 (1H, s), 8.31 (1H, d, J = 5.1 Hz), 8.07 (1H, d, J = 5.1 Hz), 7.37 (1H, d, J = 2.2 Hz), 5.78 (1H, s), 4.32 - 4.25 (1H, m), 3.87 - 3.80 (2H, br m), 3.75 - 3.68 (2H, br m), 3.26 - 3.12 (4H br m), 2.58 - 2.51 (3H, m overlapping with DMSO), 2.36-2.31 (3H, m), 2.25 -2.17 (2H, m), 2.14 - 2.05 (1H, m), 1.94 - 1.87 (2H, m), 1.76 - 1.67 (1H, m)	1-[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-cyclobutanol
2387		[B4]	Method 6: RT: 3.17 min, MI: 508 [M+H]	^{1}H NMR (500MHz, DMSO) 9.76 (1H, s), 9.06 (1H, s), 8.40 (1H, d), 8.18 (1H, s), 8.06 (1H, s), 7.98 (1H, s), 7.78 (1H, dd), 7.61 (1H, dd), 7.40 (1H, t), 6.87 (1H, d), 3.92 (4H, s), 3.34 (4H, s,), 2.69 (1H, m), 1.25 (2H, m),1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethoxy-phenyl)-amine

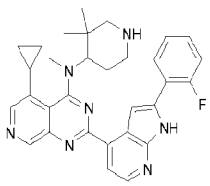
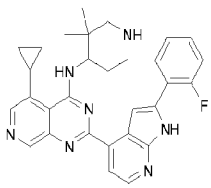
2388		[B4]	Method 6: RT: 2.66 min, MI: 522 [M+H]	^{1}H NMR (500MH, DMSO) 9.73 (1H, s), 9.13 (1H, s), 9.07 (1H, s), 8.21 (1H, s), 8.18 (1H, d), 8.05 (1H, s), 7.81 (1H, dd), 7.71 (1H, d), 7.37 (1H, s), 7.27 (1H, d), 3.91 (4H, s), 3.31 (4H, s,), 2.67 (1H, m), 2.32 (3H, s), 1.25 (2H, m),1.09 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-trifluoromethoxy-phenyl)-amine
2389		[D3]	450 (M+H)	1H NMR (400 MHz, DMSO-d6): 12.06 (1 H, s), 9.08 - 9.29 (1 H, m), 8.76 - 8.91 (1 H, m), 8.61 - 8.71 (1 H, m), 8.54 - 8.61 (1 H, m), 7.78 - 8.11 (4 H, m), 7.55 (1 H, d, J=7.8 Hz), 7.41 - 7.52 (1 H, m), 7.07 - 7.26 (1 H, m), 4.21 - 4.27 (2 H, m), 3.50 - 3.73 (2 H, m), 3.30 - 3.46 (2 H, m), 2.92 - 3.24 (2 H, m), 2.53 - 2.60 (1 H, m), 2.05 - 2.30 (3 H, m), 1.86 - 2.01 (2 H, m), 1.39 - 1.76 (2 H, m)	(S)-1-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine

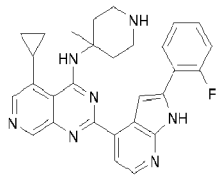
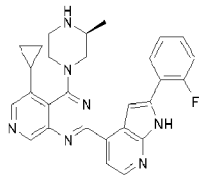
2390		[D3]	450 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.06 (1 H, s), 9.08 - 9.29 (1 H, m), 8.76 - 8.91 (1 H, m), 8.61 - 8.71 (1 H, m), 8.54 - 8.61 (1 H, m), 7.78 - 8.11 (4 H, m), 7.55 (1 H, d, J=7.8 Hz), 7.41 - 7.52 (1 H, m), 7.07 - 7.26 (1 H, m), 4.21 - 4.27 (2 H, m), 3.50 - 3.73 (2 H, m), 3.30 - 3.46 (2 H, m), 2.92 - 3.24 (2 H, m), 2.53 - 2.60 (1 H, m), 2.05 - 2.30 (3 H, m), 1.86 - 2.01 (2 H, m), 1.39 - 1.76 (2 H, m)	(R)-1-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine
2391		[D3]	437 (M+ H)	1H NMR (400 MHz, DMSO-d6) 12.04 (1 H, s), 9.18 (1 H, s), 8.82 (1 H, s), 8.64 (1 H, d, J=8.0 Hz), 8.56 (1 H, d, J=5.3 Hz), 7.86 (1 H, d, J=5.0 Hz), 7.51 - 7.59 (1 H, m), 7.42 - 7.50 (1 H, m), 7.17 (1 H, ddd, J=8.2, 7.0, 1.1 Hz), 4.33 (1 H, quin, J=8.7 Hz), 3.48 - 3.88 (8 H, m), 2.52 - 2.57 (2 H, m), 2.07 - 2.31 (3 H, m), 1.87 - 1.98 (1 H, m)	4-(5-Cyclobutyl-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole

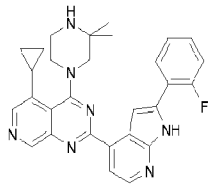
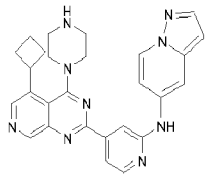
2394		[D3], [D4]	510.19	1H NMR (400 MHz, DMSO-d6) δ 12.32 (d, 1H, J = 1.6 Hz), 9.14 (m, 3H), 8.46 (d, 1H, J = 5.0 Hz), 8.21 (m, 2H), 7.93 (d, 1H, J = 2.1 Hz), 7.84 (m, 1H), 7.67 (m, 2H), 7.50 (m, 2H), 3.92 (m, 4H), 3.41 (m, 2H), 2.60 (m, 1H), 1.23 (m, 10H)	2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-(3, 3-dimethyl-piperazin-1-yl)-3,4-d ihydro-pyrido[3,4-d]pyrimidine

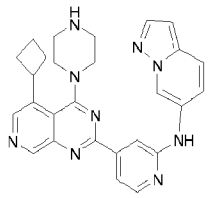
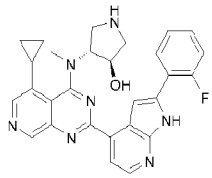
2400		[B4]	Method 6: RT: 2.68 min, MI: 508 [M+H]	^{1}H NMR (500MH, DMSO, 3IGO079) 9.06 (1H, s), 8.99 (1H, s), 8.31 (1H, d), 8.27 (1H, dd), 8.17 (1H, s), 8.11 (1H, s), 7.78 (1H, dd), 7.36-7.32 (2H, m), 7.11-7.07 (1H, m), 3.92 (4H, s), 3.33 (4H, s,), 2.69 (1H, m), 1.26 (2H, m), 1.08 (2H, m).	[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethoxy-phenyl)-amine
2401		[D3], [D4]	524.21 (M+H)	(dmso-d6) 12.25 (s, 1H), 9.13 (s, 1H), 9.03 (br d, J = 6.8 Hz, 1H), 8.50 (s, 1H), 8.45 (d, J = 5.0 Hz, 1H), 8.31 (m, 1H), 8.22 (d, J = 5.0 Hz, 1H), 7.84 (dd, J = 7.6, 1.7 Hz, 1H), 7.66 (dd, J = 8.0, 1.4 Hz, 1H), 7.60 (br d, J = 8.8 Hz, 1H), 7.55-7.45 (m, 2H), 4.87 (m, 1H), 3.34 (m, 1H), 3.21 (m, 1H), 3.11 (m, 1H), 2.61 (m, 1H), 2.17 (m, 1H), 1.96 (m, 1H), 1.27 (m, 1H), 1.20 (s, 3H), 1.23-1.10 (m, 3H), 1.12 (s, 3H)	(±)-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

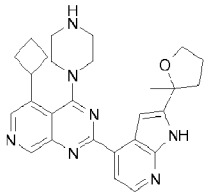
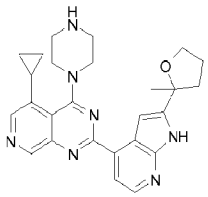
2402		[D3], [D4]	510.19 (M+H)	(dmso-d6) 12.26 (s, 1H), 9.12 (s, 1H), 8.51 (br s, 1H), 8.50 (s, 1H), 8.47 (br s, 1H), 8.46 (d, J = 5.0 Hz, 1H), 8.01 (d, J = 5.0 Hz, 1H), 7.94 (d, J = 2.2 Hz, 1H), 7.82 (dd, J = 7.8, 1.8 Hz, 1H), 7.66 (dd, J = 7.8, 1.4 Hz, 1H), 7.64 (br s, 1H), 7.56-7.44 (m, 2H), 3.29-3.14 (m, 4H), 2.79 (m, 2H), 2.65 (m, 1H), 2.07 (m, 2H), 1.78 (s, 3H), 1.22 (m, 2H), 1.18 (m, 2H)	{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine
2403		[D3], [D4]	538.23 (M+H)	(dmso-d6) 12.28 (s, 1H), 9.06 (s, 1H), 8.99 (br s, 1H), 8.46 (d, J = 5.1 Hz, 1H), 8.19 (br s, 1H), 8.18 (d, J = 4.8 Hz, 1H), 8.13 (s, 1H), 7.91 (br s, 1H), 7.84 (dd, J = 7.6, 1.3 Hz, 1H), 7.66 (dd, J = 7.8, 1.3 Hz, 1H), 7.55-7.44 (m, 2H), 5.58 (m, 1H), 4.17 (br s, exchangeable protons), 3.60-2.95 (m, 7H), 2.75 (br s, 1H), 2.23 (br s, 1H), 1.93 (br s, 1H), 1.60-0.80 (m, 8H)	(±)-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

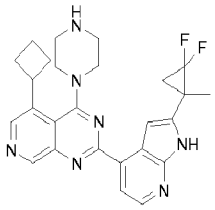
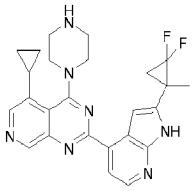
2404		[D3], [D4]	522.22 (M+H)	(dmso-d6) d: 12.37 (s, 1H), 9.06 (s, 1H), 9.01 (br s, 1H), 8.45 (d, J = 7.4 Hz, 1H), 8.22 (br s, 1H), 8.18-8.06 (m, 3H), 7.92 (br s, 1H), 7.55-7.30 (m, 3H), 5.59 (m, 1H), 4.23 (m, 1H), 3.51 (br s, exch. protons), 3.15 (br s, 5H), 2.76 (m, 1H), 2.21 (m, 1H), 1.94 (br s, 1H), 1.55-0.80 (m, 10H)	(±)-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine
2405		[D3], [D4]	508.27 (M+H)	(dmso-d6) 12.29 (s, 1H), 9.07 (s, 1H), 9.03 (m, 1H), 8.45 (s, 1H), 8.38 (d, J = 5.0 Hz, 1H), 8.29 (m, 1H), 8.14 (d, J = 5.0 Hz, 1H), 8.04 (m, 1H), 7.92 (m, 1H), 7.56 (d, J = 8.9 Hz, 1H), 7.45-7.30 (m, 3H), 4.82 (m, 1H), 3.32 (m, 1H), 3.17 (m, 1H), 3.03 (m, 2H), 2.55 (m, 1H), 2.11 (m, 1H), 1.92 (m, 1H), 1.27-1.17 (m, 1H), 1.17-1.04 (m, 3H), 1.15 (s, 3H), 1.05 (s, 3H)	(±)-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

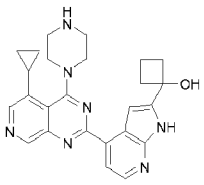
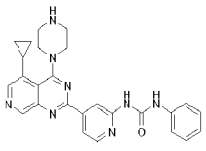
2406		[D3], [D4]	494.23 (M+H)	(dmso-d6) 12.36 (d, J = 1.6 Hz, 1H), 9.13 (s, 1H), 8.59 (br s, 1H), 8.52 (s, 2H), 8.46 (d, J = 5.0 Hz, 1H), 8.09 (m, 1H), 8.03 (d, J = 5.0 Hz, 1H), 8.00 (m, 1H), 7.66 (s, 1H), 7.51-7.35 (m, 3H), 3.29-3.10 (m, 4H), 2.80 (m, 2H), 2.66 (m, 1H), 2.09 (m, 2H), 1.80 (s, 3H), 1.22 (m, 2H), 1.19 (m, 2H)	{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine
2407		[D3], [D4]	480.22	1H NMR (400 MHz, DMSO-d6) δ 12.41 (d, 1H, J = 1.4 Hz), 9.44 (br s, 1H), 9.14 (s, 1H), 8.95 (br s, 1H), 8.46 (d, 1H, J = 5.1 Hz), 8.19 (m, 2H), 8.10 (m, 1H), 7.98 (br s, 1H), 7.44 (m, 3H), 3.47 (m, 7H), 2.82 (m, 1H), 1.21 (m, 7H)	5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)- 3-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine

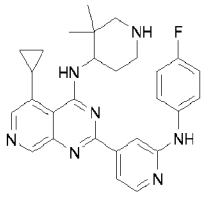
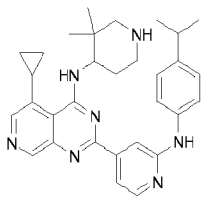
2408		[D3], [D4]	494.22	1H NMR (400 MHz, DMSO-d6) δ 12.42 (d, 1H, J = 1.4 Hz), 9.15 (m, 3H), 8.47 (d, 1H, J = 5.0 Hz), 8.22 (m, 2H), 8.10 (m, 1H), 7.98 (m, 1H), 7.44 (m, 3H), 3.94 (m, 4H), 3.42 (m, 2H), 2.61 (m, 1H), 1.22 (m, 10H)	5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-2-[2-(2-fluoro-phenyl)-1H- pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidine
2409		[B4]	478 (M+H)+	1H NMR (400 MHz, DMSO-d6) δ ppm 9.74 (s, 1 H) 9.15 (s, 1 H) 8.85 - 9.02 (m, 2 H) 8.80 (s, 1 H) 8.54 (d, J=7.5 Hz, 1 H) 8.42 - 8.48 (m, 2 H) 8.01 (s, 1 H) 7.86 (d, J=2.0 Hz, 1 H) 7.81 (dd, J=5.3, 1.3 Hz, 1 H) 6.93 (dd, J=7.5, 2.5 Hz, 1 H) 6.38 - 6.42 (m, 1 H) 4.20 - 4.31 (m, 1 H) 3.75 - 3.93 (m, 5 H) 3.14 - 3.48 (m, 4 H) 1.83 - 2.33 (m, 4 H)	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-5-yl-amine

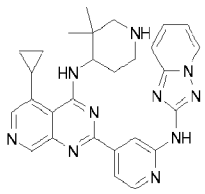
2410		[B4]	478 (M+ H)+	1H NMR (400 MHz, DMSO-d6) δ ppm 9.73 (s, 1 H) 9.59 (s, 1 H) 9.15 (s, 1 H) 8.85 - 9.06 (m, 2 H) 8.81 (s, 1 H) 8.44 (d, J=5.3 Hz, 1 H) 8.00 (s, 1 H) 7.88 (d, J=2.3 Hz, 1 H) 7.77 (dd, J=5.4, 1.4 Hz, 1 H) 7.67 (d, J=9.0 Hz, 1 H) 7.25 (dd, J=9.5, 1.8 Hz, 1 H) 6.55 (dd, J=2.1, 0.9 Hz, 1 H) 4.16 - 4.34 (m, 1 H) 3.73 - 3.93 (m, 4 H) 3.17 - 3.43 (m, 4 H) 2.22 (br. s., 3 H) 1.84 - 2.00 (m, 2 H)	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-6-yl-amine
2411		[D3], [D4]	496.19	1H NMR (400 MHz, DMSO-d6) δ 12.43 (m, 1H), 9.17 (m, 2H), 8.50 (m, 1H), 8.20 (m, 2H), 8.10 (m, 1H), 8.01 (m, 1H), 7.44 (m, 3H), 4.72 (m, 1H), 3.94 (m, 3H), 3.50 (m, 2H), 3.20 (m, 3H), 2.64 (m, 1H), 1.12 (m, 4H)	(±)-(3,4-trans)-4-({5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin- 4-yl]-3,4-dihydro-pyrido[3,4-d] pyrimidin-4-yl}-methyl-amino)-pyrrolidin- 3-ol

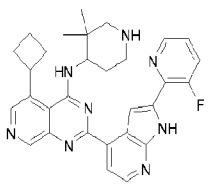
2415		[D3], [D4]	Method 5: RT: 3.57 min, MI: 470 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 11.70 (1H, s), 9.10 (1H, s), 8.68 (1H, s), 8.29 (1H, d, J = 5.0 Hz), 8.03 (1H, d, J = 5.0 Hz), 4.28 (1H, quintet, J = 8.7 Hz), 3.96 - 3.89 (2H, m), 3.65 (2H, br. s), 3.51 (2H, br. s), 2.92 (2H, br s), 2.83 (2H, br s), 2.54 - 2.51 (2H, m), 2.36 - 2.32 (1H, m), 2.22 - 2.14 (2H, m), 2.11 - 1.86 (5H, m), 1.62 (3H, s).	5-Cyclobutyl-2-[2-(2-methyl-tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2416		[D3], [D4]	Method 5: RT: 3.25 min, MI: 456 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 11.70 (1H, s), 9.03 (1H, s), 8.30 (1H, d, J = 5.1 Hz), 8.08 (1H, s), 8.05 (1H, d, J = 5.1 Hz), 7.29 (1H, d, J = 2.2 Hz), 3.94 - 3.91 (2H, m), 3.85 - 3.53 (4H, very broad d), 2.88 (4H, br. s), 2.70 - 2.65 (1H, m), 2.36 - 2.33 (1H, m), 2.00 - 1.90 (3H, m), 1.62 (3H, m), 1.26 - 1.23 (2H, m), 1.04 - 1.01 (2H, m).	5-Cyclopropyl-2-[2-(2-methyl-tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

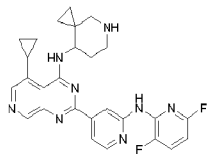
2417		[D3], [D4]	Method 6: RT: 2.78 min, MI: 476 [M+H]	^{1}H NMR (500MHz, d6-DMSO) 11.97 (1H, brs), 9.23 (1H, s), 8.75 (1H, s), 8.35 (1H, d), 8.09 (1H, d), 7.36 (1H, s), 4.28 (q, 1H), 3.91-3.58 (3H, m), 3.42-3.07 (7H, m), 2.33 (1H, m), 2.26-2.14 (2H, m), 2.08 (1H, m), 1.90 (1H, m), 1.81 (1H, m), 1.66 (s, 3H)	5-Cyclobutyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2418		[D3], [D4]	Method 5: RT: 2.21 min, MI: 462. [M+H]	1H NMR (500MHz, d6-DMSO) 11.93 (1H, brs), 9.08 (1H, s), 8.34 (1H, d), 8.08 (1H, s), 8.07 (1H, s), 7.37 (1H, d), 4.00-3.43 (5H, m), 2.96-2.79 (4H, m), 2.67 (1H, m), 2.30 (1H, m), 1.82 (1H, m), 1.65 (3H, s) 1.31-1.21 (2H, m), 1.05-0.99 (2H, m)	5-Cyclopropyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

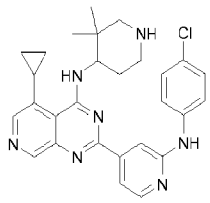
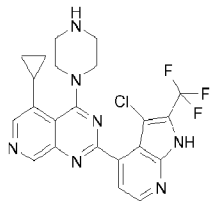
2419		[D3], [D5]	Method 6: RT: 2.24 min, MI: 442 [M+H]	^{1}H NMR (500MHz, d6-DMSO) 11.68 (1H, brs), 9.07(1H, s), 8.31 (1H, d), 8.11 (1H, s), 8.07 (1H, d), 7.39 (1H, d), 5.77 (1H, s), 4.17-3.50 (5H, m), 3.19-2.94 (4H, m), 2.70 (1H, m), 2.40-2.28 (3H, m), 1.90 (1H, m), 1.71 (m, 1H), 1.31-1.23 (2H, m), 1.07-1.01 (2H, m)	1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-cyclobutanol
2420		[B4], [D11]	Method 6: RT: 2.95 min, MI: 467 [M+H]	^{1}H NMR (500MHz, DMSO) 9.65 (1H, s), 9.00 (1H, s), 8.56 (1H, s), 8.46 (1H, dd), 8.12 (1H, s), 7.95 (1H, dd), 7.56 (2H, d), 7.33 (2H, t), 7.04 (1H, t), 3.78 (4H, m), 2.92 (4H, s), 2.63 (1H, m), 1.23 (2H, m), 1.03 (2H, m).	1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-3-phenyl-urea

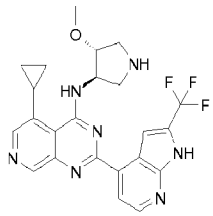
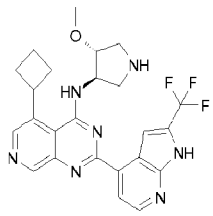
2421		[B4]	484.24 (MH)+	(400 MHz, d6-DMSO, δ): 9.41 (br s, 1H), 9.06 (s, 1H), 9.01-8.94 (m, 1H), 8.51 (s, 1H), 8.31 (d, J= 5.4 Hz, 1H), 8.25-8.14 (m, 1H), 7.90 (s, 1H), 7.80-7.72 (m, 3H), 7.61 (d, J=8.8 Hz, 1H), 7.19-7.11 (m, 2H), 4.86-4.78 (m, 1H), 3.38-3.31 (m, 2H), 3.25-3.06 (m, 3H), 2.63-2.55 (m, 1H), 2.15-2.08 (m, 1H), 1.99-1.86 (m, 1H), 1.30-1.07 (m, 10H).	5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine
2422		[B4]	507.27 (MH)+	(400 MHz, d6-DMSO, δ): 9.93 (br s, 1H), 9.06 (s, 1H), 8.97 (d, J=10.9 Hz, 1H), 8.51 (d, J=0.7 Hz, 1H), 8.27 (d, J=5.4 Hz, 1H), 8.20 (d, J=9.1 Hz, 1H), 7.93 (s, 1H), 7.76 (dd, J=5.3, 1.3 Hz, 1H), 7.63-7.60 (m, 3H), 7.20 (d, J=8.4 Hz, 2H), 4.85-4.79 (m, 1H), 3.35 (d, J=11.6 Hz, 1H), 3.22-3.07 (m, 3H), 2.91-2.82 (m, 1H), 2.63-2.54 (m,1H), 2.15-2.06 (m, 1H), 1.98-1.89 (m, 1H), 1.28-1.09 (m, 16H).	{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

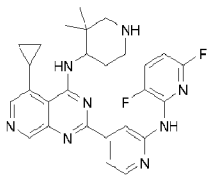
2423		[B4]	507.27 (MH)+	(400 MHz, d6-DMSO, δ): 10.69 (br s, 1H), 9.16 (s, 1H), 9.00-8.92 (m, 2H), 8.89 (d, J=6.8 Hz, 1H), 8.53 (d, J=0.5 Hz, 1H), 8.45 (d, J=5.3 Hz, 1H), 8.27-8.19 (m, 1H), 8.00 (dd, J=5.6, 0.9 Hz, 1H), 7.72-7.64 (m, 3H), 7.15 (dt, J=6.6, 1.9 Hz, 1H), 4.87-4.81 (m, 1H), 3.37-3.30 (m, 1H), 3.24-3.00 (m, 3H), 2.65-2.56 (m, 1H), 2.18-2.10 (m, 1H), 2.02-1.91 (m, 1H), 1.31-1.11 (m, 10H).	{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

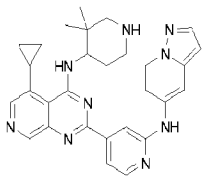
2424		[D3], [D4]	523.24 (M+H)	(dmso-d6) 12.39 (s, 1H), 9.12 (s, 1H), 9.05 (m, 1H), 8.62 (m, 1H), 8.57 (s, 1H), 8.50 (d, J = 4.9 Hz, 1H), 8.33 (m, 1H), 8.20 (d, J = 4.9 Hz, 1H), 8.18 (m, 1H), 7.93 (m, 1H), 7.54 (m, 1H), 6.58 (d, J = 8.8 Hz, 1H), 4.86 (m, 1H), 4.45 (m, 1H), 3.37 (m, 1H), 3.27 (m, 1H), 3.11 (m, 2H), 2.54 (m, 1H), 2.43-2.24 (m, 2H), 2.15-1.97 (m, 3H), 1.97-1.84 (m, 1H), 1.28 (s, 3H), 1.14 (s, 3H)	(±)-{5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

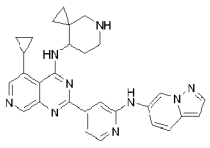
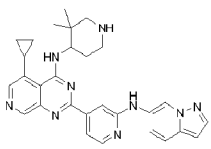
2425		[B4]	501 (M+ H)	1H NMR (CD3OD) δ ppm 9.14 (1H, s), 8.94 (1H, s), 8.57 (1H, s), 8.49 (1H, d, J= 6.3 Hz,), 8.34 (1H, dd, J= 6.3 Hz,J=1.4 Hz,) , 7.94-7.88 (1H, m), 6.88-6.85 (1H, m,), 4.34 1H, (bs),, 3.49 (1H, d, J=13.5 Hz,),, 3.44-3.41 (2H, m,), 3.08-3.05 (1H, d, J=13.4 Hz,), 2.72-2.62 (2H, m,), 2.43-2.35 (1H, m,), 1.41-1.33 (3H, m,), 1.13-1.08 (1H, m,), 0.95-0.80 (4H, m).1H), 3.49 (d, J=13.5 Hz, 1H, 3.44-3.41 (m, 2H), 3.08-3.05 (d, J=13.4 Hz, 1H), 2.72-2.62 (m, 2H), 2.43-2.35 (m, 1H), 1.41-1.33 (m, 3H), 1.13-1.08 (m, 1H), 0.95-0.80 (m, 4H).	(5-Aza-spiro[2.5]oct-8-yl)-{5-cyclo propyl-2-[2-(3,6-difluoro-pyridin-2 -ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine

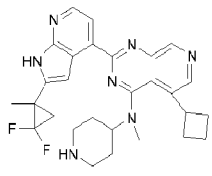
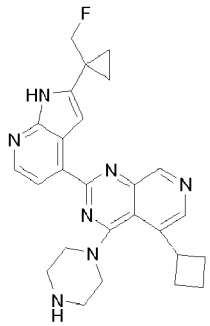
2426		[B4]	500.22 (MH)+	(400 MHz, d6-DMSO, δ): 9.50 (s, 1H), 9.06 (s, 1H), 8.96 (d, J=10.2 Hz, 1H), 8.51 (d, J=.7 Hz, 1H), 8.36 (d, J=5.2 Hz, 1H), 8.25-8.12 (m, 1H), 7.93 (s, 1H), 7.83-7.77 (m, 3H), 7.61 (d, J=8.7 Hz, 1H), 7.36-7.31 (m, 2H), 4.87-4.79 (m, 1H), 3.35 (d, J=12.4 Hz, 1H), 3.25-3.01 (m, 3H), 2.63-2.53 (m, 1H), 2.15-2.05 (m, 1H), 1.98-1.88 (m, 1H), 1.31-1.07 (m, 10H).	{2-[2-(4-Chloro-phenylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine
2427		[D3], [D7]	Method 5: RT: 3.45 min, MI: 474 [M+H]	^{1}H NMR (500MHz, d6-DMSO) 8.96 (1H, s), 8.59 (1H, d), 8.13 (1H, s), 7.57 (1H, d), 3.89-3.46 (4H, m), 2.84 (4H, s), 2.71-2.59 (1H, m), 1.29-1.24 (2H, m), 1.06-1.01 (2H, m).	2-(3-Chloro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

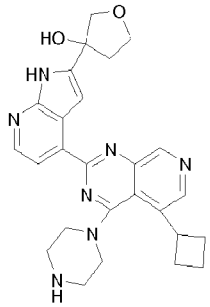
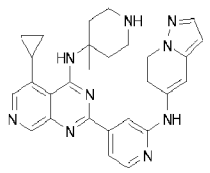
2429		[D3], [D4]	470.17 (M+H)	(dmso-d6) 13.15 (s, 1H), 9.41 (br s, 2H), 9.23 (s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.53 (s, 1H), 8.29 (d, J = 4.9 Hz, 1H), 8.02 (s, 1H), 7.80 (d, J = 5.9 Hz, 1H), 5.09 (m, 1H), 4.36 (m, 1H), 3.82 (m, 1H), 3.60-3.51 (m, 3H), 3.50 (s, 3H), 2.64(m, 1H), 1.25 (m, 2H), 1.06 (m, 2H)	(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3,4-trans)-4-methoxy-pyrrolidin-3-yl)-amine
2430		[D3], [D4]	484.18 (M+H)	(dmso-d6) 13.15 (s, 1H), 9.34 (br s, 2H), 9.23 (s, 1H), 8.64 (d, J = 4.9 Hz, 1H), 8.50 (s, 1H), 8.28 (d, J = 4.9 Hz, 1H), 8.03 (s, 1H), 7.18 (d, J = 6.5 Hz, 1H), 5.12 (m, 1H), 4.55 (m, 1H), 4.31 (m, 1H), 3.81 (m, 1H), 3.60-3.40 (m, 3H), 3.40 (s, 3H), 2.55 (m, 2H), 2.24 (m, 2H), 2.13 (m, 1H), 1.84 (m, 1H)	(±)-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3,4-trans)-4-methoxy-pyrrolidin-3-yl)-amine

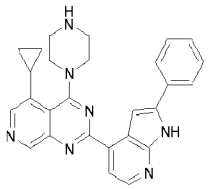
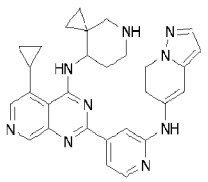
2436		[B4]	503(M+H)	1H NMR (400 MHz, METHANOL-d4) δ ppm 9.12 (1 H, s) 9.01 (1 H, s) 8.54 (1 H, s) 8.48 (1 H, d, J=6.0 Hz) 8.33 (1 H, d, J=5.8 Hz) 7.81 - 7.92 (1 H, m) 6.80 (1 H, d, J=8.0 Hz) 5.05 (1 H, dd, J=11.7, 4.4 Hz) 3.43 - 3.59 (2 H, m) 3.07 - 3.23 (2 H, m) 2.54 (1 H, t, J=6.5 Hz) 2.29 (1 H, dd, J=14.2, 2.9 Hz) 2.10 (1 H, d, J=14.1 Hz) 1.36 - 1.47 (4 H, m) 1.22 (3 H, s) 1.14 (1 H, d, J=5.5 Hz)	{5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

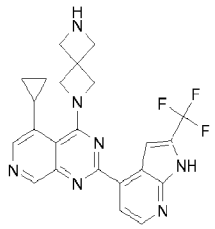
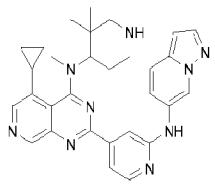
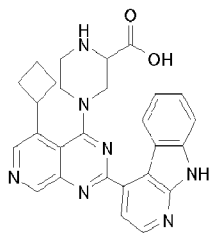
2437		[B4]	506 (M+H)	1H NMR (400 MHz, DMSO-d6) δ ppm 9.70 (1 H, s) 9.07 (1 H, s) 8.98 (1 H, d, J=10.8 Hz) 8.49 - 8.57 (2 H, m) 8.42 - 8.48 (2 H, m) 8.22 (1 H, br. s.) 8.01 (1 H, s) 7.88 (1 H, dd, J=5.4, 1.4 Hz) 7.85 (1 H, d, J=2.0 Hz) 7.62 (1 H, d, J=8.8 Hz) 6.94 (1 H, dd, J=7.7, 2.4 Hz) 6.39 (1 H, d, J=2.0 Hz) 4.85 (2 H, d, J=8.0 Hz) 3.35 (1 H, d, J=11.5 Hz) 3.06 - 3.28 (3 H, m) 2.54 - 2.71 (1 H, m) 2.28 - 2.36 (1 H, m) 2.04 - 2.16 (1 H, m) 1.85 - 1.99 (1 H, m) 1.21 - 1.32 (1 H, m) 1.19 (5 H, s) 1.10 (3 H, s)	{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine

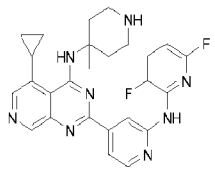
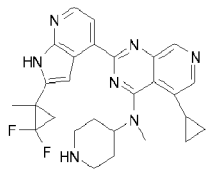
2438		[B4]	504 (M+ H)	1H NMR (400 MHz, METHANOL-d4) δ ppm 9.17 (1 H, br. s.) 8.16 (3 H, br. s.) 8.01 (1 H, d, J=5.8 Hz) 7.83 (1 H, d, J=9.0 Hz) 7.28 (1 H, d, J=9.5 Hz) 6.77 (1 H, br. s.) 4.26 (1 H, br. s.) 3.32 - 3.57 (3 H, m) 3.02 (2 H, d, J=13.6 Hz) 2.48 - 2.70 (2 H, m) 2.19 - 2.36 (1 H, m) 1.33 (3 H, d, J=4.8 Hz) 0.66 - 0.93 (3 H, m)	(5-Aza-spiro[2.5]oct-8-yl)-{5-cyclo propyl-2-[2-(pyrazolo[1,5-a]pyridin -6-ylamino)-pyridin-4-yl]-pyrido[3, 4-d]pyrimidin-4-yl}-amine
2439		[B4]	506 (M+ H)	1H NMR (400 MHz, METHANOL-d4) δ ppm 9.42 (1 H, s) 9.08 (1 H, br. s.) 8.50 (1 H, br. s.) 8.27 (1 H, d, J=5.8 Hz) 8.04 (1 H, s) 7.88 - 7.96 (2 H, m) 7.70 (1 H, d, J=9.5 Hz) 7.27 (1 H, dd, J=9.5, 1.8 Hz) 6.63 (1 H, d, J=1.8 Hz) 3.44 - 3.56 (2 H, m) 2.46 - 2.58 (1 H, m) 2.25 (1 H, d, J=14.8 Hz) 2.01 - 2.15 (1 H, m) 1.36 - 1.44 (1 H, m) 1.28 (6 H, s) 1.07 - 1.19 (4 H, m)	{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-p yrido[3,4-d]pyrimidin-4-yl}-(3,3-di methyl-piperidin-4-yl)-amine

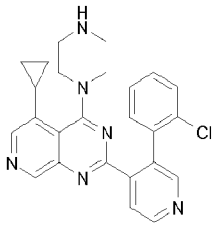
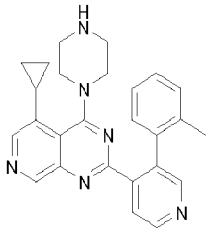
2440		[D3], [D4]	Method 6: RT: 2.76 min, MI: 504 [M+H]	^{1}H NMR (500MHz, d6-DMSO) 11.93 (1H, brs), 9.08 (1H, s), 8.61 (1H, s), 8.33 (1H, s), 8.07 (1H, m), 7.36 (1H, d), 4.58 (1H, m), 4.16 (1H, m), 3.17 (1H, m), 3.00 (3H, s), 2.75-2.55 (3H, m), 2.44-2.17 (4H, m), 2.12-1.74 (6H, m), 1.65 (3H, s), 1.63-1.47 (2H, m)	{5-Cyclobutyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine
2441		[D3], [D4]	Method 6: RT: 2.61 min, MI: 458 [M+H]	^{1}H NMR (500MHz, d6-DMSO) 11.63 (1H, brs), 9.12 (1H, s), 8.68 (1H, s), 8.27 (1H, d), 8.03 (1H, d), 7.35 (1H, s),4.71 (2H, d, J = 50 Hz), 4.28 (1H, m), 3.76-3.43 (5H, m), 3.04-2.74 (5H, m), 2.26-2.14 (2H, m), 2.06 (1H, m), 1.89 (1H, m), 1.30-1.24 (2H, m) 1.16-1.10 (2H, m)	5-Cyclobutyl-2-[2-(1-fluoromethyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

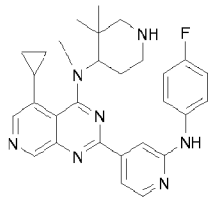
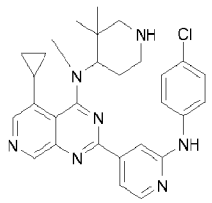
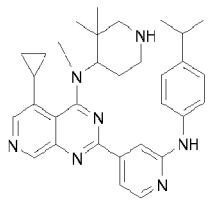
2442		[D3], [D5]	Method 5: RT: 3.12 min, MI: 472 [M+H]	^{1}H NMR (500MHz, d6-DMSO) 11.77 (1H, s), 9.12 (1H, s), 8.69 (1H, s), 8.32 (1H, d, J = 5.1 Hz), 8.06 (1H, d, J = 5.1 Hz), 7.42 (1H, d, J = 2.2 Hz), 5.70 (1H, s), 4.32 - 4.261H, m), 4.08 - 4.00 (2H, m), 3.96 - 3.91 (2H, m), 3.70 (2H, br m), 3.50 (2H, br. m), 2.93 (2H, br. m), 2.84 (2H, br m), 2.50 - 2.40 (3H, m), 2.27 - 2.22 (1H, m), 2.21 - 2.15 (2H, m), 2.12 - 2.04 (1H, m), 1.93 - 1.88 (1H, m).	3-[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-tetrahydro-furan-3-ol
2443		[B4]	492 (M+H)	1H NMR (400 MHz, DMSO-d6) δ ppm 9.70 (1 H, s) 9.06 (1 H, s) 8.50 - 8.58 (2 H, m) 8.39 - 8.49 2 H, m) 7.95 (1 H, s) 7.85 (1 H, d, J=2.3 Hz) 7.71 (2 H, dd, J=5.4, 1.4 Hz) 6.94 (1 H, dd, J=7.4, 2.4 Hz) 6.39 (1 H, d, J=2.8 Hz) 2.56 - 2.81 (6 H, m) 2.27 - 2.37 (2 H, m) 1.99 - 2.13 (2 H, m) 1.75 (3 H, s) 1.12 - 1.27 (6 H, m)	{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine

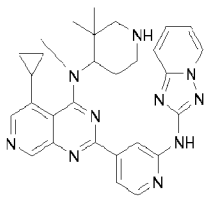
2444		[D3], [D4]	448.23	1H NMR (400 MHz, DMSO-d6) δ 12.42 (m, 1H), 9.29 (s, 1H), 9.01 (br s, 2H), 8.41 (d, 1H, J = 5.1 Hz), 8.20 (s, 1H), 8.15 (d, 1H, J = 5.0 Hz), 8.08 (m, 2H), 7.94 (d, 1H, J = 2.2 Hz), 7.53 (m, 2H), 7.41 (m, 1H), 3.98 (m, 4H), 3.39 (m, 4H), 2.77 (m, 1H), 1.28 (m, 2H), 1.10 (m, 2H)	5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1- yl-3,4-dihydro-pyrido[3,4-d]pyrimidine
2445		[B4]	504 (M+H)	1H NMR (400 MHz, DMSO-d6) δ ppm 9.68 (1 H, s) 9.08 (1 H, s) 8.50 - 8.56 (2 H, m) 8.45 (2 H, d, J=4.5 Hz) 7.99 (1 H, s) 7.76 - 7.88 (2 H, m) 6.90 - 6.96 (1 H, m) 6.52 (2 H, br. s.) 6.39 (1 H, d, J=2.0 Hz) 4.15 (1 H, br. s.) 2.94 (1 H, d, J=13.1 Hz) 2.74 (1 H, s) 2.20 (1 H, s) 1.11 - 1.34 (6 H, m) 1.03 (1 H, s) 0.65 - 0.88 4 H, m)	{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine

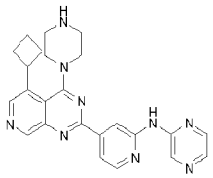
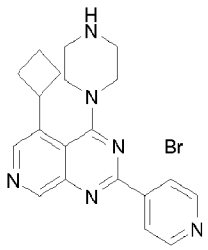
2448		[D3], [D4]	Method 5: RT: 3.66 min, MI: 442 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 9.03 (1H, s), 8.61 (1H, d), 8.26 (1H, d), 8.14 (1H, s), 7.94 (1H, s), 4.55 (4H, s), 3.76 (4H, s), 2.39-2.31 (1H, m), 1.34-1.27 (2H, m), 1.03-0.93 (2H, m).	5-Cyclopropyl-4-(2,6-diaza-spiro[3.3]hept-2-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine
2449		[B4]	520 (M+H)	1H NMR (400 MHz, DMSO-d6) δ ppm 9.75 (1 H, s) 9.50 (1 H, s) 8.98 (2 H, s) 8.45 (1 H, d, J=5.3 Hz) 8.13 (2 H, bs) 7.97 (1 H, s) 7.87 (1 H, d, J=2.3 Hz) 7.80 (1 H, d, J=5.5 Hz) 7.66 (1 H, d, J=9.5 Hz) 7.24 (1 H, dd, J=9.4, 1.9 Hz) 6.54 (1 H, dd, J=2.3, 0.8 Hz) 3.05 - 3.54 (11 H, m) 1.03 - 1.36 (9 H, m)	{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine
2450		[D3]	M+H = 480 m/z	1H NMR (400 MHz, METHANOL-d4) δ ppm 9.04 - 9.66 (m, 1 H) 8.89 (br. s., 1 H) 8.45 - 8.70 (m, 2 H) 7.90 - 8.23 (m, 1 H) 7.46 - 7.73 (m, 2 H) 7.16 - 7.35 (m, 1 H) 4.11 - 4.75 (m, 3 H) 3.38 - 4.11 (m, 3 H) 1.98 - 2.90 (m, 5 H)	4-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-2-carboxylic acid

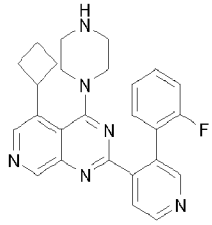
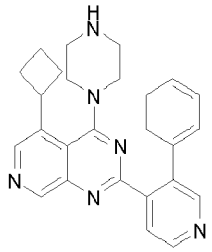
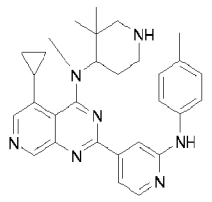
2451		[B4]	489 (M+ H)	1H NMR (400 MHz, METHANOL-d4) δ ppm 9.11 (1 H, br. s.) 8.96 (1 H, s) 8.54 (1 H, s) 8.47 (1 H, d, J=5.8 Hz) 8.23 (1 H, d, J=5.8 Hz) 7.82 (1 H, td, J=9.1, 6.1 Hz) 6.74 (1 H, d, J=8.5 Hz) 2.94 (2 H, d, J=14.8 Hz) 2.57 (1 H, t, J=5.5 Hz) 2.24 (2 H, ddd, J=14.9, 10.8, 4.1 Hz) 1.88 (3 H, s) 1.17 - 1.40 (8 H, m)	{5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine
2452		[D3], [D4]	Method 6: RT: 2.53 min, MI: 490 [M+ H]	^{1}H NMR (500 MHz, d6-DMSO) 11.97 (1H, brs), 9.03 (1H, s), 8.31 (1H, d), 8.09 (2H, m), 7.39 (1H, s), 4.66 (1H, m), 3.18-2.92 (2H, m), 3.12 (3H, s), 2.76-2.64 (2H, m), 2.45 (1H, m), 2.33 (m, 1H), 2.03-1.81 (3H, m), 1.81-1.40 (2H, m), 1.66 (3H, s), 1.40-1.05 (2H, m), 1.06-0.89 (2H, m)	{5-Cyclopropyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine

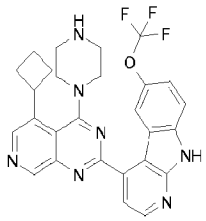
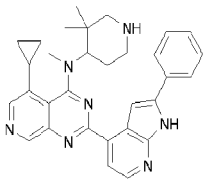
2458		[D16]	443.14 (MH)+	(400 MHz, d6-DMSO,δ): 8.88 (s, 1H), 8.84 (d, J=5.1 Hz, 1H), 8.74 (br s, 2H), 8.57 (s, 1H), 8.35 (d, J=5.1 Hz, 1H), 8.15 (s, 1H), 7.50-7.36 (m, 4H), 3.70-2.96 (m, 8H), 2.56-2.48 (m, 1H), 1.23-1.17 (m, 2H), 1.04-0.99 (m, 2H).	2-[3-(2-Chloro-phenyl)-pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2459		[D16]	423.20 (MH)+	(400 MHz, d6-DMSO,δ): 8.95 (s, 1H), 8.81 (d, J=5.1 Hz, 1H), 8.77 (br s, 2H), 8.56 (s, 1H), 8.31 (d, J=5.1 Hz, 1H), 8.15 (s, 1H), 7.30-7.17 (m, 3H), 7.05 (d, J=7.4 Hz, 1H), 3.40-2.90 (m, 8H), 2.52-2.45 (m, 1H), 1.88 (s, 3H), 1.21-1.15 (m, 2H), 1.03-0.97 (m, 2H).	5-Cyclopropyl-4-piperazin-1-yl-2-(3-o-tolyl-pyridin-4-yl)-pyrido[3,4-d]pyrimidine

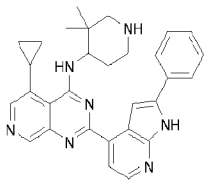
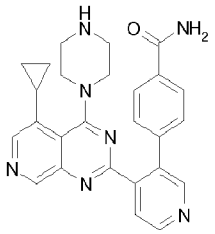
2464		[B4]	498.22 (MH)+	(400 MHz, d6-DMSO, δ): 9.45 (s, 1H), 8.98 (s, 1H), 8.34-8.09 (m, 3H), 7.89 (s, 1H), 7.74 (dd, J=9.2, 5.3 Hz, 3H), 7.15 (t, J=8.9 Hz, 2H), 3.52-3.42 (d, J=11.6 Hz, 2H), 3.14 (br s, 6H), 2.47-2.37 (m, 2H), 2.28-1.76 (m, 2H), 1.57-0.87 (m, 9H).	{5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine
2465		[B4]	514.18 (MH)+	(400 MHz, d6-DMSO, δ): 9.53 (s, 1H), 8.98 (s, 1H), 8.37-8.10 (m, 3H), 7.92 (s, 1H), 7.83-7.75 (m, 3H), 7.37-7.30 (m, 2H), 3.50-3.42 (d, J=10.1 Hz, 3H), 3.30-3.05 (m, 6H), 2.46-2.36 (m, 1H), 2.29-1.72 (m, 2H), 1.5-0.91 (m, 9H).	{2-[2-(4-Chloro-phenylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine
2466		[B4]	522.28 (MH)+	(400 MHz, d6-DMSO, δ): 9.46-9.26 (m, 1H), 9.07-8.88 (m, 2H), 8.27 (d, J=5.5 Hz, 1H), 8.23-8.08 (m, 2H), 7.89 (s, 1H), 7.71 (d, J=4.1 Hz, 1H), 7.61 (d, J=8.2 Hz, 2H), 7.18 (d, J=8.2 Hz, 2H), 4.0-1.0 (m, 28H).	{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

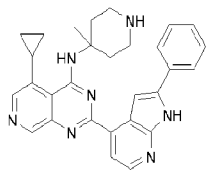
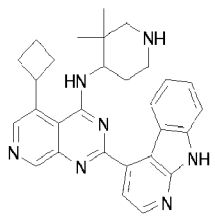
2467		[B4]	521.22 (MH)+	(400 MHz, d6-DMSO, δ): 10.65-10.54 (m, 1H), 9.06 (s, 1H), 8.96-881 (m, 2H), 8.44 (d, J=5.0 Hz, 1H), 8.25-8.10 (s, 2H), 7.94 (d, J=4.2 Hz, 1H), 7.66 (d, J=5.9 Hz, 2H), 7.17-7.12 (m, 1H), 4.0-1.0 (m, 21H).	{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

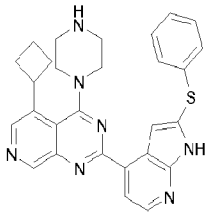
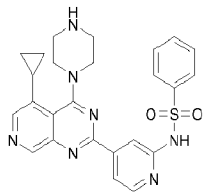
2470		[B4]	Method 6: RT: 1.95 min, MI: 440 [M+H]	^{1}H NMR (500MHz, DMSO) 9.16 (1H, s), 9.12 (1H, d), 8.80 (1H, s), 8.78 (1H, s), 8.47 (1H, d), 8.31 (1H, m), 8.16 (1H, d), 7.93 (1H, dd), 4.26 (1H, m), 3.86 (4H, m), 3.35 (2H, m), 3.26 (2H, m), 2.46 (2H, m), 2.22 (2H, m), 2.11 (1H, m), 1.93 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine
2471		[D16]	427.00 (MH)+	(400 MHz, d6-DMSO,δ): 9.02 (s, 1H), 8.88 (s, 1H), 8.75 (s, 1H), 8.68 (d, J=4.9 Hz, 1H), 7.87 (d, J=4.9 Hz, 1H), 4.27-4.17 (m, 1H), 3.65-3.45 (m, 4H), 2.91-2.69 (m, 4H), 2.52-2.42 (m, 2H), 2.25-2.02 (m, 3H), 1.95-1.86 (m, 1H).	2-(3-Bromo-pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

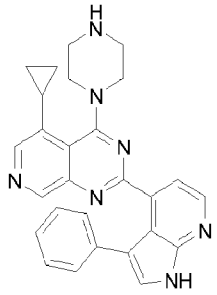
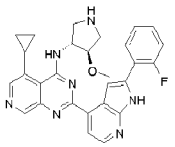
2472		[D16]	441.12 (MH)+	(400 MHz, d6-DMSO,δ): 8.99 (s, 1H), 8.87-8.65 (m, 5H), 8.27 (dd, J=5.1, 0.5 Hz, 1H), 7.47-7.37 (m, 2H), 7.27 (dt, J=7.5, 1.1 Hz, 1H), 7.14-7.08 (m, 1H), 4.16-4.06 (m, 1H), 3.41-2.88 (m, 8H), 2.44-2.34 (m, 2H), 2.18-1.84 (m, 4H).	5-Cyclobutyl-2-[3-(2-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2473		[D16]	423.10 (MH)+	(400 MHz, d6-DMSO,δ): 8.96 (s, 1H), 8.72 (d, J=5.0 Hz, 1H), 8.66 (s, 1H), 8.60 (s, 1H), 7.94 (d, J=5.0 Hz, 1H), 7.31-7.25 (m, 3H), 7.16-7.12 (m, 2H), 4.15-4.05 (m, 1H), 3.15-2.85 (m, 4H), 2.65-2.35 (m, 6H), 2.12-1.98 (m, 3H), 1.90-1.80 (m, 1H).	5-Cyclobutyl-2-(3-phenyl-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2474		[B4]	494.24 (MH)+	(400 MHz, d6-DMSO, δ): 9.37-9.22 (m, 1H), 9.00-8.87 (m, 2H), 8.28 (d, J=5.4 Hz, 1H), 8.21-8.08 (m, 2H), 7.89 (br s, 1H), 7.71 (d, J=6.1 Hz, 1H), 7.60 (d, J=8.1, Hz, 2H), 7.12 (d, J=8.3 Hz, 2H), 4.0-1.0 (m, 24H).	[5-Cyclopropyl-2-(2-p-tolylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

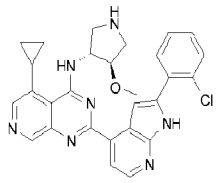
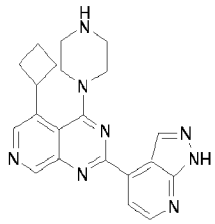
2475		[D3]	520.16 (MH)+	(400 MHz, d6-DMSO,δ): 12.38 (s, 1H), 9.16 (s, 1H), 8.99 (s, 1H), 8.95-8.75 (m, 3H), 8.67 (d, J=5.1 Hz, 1H), 8.07 (d, J=5.1 Hz, 1H), 7.65 (d, J=8.8 Hz, 1H), 7.52 (dd, J=8.7, 2.5 Hz, 1H), 4.35-4.25 (m, 1H), 3.90-3.80 (m, 4H), 3.40-3.20 (m, 4H), 2.52-2.46 (m, 2H), 2.33-2.21 (m, 2H), 2.20-2.09 (m, 1H), 2.00-1.89 (m, 1H).	4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6-trifluoromethoxy-9H-pyrido[2,3-b]indole
2476		[D3], [D4]	504.2	1H NMR (400 MHz, DMSO-d6) δ 12.38 (s, 1H), 9.21 (s, 1H), 9.00 (br s, 1H), 8.40 (d, 1H, J = 5.1 Hz), 8.25 (br s, 1H), 8.15 (m, 2H), 8.06 (d, 2H, J = 7.4 Hz), 7.93 (m, 1H), 7.53 (m, 2H), 7.41 (m, 1H), 3.16 (m, 8H), 1.98 (m, 4H), 1.21 (m, 9H)	[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin- 4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine

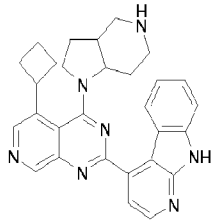
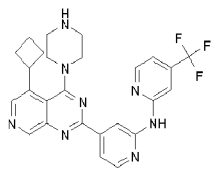
2477		[D3], [D4]	490.19	1H NMR (400 MHz, DMSO-d6) δ 12.37 (d, 1H, J = 1.6 Hz), 9.31 (s, 1H), 9.10 (m, 1H), 8.51 (s, 1H), 8.40 (m, 2H), 8.20 (d, 1H, J = 5.0 Hz), 8.08 (m, 2H), 7.98 (d, 1H, J = 2.2 Hz), 7.61 (d, 1H, J = 8.8 Hz), 7.53 (m, 2H), 7.41 (m, 1H), 7.53 (m, 2H), 4.91 (m, 1H), 3.39 (m, 1H), 3.16 (m, 3H), 2.62 (m, 1H), 2.19 (m, 1H), 1.98 (m, 1H), 1.21 (m, 10H)	[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin- 4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine
2478		[D16]	452.13 (MH)+	(400 MHz, d6-DMSO,δ): 8.96 (s, 1H), 8.81 (d, J=5.0 Hz, 1H), 8.75-8.60 (m, 3H), 8.20 (d, J=5.1 Hz, 1H), 8.17 (s, 1H), 7.99 (br s, 1H), 7.82 (d, J=8.4 Hz, 2H), 7.41 (br s, 1H), 7.28 (d, J=8.3 Hz, 2H), 3.29 (br s, 4H), 3.03 (br s, 4H), 2.57-2.50 (m, 1H), 1.23-1.17 (m, 2H), 1.06-1.00 (m, 2H).	4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-benzamide

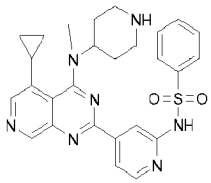
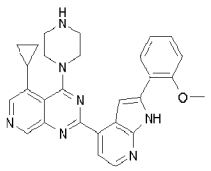
2479		[D3], [D4]	476.17	1H NMR (400 MHz, DMSO-d6) δ 12.36 (d, 1H, J = 1.6 Hz), 9.32 (s, 1H), 8.53 (m, 3H), 8.40 (d, 1H, J = 5.0 Hz), 8.08 (m, 2H), 8.01 (m,2H), 7.63 (s, 1H), 7.52 (m, 2H), 7.40 (m, 1H), 3.22 (m, 4H), 2.79 (m, 2H), 2.66 (m, 1H), 2.09 (m, 2H), 1.80 (s, 3H), 1.20 (m, 4H)	[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin- 4-yl]-(4-methyl-piperidin-4-yl)-amine
2480		[D3]	478.18 (MH)+	(400 MHz, d6-DMSO,δ): 12.04 (s, 1H), 9.15 (s, 1H), 8.88-8.80 (m, 1H), 8.64 (s, 1H), 8.58-8.54 (m, 2H), 8.20-8.10 (m, 1H), 7.82 (d, J=5.1 Hz, 1H), 7.54 (d, J=7.9 Hz, 1H), 7.50-7.45 (m, 1H), 7.17-7.11 (m, 1H), 6.60 (d, J=9.1 Hz, 1H), 4.80-4.70 (m, 1H), 4.52-4.42 (m, 1H), 3.31-3.24 (m, 1H), 3.18-3.12 (m, 1H), 3.03-2.93 (m, 2H), 2.63-2.28 (m, 4H), 2.12-1.88 (m, 4H), 1.26 (s, 3H), 1.09 (s, 3H).	[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine

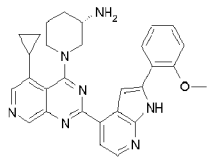
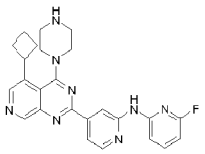
2481		[D3], [D5]	Method 5: RT: 4.32 min, MI: 494 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 12.39 (1H, s), 9.10 (1H, s), 8.69 (1H, s), 8.41 (1H, d, J = 5.0 Hz), 8.12 (1H, d, J = 5.0 Hz), 7.57 (1H, br. d, J = 1.1 Hz), 7.40 - 7.33 (4H, m), 7.31 - 7.28 (1H, m), 4.30 - 4.23 (1H, m) 3.66 - 3.59 (2H, br. m), 3.47 - 3.40 (2H, br. s), 2.92 - 2.86 (2H, br m), 2.38 - 2.75 (2H, br. m), 2.48 - 2.44 (2H, m), 2.20 - 2.14 (2H, m), 2.11 - 2.01 (1H, m), 1.93 - 1.89 (1H, m).	5-Cyclobutyl-2-(2-phenylsulfanyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2482		[D3], [D12]	Method 6: RT: 2.25 min, MI: 488 [M+H]	^{1}H NMR (400MHz, DMSO, 90°C) 8.99 (1H, s), 8.22 (2H, m), 8.15 (1H, s), 7.97 (2H, d), 7.84 (1H, d), 7.57 (4H, m), 3.78 (4H, m), 2.97 (4H, m), 2.62 (1H, m), 1.26 (2H, m), 0.99 (2H, m).	N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-benzenesulfonamide

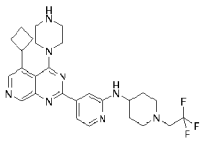
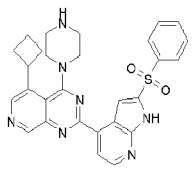
2483		[D3], [D6]	Method 6: RT: 2.97 min, MI: 448 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 12.04 (1H, s), 8.69 (1H, s), 8.39 (1H, d), 8.01 (1H, s), 7.61 (1H, d), 7.52 (1H, d), 7.00-6.92 (1H, m), 6.84-6.77 (4H, m), 3.19-2.89 (4H, m), 2.71-2.59 (4H, m), 2.45-2.38 (1H, m), 1.32-1.23 (2H, m), 1.05-1.00 (2H, m).	5-Cyclopropyl-2-(3-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine
2484		[D3], [D4]	496.16	1H NMR (400 MHz, DMSO-d6) δ ppm 1.07 (d, J=3.51 Hz, 2 H) 1.21 - 1.31 (m, 2 H) 2.59 - 2.68 (m, 1 H) 3.43 (s, 3 H) 3.45 - 3.63 (m, 4 H) 4.35 - 4.40 (m, 1 H) 5.11 (m, 1 H) 7.36 - 7.50 (m, 3 H) 7.77 (d, J=5.8 Hz, 1 H) 7.97 - 8.01 (m, 1 H) 8.09 (td, J=7.91, 1.51 Hz, 1 H) 8.15 - 8.21 (m, 1 H) 8.46 (d, J=5.0 Hz, 1 H) 8.49 - 8.55 (m, 1 H) 9.17 (s, 1 H) 9.37 (br s, 2 H) 12.33 - 12.39 (m, 1H)	{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3, 4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-((3R,4R)-4-methoxy-pyrrolidin-3- yl)-amine

2485		[D3], [D4]	512.14	1H NMR (400 MHz, DMSO-d6) δ 12.27 (d, 1H, J = 1.3 Hz), 9.37 (m, 2H), 9.16 (s, 1H), 8.51 (s, 1H), 8.45 (d, 1H, J = 5.0 Hz), 8.19 (d, 1H, J = 5.0 Hz), 7.93 (d, 1H, J = 2.2 Hz), 7.83 (m, 1H), 7.76 (m, 1H), 7.66 (m, 1H), 7.50 (m, 2H), 5.10 (m, 1H), 4.36 (m, 1H), 3.54 (m, 4H), 3.37 (s, 3H), 2.64 (m, 1H), 1.25 (m, 2H), 1.06 (m, 2H)	{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3, 4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-((3R,4R)-4-methoxy-pyrrolidin-3- yl)-amine
2486		[D3], [D13]	Method 5: RT: 3.37 min, MI: 387 [M+H]	^{1}H NMR (500MHz, DMSO) 13.82 (brs, 1H), 9.21 (s, 1H), 8.93 (s, 1H), 8.74 (s, 1H), 8.70 (d, 1H), 8.17 (d, 1H), 4.32-4.22 (m, 1H), 3.79-3.51 (m, 4H), 3.06-2.83 (m, 2H), 2.24-2.15 (m, 2H), 2.12-2.02 (m, 1H), 1.94-1.85 (m, 1H), 1.32-1.03 (m, 2H).	5-Cyclobutyl-4-piperazin-1-yl-2-(1H-pyrazolo[3,4-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine

2487		[D3]	476.19 (MH)+	(400 MHz, d6-DMSO,δ): 12.06 (s, 1H), 9.13 (s, 1H), 8.77 (s, 1H), 8.72 (d, J=8.1 Hz, 1H), 8.65-8.50 (m, 3H), 7.87 (d, J=5.1 Hz, 1H), 7.54 (d, J=7.9 Hz, 1H), 7.50-7.45 (m, 1H), 7.20-7.15 (m, 1H), 4.54-4.48 (m, 1H), 4.32-4.22 (m, 1H), 4.13-4.03 (m, 1H), 3.45-3.36 (m, 1H), 3.29-3.15 (m, 1H), 3.10-2.88 (m, 3H), 2.80-2.58 (m, 2H), 2.50-2.38 (m, 2H), 2.18-1.65 (m, 7H).	4-[5-Cyclobutyl-4-(octahydro-pyrrolo[3,2-c]pyridin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole
2488		[B4]	Method 6: RT: 2.78 min, MI: 507 [M+H]	^{1}H NMR (500MHz, DMSO) 9.16 (1H, s), 8.80 (1H, s), 8.70 (1H, s), 8.56 (1H, d), 8.48 (1H, d), 8.26 (1H, s), 7.93 (1H, dd), 7.27 (1H, d), 4.26 (1H, m), 3.87 (4H, s), 3.35 (2H, m), 3.26 (2H, m), 2.46 (2H, m), 2.22 (2H, m), 2.11 (1H, m), 1.93 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine

2489		[D3], [D12]	Method 6: RT: 2.29 min, MI: 516 [M+H]	^{1}H NMR (400MHz, DMSO, 90°C) 8.94 (1H, s), 8.25 (1H, m), 8.15 (2H, m), 7.96 (2H, d), 7.78(1H, d), 7.54 (3H, m), 4.61 (1H, m), 3.15 (4H, m), 2.75 (2H, m), 2.47 (1H, m), 1.81 (5H, m), 1.23 (2H, m), 0.94 (2H, m).	N-{4-[5-Cyclopropyl-4-(methyl-piperidin-4-yl-amino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzenesulfonamide
2490		[D3], [D4]	478.17	1H NMR (400 MHz, DMSO-d6) δ 12.08 (d, 1H, J = 1.6 Hz), 9.21-8.91 (m, 3H), 8.41 (d, 1H, J = 5.1 Hz), 8.20-8.17 (m, 2H), 8.00 (d, 1H, J = 2.2 Hz), 7.97-7.95 (m, 1H), 7.44-7.40 (m, 1H), 7.23 (d, 1H, J = 7.8 Hz), 7.14-7.10 (m, 1H), 4.05 (m, 7H), 3.39 (m, 4H), 2.81-2.74 (m, 1H), 1.31-1.26 (m, 2H), 1.13-1.09 (m, 2H)	5-Cyclopropyl-2-[2-(2-methoxy-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-3,4-dihydro-pyrido[3,4-d]pyrimidine

2491		[D3], [D4]	492.2	1H NMR (400 MHz, DMSO-d6) δ 12.03 (d, 1H, J = 1.6 Hz), 9.16 (br s, 1H), 8.41 (d, 1H, J = 5.1 Hz), 8.18-8.04 (m, 6H), 7.97-7.94 (m, 1H), 7.44-7.40 (m, 1H), 7.23 (d, 1H, J = 7.8 Hz), 7.14-7.10 (m, 1H), 4.47-4.44 (m, 1H), 4.00 (s, 3H), 3.56-2.64 (m, 5H), 2.05-1.64 (m, 4H), 1.28 (m, 2H), 1.08 (m, 2H)	(S)-1-{5-Cyclopropyl-2-[2-(2-methoxy-phenyl)-1H-pyrrolo[2,3-b]pyridin-4- yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine
2492		[B4]	Method 6: RT: 2.41 min, MI: 457 [M+H]	^{1}H NMR (500MHz, DMSO) 10.14 (1H, s), 9.04 (1H, s), 8.74 (1H, s), 8.69 (1H, s), 8.40 (1H, d), 7.84 (2H, m), 7.75 (1H, dd), 6.59 (1H, dd), 4.23 (1H, m), 3.66 (2H, s), 3.54 (2H, s), 2.90 (2H, s), 2.79 (2H, s), 2.44 (2H, m), 2.16 (2H, m), 2.06 (1H, m), 1.89 (1H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine

2493		[B4]	Method 6: RT: 2.02 min, MI: 527 [M+H]	^{1}H NMR (500MHz, DMSO) 9.00 (1H, s), 8.66 (1H, s), 8.08 (1H, d), 7.50 (1H, s), 7.37 (1H, dd), 6.69 (1H, d), 4.23 (1H, m), 3.76 (1H, m), 3.62 (2H, s), 3.45 (2H, s), 3.30 (2H, s), 3.14 (2H, m), 2.90 (4H, m), 2.77 (2H, m), 2.45 (3H, m), 2.16 (2H, m), 2.05 (1H, m), 1.89 (3H, m), 1.46 (2H, m).	[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine
2494		[D3], [D5], [D14]	Method 5: RT: 3.95 min, MI: 526 [M+H]	^{1}H NMR (500 MHz, d6-DMSO) 9.14 (1H, s), 8.73 (1H, s), 8.62 (1H, d, J = 4.9 Hz), 8.19 (1H, d, J = 4.9 Hz), 8.12 - 8.08 (3H, m), 7.75 - 7.71 (1H, m), 7.69 - 7.65 (2H, m), 4.30 - 4.23 (1H, m), 3.71 - 3.64 (2H, br. m), 3.58 - 3.52 (2H, br. m), 2.97 - 2.90 (2H, br. m), 2.85 - 2.76 (2H, br. m), 2.50 - 2.47 (2H, m), 2.23 - 2.15 (2H, m), 2.12 - 2.03 (1H, m), 1.93 - 1.88 (1H, m).	2-(2-Benzenesulfonyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine

VI. Biology

PKCι IC_{50} Assay

Assays are based on the ability of PKCι to phosphorylate a commercially available peptide substrate *in vitro*. The peptide substrate is FAM-PKCε pseudopeptide derived peptide, and comprises the amino acid sequence 5FAM-ERMRPRKRQGSVRRRV-NH_2. Recombinant, full-length human PKCι expressed in Sf21 insect cells is also commercially available. Recombinant, kinase-domain human PKCι is expressed and purified in-house.

The procedure below explains how dose response curves for inhibitors of PKCι are obtained. The screen described is for a 384 well format but the assay can be adapted to 1536 or other formats as required.

Compounds to be tested are dissolved in 100% DMSO. Compounds are diluted as required to give a final concentration of 4% DMSO (v/v) in the assay. 1μl is plated into 384 well black low-binding flat bottomed assay plates which are used immediately. Dilutions and additions of compound to assay plates are carried out using Matrix WellMate® and Matrix PlateMate® Plus liquid handling systems.

On the day of the screen PKCι / substrate working solution, and ATP working solution, are prepared in buffer containing 20mM tris-HCl pH7.5, 10mM $MgCl_2$, 0.01% Triton X100, 250μM EGTA and 1mM DTT. The final concentration of PKCι used varies depending on the batch of protein but is typically 15pM. The final concentration of peptide substrate in the assay is 100nM. ATP is used at a final concentration of 150μM or 25μM in the assays containing full-length or kinase-domain PKCι respectively, which corresponds to five times or equal to the K_M^{APP} for ATP for each enzyme, respectively. The final buffer concentration in the assay is 18mM tris-HCl pH7.5, 9mM $MgCl_2$, 0.009% Triton X100, 225μM EGTA and 0.9mM DTT. Relevant controls are included, namely no compound and no enzyme. 5μl PKCι / substrate working solution at 30pM and 200nM, respectively, is added to the wells, followed by 4μl ATP working solution at 375μM or 62.5μM for full-length or kinase-domain PKCι respectively, using a 16 channel Matrix pipette. The reaction is allowed to incubate for 60 minutes at room temperature, before the reaction is stopped and developed by the addition of 20μl IMAP™ development reagent (Molecular Devices). IMAP development reagent consists of 0.25% (v/v) IMAP progressive binding reagent, 17% (v/v) IMAP progressive binding buffer A and 3% (v/v) IMAP progressive binding buffer B. The plates are then incubated for 2 hours at room temperature before being read using an appropriate plate reader, for example a Molecular

Devices HT Analyst or a BMG Pherastar. Plates are read using a fluorescence polarisation protocol with excitation at 485nm and emission at 530nm, and dichroic mirror at 505nm.

Percentage inhibition values are calculated from fluorescence polarisation values, using the no compound and no enzyme control values as 0% and 100% inhibition, respectively. IC50 determination is performed with ExcelFit software (IDBS) using curve fit 205. Z′ factors are determined for each plate tested and are all above 0.5.

Alternatively, compounds were tested for their ability to inhibit the kinase activity of recombinant human baculovirus-expressed PKCíota using the immobilized metal-ion affinity particle (IMAP®) fluorescence polarization detection system (Molecular Devices, Sunnyvale, CA). PKCíota/IMAP® substrate mixture (2X) was prepared in 1X IMAP assay buffer (Molecular Devices) containing 1 mM DTT so that the final assay concentrations were 15 pM PKCíota (EMD Millipore, Billerica, MA) and 100 nM 5-fluorescein-amidite (FAM)-PKC€-pseudosubstrate (5-FAM-ERMRPRKRQGSVRRRV-NH2) (Molecular Devices). The 2X working solution was added at 5 µL/well into a 384-well black, non-binding, flat bottom assay plate (Corning, Corning, NY). Compound serial dilutions were carried out in 100% DMSO, then 100 nL transferred to the assay plate containing 5 µL of the 2X enzyme/substrate solution using a BioMek NX pin tool (Beckman Coulter, Indianapolis, IN). Enzyme reaction was initiated by the addition of 5 µL 2X ATP, so that the final assay concentration was 150 µM. Assay plates were incubated for 1 hour in a 25°C incubator, followed by addition of 20 µL IMAP® detection reagent. The detection reagent was comprised of 85% 1X buffer A and 15% 1X buffer B and the IMAP® Binding Reagent diluted 1:400. Assay plates were then incubated for 2 hours in a 25°C incubator. Following the incubation, fluorescence polarization was measured using a PerkinElmer Envision™ 2102 plate reader (PerkinElmer, Waltham, MA) with an excitation wavelength of 480 nm and an emission wavelength of 535 nm.

Results

Biological data for the Example compounds is presented in the following table. Activities are set forth as follows:

IC50 in IMAP assay against full length PKCi at 150 µM ATP:

++++	=	< 100 nM
+++	=	100 nM to 1,000 nM
++	=	1,000 nM to 10,000 nM
+	=	10,000 nM to 40,000 nM

Example	Activity
1	+++
2	+++
3	+
4	++
5	+
6	++++
7	++++
8	+++
9	++++
10	+++
11	++++
12	++++
13	++
14	+++
15	++
16	+++
17	++
18	+
19	+
20	+
21	+
22	+
23	+
24	+
25	+++
26	+
27	+
28	+++
29	++
30	++
31	+++
32	+++
33	++
34	+
35	+
36	+
37	++++
38	+++
39	+
40	++
41	++++
42	+
43	++
44	+++
45	++
46	++++
47	++++

Example	Activity
48	++
49	++
50	+
51	++
52	++
53	+++
54	++
55	++
56	+
57	+
58	+++
59	+
60	++
61	++
62	++
63	+++
64	+
65	+
66	+
67	+
68	+++
69	+
70	++
71	++
72	++
73	+
74	++++
75	++
76	++++
77	++++
78	++
79	+
80	+++
81	+++
82	++
83	+
84	+
85	+
86	++
87	+
88	+++
89	++++
90	+++
91	+++
92	++
93	+++
94	+++

Example	Activity
95	+++
96	+++
97	+++
98	++
99	+++
100	+++
101	++
102	+++
103	+++
104	++
105	++++
106	++
107	++
108	+++
109	+++
110	+++
111	+++
112	+
113	+++
114	+++
115	++++
116	++
117	++
118	++
119	++
120	++
121	+++
122	+++
123	++
124	++
125	++
126	+++
127	+
128	++
129	+++
130	++
131	++++
132	++++
133	++++
134	++++
135	++++
136	++++
137	++++
138	++++
139	++++
140	+++
141	+++

Example	Activity
142	++
143	++++
151	+++
152	++
153	++
154	+++
155	++
156	++
157	++
158	++
159	+
160	+
200	++++
201	++++
202	++++
203	++++
204	++++
205	+++
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207	+++
208	++++
209	+++
210	+++
211	++++
212	++++
213	+++
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215	+++
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218	++++
219	+++
220	++++
221	++++
222	++++
223	++
224	++++
225	+++
226	++++
227	++++
228	++++
229	++++
230	++++
231	+
232	+++
233	+++
234	+++

Example	Activity
235	+++
236	+++
237	++
238	++++
239	++++
240	++++
241	++++
242	++++
243	++
244	++
245	++
246	+++
247	+++
248	++++
249	++++
250	+++
251	+++
252	+++
253	++++
254	++++
255	+++
256	++++
257	+++
258	++++
259	++++
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261	+++
262	+++
263	++++
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267	++++
268	+++
269	++++
270	+++
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272	++++
273	++++
274	+++
275	++++
276	++++
277	++++
278	+
279	++++
280	++++
281	++++

Example	Activity
282	++++
283	++++
284	+++
285	++++
303	+++
304	+++
305	+++
306	++
307	+++
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310	+++
311	++++
313	++++
314	++++
316	+++
317	+++
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321	++++
322	+++
323	++++
324	++++
325	+
326	+++
327	++++
328	++
329	++++
330	++++
331	++++
332	++++
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334	++
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348	++++

Example	Activity
349	++++
350	++++
351	++++
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357	++++
358	+++
359	+++
360	+++
361	++++
362	++++
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367	++++
368	++++
369	++++
370	++++
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372	++++
373	++++
374	++++
375	++++
376	+++
377	+++
378	++++
379	++++
380	++++
382	++++
383	++++
384	+++
385	+++
386	+++
387	++++
388	+
389	+++
390	+++
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392	++++
393	++++
394	++++
395	+++
396	++++

Example	Activity
397	+++
398	+++
399	++++
400	++++
401	++++
402	+++
403	+++
404	+++
405	++++
406	+++
407	+++
408	+++
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Example	Activity
444	++++
445	+++
446	+++
447	++++
448	++++
449	++++
450	++++
451	++++
452	+++
453	++++
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455	+++
456	+++
457	+++
458	++
459	+
460	+
461	++
462	+
463	++
464	+++
465	++
466	++
467	++
468	+++
469	++
470	++
471	++
473	++++
474	++++
475	++++
476	++++
477	++++
478	++++
481	++++
482	+++
483	++++
484	++++
485	++++
486	++++
487	++++
488	+++
489	++++
490	++++
491	++++
492	++++
493	++++

Example	Activity
494	+++
495	++++
496	+
497	+
498	+
499	+
500	+++
501	+
502	++
503	++
504	++++
505	++++
506	+++
507	++++
508	++++
509	++++
510	++++
511	+++
512	++++
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515	++++
516	++++
517	+++
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519	+++
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522	+++
523	++++
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525	+++
526	++++
527	++++
528	+++
529	++++
530	++++
531	++++
532	++++
533	+++
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535	+++
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537	++++
538	++++
539	++++
540	++++

Example	Activity
541	++++
542	+++
543	++++
544	++++
545	++++
546	++++
547	++++
548	++++
549	++++
550	++++
551	++++
552	++++
553	++++
554	+++
555	+++
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577	++++
578	++++
579	+
580	++++
581	++++
582	++++
583	++++
584	++++
585	++++
586	++++
587	++++

Example	Activity
588	++++
589	++++
590	++++
591	++++
592	++++
593	+
594	++++
595	++++
596	+
597	+
598	++++
599	++++
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604	++++
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619	++++
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621	++++
622	++++
623	++++
624	+++
625	+++
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629	++++
630	++++
631	+++
632	++++
633	++++
634	++++

Example	Activity
635	++++
636	++++
637	++++
638	+++
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640	++++
641	++++
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663	+++
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672	++++
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674	++
675	+++
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681	++++
682	+++
683	++

Example	Activity
684	+++
685	+++
686	+++
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688	++++
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691	++++
692	++++
693	++++
694	++++
695	++++
696	++++
697	+++
698	+++
699	++++
700	++++
701	+
702	+++
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704	++++
705	++++
706	+++
707	+
708	+++
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711	+++
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718	++++
719	++++
720	++++
721	++++
722	++++
723	++
724	++++
725	++++
726	+++
727	++++
728	+++
729	++++
730	++++

Example	Activity
731	++++
732	++++
733	++
734	++++
735	+++
736	++++
737	++++
738	++++
739	+++
740	+++
741	+++
742	++++
743	++++
744	++++
745	+++
746	++++
747	++++
748	++++
749	++++
750	++++
751	++++
752	++++
753	++++
754	++++
756	++++
757	+++
758	++++
760	+++
761	+++
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763	++++
764	++++
765	++++
766	+++
767	+++
768	++++
769	++++
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779	++++

Example	Activity
780	++++
781	+++
782	+++
783	++++
784	++++
785	++++
786	++++
787	++++
788	+++
789	+++
790	++++
791	++++
793	+++
794	++++
795	++++
796	++++
797	+++
798	++++
799	++++
800	++++
801	++++
802	++++
803	+++
804	+++
805	+++
806	++
807	++++
808	++++
809	++++
810	++++
811	++++
812	++++
813	++++
814	++++
815	++++
816	++++
817	++++
818	++++
819	+
820	++++
821	++++
822	++
823	++++
824	++++
825	++++
826	+++
827	++++

Example	Activity
828	++++
829	++++
830	++
831	++++
832	++++
833	++++
834	++++
835	++++
836	++++
837	++++
838	++++
839	++++
840	++++
841	++++
842	++++
843	++++
844	++++
845	++++
846	++++
1000	++
1001	++
1002	++++
1003	+++
1004	++
1005	+++
1006	+++
1007	++
1008	+++
1009	++
1010	+++
1011	++
1012	++
1013	+++
1014	+++
1015	+++
1016	++++
1017	++++
1018	++++
1200	++++
1201	++++
1202	++++
1203	++++
1204	+++
1205	+++
1206	++++
1207	+++
1208	+++

Example	Activity
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1211	++++
1212	++++
1213	++++
1214	++++
1215	++++
1216	++++
1217	++++
1218	++++
1219	++++
1220	++++
1221	++++
1222	++++
1223	++++
1224	+
1226	++++
1227	+
1228	++++
1229	++++
1230	++++
1231	++++
1232	++++
1233	++++
1234	+++
1235	+++
1236	++
1237	+++
1238	++++
1239	++++
1240	++++
1241	+++
1242	++
1243	++
1244	++++
1245	+
1246	+
1247	++++
1248	+
1249	++++
1250	++++
1251	++++
1252	++++
1253	++++
1254	+++
1255	++++
2001	++++

Example	Activity
2002	++++
2003	++++
2004	++++
2005	++++
2006	++++
2007	++++
2008	++++
2009	++++
2010	++++
2011	++++
2012	++++
2013	++++
2014	++++
2015	++++
2016	++++
2017	++++
2018	++++
2019	++++
2020	++++
2021	++++
2022	++++
2023	++++
2024	++++
2025	++++
2026	++++
2027	++++
2028	++++
2029	++++
2030	++++
2031	++++
2032	++++
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2034	++++
2035	++++
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2040	++++
2041	++++
2042	++++
2043	++++
2044	++++
2045	++++
2046	++++
2047	++++
2048	++++

Example	Activity
2049	++++
2050	++++
2051	++++
2052	++++
2053	++++
2054	++++
2055	++++
2056	++++
2057	++++
2058	++++
2059	++++
2060	++++
2061	++++
2062	++++
2063	++++
2064	++++
2065	++++
2066	++++
2067	++++
2068	++++
2069	++++
2070	++++
2071	++++
2072	++++
2073	++++
2074	++++
2075	++++
2076	+++
2077	+
2078	++++
2079	++++
2080	++++
2081	++++
2082	++++
2083	++++
2084	++++
2085	+++
2086	++++
2087	++++
2088	++++
2089	++++
2090	+++
2091	++++
2092	++++
2093	++++
2094	++++
2095	++++

Example	Activity
2096	+++
2097	++++
2098	++++
2099	++++
2100	++++
2101	++++
2102	++++
2103	+++
2104	++++
2105	++++
2106	++++
2107	++++
2108	++++
2109	++++
2110	+++
2111	++++
2112	++++
2113	++++
2114	++++
2115	++++
2116	++++
2117	++++
2118	++++
2119	++++
2120	++++
2121	++++
2122	++++
2123	+++
2124	++++
2125	++++
2126	++++
2127	++++
2128	+++
2129	++++
2130	++++
2131	++++
2132	++++
2133	++++
2134	++++
2135	++++
2136	++++
2137	++++
2138	++++
2139	++++
2140	++++
2141	++++
2142	+++

Example	Activity
2143	++++
2144	++++
2145	++++
2146	++++
2147	++++
2148	++++
2149	++++
2150	++++
2151	++++
2152	++++
2153	++++
2154	++++
2155	+++
2156	+++
2157	++++
2158	++++
2159	+++
2160	++++
2161	++++
2162	++++
2163	++++
2164	++++
2165	++++
2166	++++
2167	++++
2168	+
2169	++++
2170	++++
2171	++++
2172	++
2173	++
2174	++++
2175	++++
2176	++++
2177	++++
2178	++++
2179	++++
2180	++++
2181	++++
2182	++++
2183	++++
2184	++++
2185	++++
2186	+++
2187	+++
2188	+++
2189	+++

Example	Activity
2190	++++
2191	++++
2192	++++
2193	++++
2194	++++
2195	++++
2196	++++
2198	++++
2199	+++
2200	++++
2201	++++
2202	++++
2203	++++
2204	++++
2205	++++
2206	+
2207	++++
2208	+++
2209	++++
2210	++++
2211	++
2301	++
2302	++++
2303	++++
2304	++++
2305	++++
2306	++++
2307	++++
2308	++++
2309	++++
2310	++++
2311	++++
2312	++++
2313	++++
2314	++++
2315	++++
2316	++++
2317	++++
2318	++++
2319	++++
2320	++++
2321	++++
2322	++++
2323	++++
2324	++++
2325	++++
2326	++++

Example	Activity
2327	++++
2328	++++
2329	++++
2330	++++
2331	++++
2332	++++
2333	++++
2334	++++
2335	++++
2336	++++
2337	++++
2338	++++
2339	+++
2340	+++
2341	++++
2342	++++
2343	+++
2344	+++
2345	+++
2346	+++
2347	++++
2348	++++
2349	++++
2350	++++
2351	++++
2352	+++
2353	++++
2354	++++
2355	++++
2356	++++
2357	++++
2358	++++
2359	++++
2360	++
2361	++++
2362	++++
2363	++++
2364	+++
2365	++
2366	+++
2367	+++
2368	+++
2369	++++
2370	++++
2371	++++
2372	+++
2373	+++

Example	Activity
2374	++++
2375	++++
2376	++++
2377	++++
2378	++++
2379	++++
2380	++++
2381	++++
2382	+++
2383	+++
2384	++++
2385	++++
2386	++++
2387	+++
2388	+++
2389	+++
2390	+++
2391	+
2392	++++
2393	++++
2394	++++
2395	+++
2396	+++
2397	++++
2398	++++
2399	+++
2400	++
2401	++++
2402	+++
2403	++++
2404	++++
2405	++++
2406	++++
2407	++++
2408	++++
2409	++++
2410	++++
2411	++++
2412	++++
2413	++++
2414	++++

Example	Activity
2415	++++
2416	++++
2417	++++
2418	++++
2419	++++
2420	++++
2421	++++
2422	++++
2423	++++
2424	++++
2425	++++
2426	++++
2427	++
2429	++++
2430	++++
2431	+++
2432	++++
2433	++++
2434	++++
2435	++++
2436	++++
2437	++++
2438	+++
2439	+++
2440	++++
2441	++++
2442	++++
2443	++++
2444	++++
2445	++
2446	++++
2447	++++
2448	+++
2449	++++
2450	++
2451	++++
2452	++++
2453	++++
2454	++++
2455	++++
2456	++++

Example	Activity
2457	++++
2458	++++
2459	+++
2460	++
2461	++
2462	++++
2463	++++
2464	++++
2465	+++
2466	++++
2467	++++
2468	++++
2469	++++
2470	++++
2471	+++
2472	++++
2473	++++
2474	++++
2475	+++
2476	++++
2477	++++
2478	+++
2479	++++
2480	++++
2481	++++
2482	++
2483	+++
2484	++++
2485	++++
2486	+++
2487	++++
2488	++++
2489	++
2490	++++
2491	++++
2492	++++
2493	++++
2494	++++

5

10

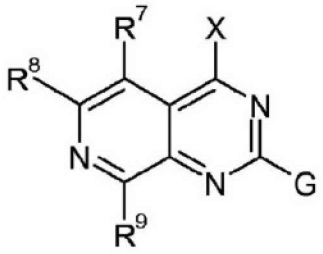
Preferably, a compound of the present invention (i.e., a compound of formula (I) or a salt thereof) has an IC_{50} in an IMAP assay against full length PKCι at 150 μM ATP of < 40 μM. In one embodiment, a compound of the present invention has an IC_{50} in an IMAP assay against full length PKCι at 150 μM ATP of 40 μM – 10 μM. More preferably, a compound of the present invention has an IC_{50} in an IMAP assay against full length PKCι at 150 μM ATP of 10 μM – 1 μM. In one embodiment, a compound of the present invention has an IC_{50} in an IMAP assay against full length PKCι at 150 μM ATP of 1 μM – 0.1 μM. More preferably, a compound of the present invention has an IC_{50} in an IMAP assay against full length PKCι at 150 μM ATP of < 0.1 μM.

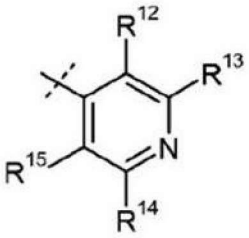
Preferably, a compound of the present invention (i.e., a compound of formula (I) or a salt thereof) has an IC_{50} in an IMAP assay against kinase domain PKCι at 25 μM ATP of < 40 μM. In one embodiment, a compound of the present invention has an IC_{50} in an IMAP assay against kinase domain PKCι at 25 μM ATP of 40 μM – 10 μM. More preferably, a compound of the present invention has an IC_{50} in an IMAP assay against kinase domain PKCι at 25 μM ATP of 10 μM – 1 μM. In one embodiment, a compound of the present invention has an IC_{50} in an IMAP assay against kinase domain PKCι at 25 μM ATP of 1 μM – 0.1 μM. More preferably, a compound of the present invention has an IC_{50} in an IMAP assay against kinase domain PKCι at 25 μM ATP of < 0.1 μM.

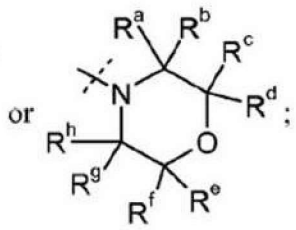
As those skilled in the art will appreciate, numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore understood that within the scope of the appended claims, the invention may be practiced otherwise than as specifically described herein, and the scope of the invention is intended to encompass all such variations.

Each publication referenced herein is incorporated by reference in its entirety for all purposes.

Claims:

1. A compound of formula (I)  or a salt form thereof, wherein (I)



G is a group of formula  ;

X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-9 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{28}$, $–C(=O)OR^{28}$, $–C(=O)NR^{24}R^{28}$, $–C(O)C(=O)R^{28}$, $–NR^{24}R^{28}$, $–NR^{24}NR^{24}R^{28}$, $–N=NR^{28}$, $–NR^{24}OR^{28}$, $–NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)C(=O)R^{28}$, $–NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)OR^{28}$, $–NR^{24}C(=O)NR^{24}R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $–NR^{24}S(=O)_2R^{28}$, $–NR^{24}S(=O)_2NR^{24}R^{28}$, $–OR^{28}$, $–OC(=O)R^{28}$, $–OC(=O)NR^{24}R^{28}$, $–OC(=O)OR^{28}$, $–OS(=O)R^{28}$, $–OS(=O)_2R^{28}$, $–OS(=O)_2OR^{28}$, $–OS(=O)_2NR^{24}R^{28}$, $–S(=O)_nR^{28}$, $–S(=O)_2NR^{24}R^{28}$, and $–S(=O)NR^{24}R^{28}$;

R^7, R^8, R^9, R^{12}, R^{13}, R^{14}, R^{15}, R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally

substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(\ NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$ $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})$ $(NR^{22}R^{23})$ $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$;

or any of R^7 and R^8, R^{12} and R^{13}, R^{14} and R^{15}, R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a $C6_{-11}$aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl

optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19};

R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11} aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-C(=NR^{35})R^{30}$, $-C(=NR^{35})NR^{32}R^{33}$, $-C(=NOH)NR^{32}R^{33}$, $-C(=NOR^{36})R^{30}$, $-C(=NNR^{32}R^{33})R^{30}$, $-C(=NNR^{34}C(=O)R^{31})R^{30}$, $-C(=NNR^{34}C(=O)OR^{31})R^{30}$, $-C(=S)NR^{32}R^{33}$, –NC, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}C(=S)R^{30}$, $-NR^{34}C(=S)OR^{30}$, $-NR^{34}C(=S)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-NR^{34}P(=O)R^{78}R^{78}$, $-NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-NR^{34}P(=O)(OR^{30})(OR^{30})$, $-NR^{34}P(=O)(SR^{30})(SR^{30})$, $-OR^{30}$, =O, –OCN, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-OS(=O)R^{30}$, $-OS(=O)2R^{30}$, $-OS(=O)_2OR^{30}$, $-OS(=O)_2NR^{32}R^{33}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-OP(=O)(OR^{30})(OR^{30})$, $-OP(=O)(SR^{30})(SR^{30})$, $-Si(R^{34})_3$, –SCN, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-SP(=O)(OR^{30})(OR^{30})$, $-SP(=O)(SR^{30})(SR^{30})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$;

R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-}

$_6$alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{28} at each occurrence is independently chosen from C_{1-10}alkyl optionally substituted by 1-13 R^{49}, C_{2-10}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69};

R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79},

C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–C(=O)C(=O)R^{70}$, $–C(=NR^{75})R^{70}$, $–C(=NR^{75})NR^{72}R^{73}$, $–C(=NOH)NR^{72}R^{73}$, $–C(=NOR^{76})R^{70}$, $–C(=NNR^{72}R^{73})R^{70}$, $–C(=NNR^{74}C(=O)R^{71})R^{70}$, $–C(=NNR^{74}C(=O)OR^{71})R^{70}$, $–C(=S)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}NR^{72}R^{73}$, $–N=NR^{74}$, $=NR^{70}$ $=NOR^{70}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)C(=O)OR^{71}$,$–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}C(=O)NR^{74}C(–O)R^{70}$, $–NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $–NR^{74}C(=NR^{75})NR^{72}R^{73}$, $–NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $–NR^{74}C(=S)R^{70}$, $–NR^{74}C(=S)OR^{70}$, $–NR^{74}C(=S)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–NR^{74}P(=O)R^{78}R^{78}$, $–NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–NR^{74}P(=O)(OR^{70})(OR^{70})$, $–NR^{74}P(=O)(SR^{70})(SR^{70})$, $–OR^{70}$, =O, –OCN, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OC(=O)OR^{70}$, $–OC(=NR^{75})NR^{72}R^{73}$, $–OS(=O)R^{70}$, $–OS(=O)_2R^{70}$, $–OS(=O)_2OR^{70}$, $–OS(=O)_2NR^{72}R^{73}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–OP(=O)(OR^{70})(OR^{70})$, $–OP(=O)(SR^{70})(SR^{70})$, $–Si(R^{74})_3$, –SCN, =S, $–S(=O)_nR^{70}$, $–S(=O)_2OR^{70}$, SO_3R^{77}, $–S(=O)_2NR^{72}R^{73}$, $–S(=O)NR^{72}R^{73}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–SP(=O)(OR^{70})(OR^{70})$, $–SP(=O)(SR^{70})(SR^{70})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–P(=O)(OR^{70})(OR^{70})$, and $–P(=O)(SR^{70})(SR^{70})$;

R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by

1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkenyl optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109};

R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89};

R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{119}, C_{2-6}alkenyl optionally substituted by 1-11 R^{119} optionally substituted by 1-9 R^{119} C_{6-11}aryl optionally substituted by 1-11 R^{119}, C_{2-6}arylalkyl optionally substituted by 1-19 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{119} C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{119},

3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{119}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{115})R^{110}$, $–C(=NR^{115})NR^{112}R^{113}$, $–C(=NOH)NR^{112}R^{113}$, $–C(=NOR^{116})R^{110}$, $–C(=NNR^{112}R^{113})R^{110}$, $–C(=NNR^{114}C(=O)R^{111})R^{110}$, $–C(=NNR^{114}C(=O)OR^{111})R^{110}$, $–C(=S)NR^{112}R^{113}$, –NC, $–NO_2$, $–NR^{112}R^{113}$, $NR^{114}NR^{112}R^{113}$, $–N=NR^{114}$,= NR^{110}, NOR^{110}, $–NR^{114}OR^{116}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}NR^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $–NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $NR^{114}C(=NR^{115})NR^{112}R^{113}$, $–NR^{114}C(=O)C(=O)NR^{112}R^{113}$, $–NR^{114}C(=S)R^{110}$, $–NR^{114}C(=S)OR^{110}$, $–NR^{114}C(=S)NR^{114}S(=O)_2R^{111,}$ $–NR^{114}S(=O)_2NR^{112}R^{138}$,$–NR^{114}P(=O)R^{118}R^{118}$, $–NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–NR^{114}P(=O)(OR^{110})(OR^{110})$, $–NR^{114}P(=O)(SR^{110})(SR^{110})$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–OC(=NR^{115})NR^{112}R^{113}$, $–OS(=O)R^{110}$, $OS(=O)_2R^{110}$, $–OS(=O)_2OR^{110}$, $–OS(=O)_2NR^{112}R^{113}$, $–OP(=O)R^{118}R^{118}$ $–OP(=O)(NR^{112}R^{113})(NR^{112}R^{113},)$ $OP(=O)(OR^{110})(OR^{110})$, $OP(=O)(SR^{110})(SR^{110})$, $–Si(R^{114})_3$, –SCN, =S, $–S(=O)_nR^{110}$, $–S(=O)_2OR^{110}$, , $–S(=O)_2NR^{112}R^{113}$, $–S(=O)NR^{112}R^{113}$, $–SP(=O)R^{118}R^{118}$ $–SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$ $–SP(=O)(OR^{110})(OR^{110})$, $SP(=O)(SR^{110})(SR^{110})$, $–P(=O)R^{118}R^{118}$, $–P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–P(=O)(OR^{110})(OR^{110})$, and $–P(=O)(SR^{110})(SR^{110})$;

R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, $C_{7-1}6$arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40

R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149};

R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{119} R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{159}, C_{2-6}alkenyl optionally substituted by 1-11 R^{159}, C_{2-6}alkynyl optionally substituted by 1-9 R^{159}, C_{6-11}aryl optionally substituted by 1-11 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{159}, 6-21

membered heteroarylalkyl optionally substituted by 1-27 R^{159}, halogen, –CN, –$C(=O)R^{150}$, –$C(=O)OR^{150}$, –$C(=O)NR^{152}R^{153}$, –$C(=O)C(=O)R^{150}$, –$C(=NR^{155})R^{150}$, –$C(=NR^{155})NR^{152}R^{153}$, –$C(=NOH)NR^{152}R^{153}$, –$C(=NOR^{156})R^{150}$, –$C(=NNR^{152}R^{153})R^{150}$, –$C(=NNR^{154}C(=O)R^{151})R^{150}$, –$C(=NNR^{154}C(=O)OR^{151})R^{150}$, –$C(=S)NR^{152}R^{153}$, –NC, –$NO_2$, –$NR^{152}R^{153}$, –$NR^{154}NR^{152}R^{153}$, –$N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, –$NR^{154}OR^{156}$, –$NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)C(=O)R^{150}$, –$NR^{154}C(=O)OR^{151}$, –$NR^{154}C(=O)C(=O)OR^{151}$, –$NR^{154}C(=O)NR^{152}R^{153}$, $NR^{154}C(=O)NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, –$NR^{154}C(=NR^{155})NR^{152}R^{153}$, –$NR^{154}C(=O)C(=O)NR^{152}R^{153}$, –$NR^{154}C(=S)R^{150}$, –$NR^{154}C(=S)OR^{150}$, –$NR^{154}C(=S)NR^{152}R^{153}$, –$NR^{154}S(=O)_2R^{151}$, –$NR^{154}S(=O)_2NR^{152}R^{153}$, –$NR^{154}P(=O)R^{158}R^{158}$, –$NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$NR^{154}P(=O)(OR^{150})(OR^{150})$, –$NR^{154}P(=O)(SR^{150})(SR^{150})$, –$OR^{150}$, =O, –OCN, –$OC(=O)R^{150}$, –$OC(=O)NR^{152}R^{153}$, –$OC(=O)OR^{150}$, –$OC(=NR^{155})NR^{152}R^{153}$, –$OS(=O)R^{150}$ –$OS(=O)_2R^{150}$, –$OS(=O)_2OR^{150}$, –$OS(=O)_2NR^{152}R^{153}$, –$OP(=O)R^{158}R^{158}$, –$OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$OP(=O)(OR^{150})(OR^{150})$, –$OP(=O)(SR^{150})(SR^{150})$, –$Si(R^{154})_3$, –SCN, =S, –$S(=O)_nR^{150}$, –$S(=O)_2OR^{150}$, , –$S(=O)_2NR^{152}R^{153}$, –$S(=O)NR^{152}R^{153}$, –$SP(=O)R^{158}R^{158}$, –$SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$SP(=O)(OR^{150})(OR^{150})$, –$SP(=O)(SR^{150})(SR^{150})$, –$P(=O)R^{158}R^{158}$, –$P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$P(=O)(OR^{150})(OR^{150})$, and –$P(=O)(SR^{150})(SR^{150})$;

R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179};

or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{189};

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169} C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{199}, C_{2-6}alkenyl optionally substituted by 1-11 R^{199}, C_{2-6}alkynyl optionally substituted by 1-9 R^{199}, C_{6-11}aryl optionally substituted by 1-11 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{199}, halogen, –CN, –$C(=O)R^{190}$, –$C(=O)OR^{190}$, –$C(=O)NR^{192}R^{193}$, –$C(=O)C(=O)R^{190}$, –$C(=NR^{195})R^{190}$,

–C(=NR^{195})NR^{192}R^{193}, –C(=NOH)NR^{192}R^{193}, –C(=NOR^{196})R^{190}, –C(=NNR^{192}R^{193})R^{190}, –C(=NNR^{194}C(=O)R^{191})R^{190}, –C(=NNR^{194}C(=O)OR^{191})R^{190}, –C(=S)NR^{192}R^{193}, –NC, –NO$_2$, –NR^{192}R^{193}, –NR^{194}NR^{192}R^{193}, –N=NR^{194}, =NR^{190}, =NOR^{190}, –NR^{194}OR^{196}, –NR^{194}C(=O)R^{190}, –NR^{194}C(=O)C(=O)R^{190}, –NR^{194}C(=O)OR^{191}, –NR^{194}C(=O)C(=O)OR^{191}, –NR^{194}C(=O)NR^{192}R^{193}, –NR^{194}C(=O)NR^{194}C(=O)R^{190}, –NR^{194}C(=O)NR^{194}C(=O)OR^{190}, –NR^{194}C(=NR^{195})NR^{192}R^{193}, –NR^{194}C(=O)C(=O)NR^{192}R^{193}, –NR^{194}C(=S)R^{190}, –NR^{194}C(=S)OR^{190}, –NR^{194}C(=S)NR^{192}R^{193}, –NR^{194}S(=O)$_2$R^{191}, –NR^{194}S(=O)2NR^{192}R^{193}, –NR^{194}P(=O)R^{198}R^{198}, –NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193}), –NR^{194}P(=O)(OR^{190})(OR^{190}), –NR^{194}P(=O)(SR^{190})(SR^{190}), –OR^{190}, =O, –OCN, –OC(=O)R^{190}, OC(=O)NR^{192}R^{193}, –OC(=O)OR^{190}, –OC(=NR^{195})NR^{192}R^{193}, –OS(=O)R^{190}, –OS(=O)$_2$R^{190}, –OS(=O)$_2$OR^{190}, –OS(=O)$_2$NR^{192}R^{193}, –OP(=O)R^{198}R^{198}, –OP(=O)(NR^{192}R^{193})(NR^{192}R^{193}), –OP(=O)(OR^{190})(OR^{195}), –OP(=O)(SR^{190})(SR^{190}), –Si(R^{194})$_3$, –SCN, =S, –S(=O)$_n$R^{190}, –S(=O)$_2$OR^{190}, , –S(=O)$_2$NR^{192}R^{193}, –S(=O)NR^{192}R^{193}, –SP(=O)R^{198}R^{198}, –SP(=O)(NR^{192}R^{193})(NR^{192}R^{193}), –SP(=O)(OR^{190})(OR^{190}), –SP(=O)(SR^{190})(SR^{190}), –P(=O)R^{198}R^{198}, –P(=O)(NR^{192}R^{193})(NR^{192}R^{193}), P(=O)(OR^{190})(OR^{190}), and –P(=O)(SR^{190})(SR^{190});

R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C$_{1-6}$alkyl optionally substituted by 1-13 R^{209}, C$_{2-6}$alkenyl optionally substituted by 1-11 R^{209}, C$_{2-6}$alkynyl optionally substituted by 1-9 R^{209}, C$_{6-11}$aryl optionally substituted by 1-11 R^{209}, C$_{7-16}$arylalkyl optionally substituted by 1-19 R^{209}, C$_{3-11}$cycloalkyl optionally substituted by 1-21 R^{209}, C$_{4-17}$cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{192} and R^{193} at each occurrence is independently chosen from H, C$_{1-6}$alkyl optionally substituted by 1-13 R^{219}, C$_{2-6}$alkenyl optionally substituted by 1-11 R^{219}, C$_{2-6}$alkynyl optionally substituted by 1-9 R^{219}, C$_{6-11}$aryl optionally substituted by 1-

11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219};

or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229};

R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(–O)C(–O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}OR^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=NR^{230})NR^{230}R^{230}$, –

$NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $-NR^{230}C(=S)R^{230}$, $-NR^{230}C(=S)OR^{230}$, $-NR^{230}C(=S)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-NR^{230}P(=O)R^{231}R^{231}$, $-NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-NR^{230}P(=O)(OR^{230})(OR^{230})$, $-NR^{230}P(=O)(SR^{230})(SR^{230})$, $-OR^{230}$, =O, –OCN, $-OC(=O)R^{230}$, $-OC(=O)NR^{230}R^{230}$, $-OC(=O)OR^{230}$, $-OC(=NR^{230})NR^{230}R^{230}$, $-OS(=O)R^{230}$, $-OS(=O)_2R^{230}$, $-OS(=O)_2OR^{230}$, $-OS(=O)_2NR^{230}R^{230}$, $-OP(=O)R^{231}R^{231}$, $-OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-OP(=O)(OR^{230})(OR^{230})$, $-OP(=O)(SR^{230})(SR^{230})$, $-Si(R^{230})_3$, –SCN, =S, $-S(=O)_nR^{230}$, $-S(=O)_2OR^{230}$, $-SO_3R^{230}$, $-S(=O)_2NR^{230}R^{230}$, $-S(=O)NR^{230}R^{230}$, $-SP(=O)R^{231}R^{231}$, $-SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-SP(=O)(OR^{230})(OR^{230})$, $-SP(=O)(SR^{230})(SR^{230})$, $-P(=O)R^{231}R^{231}$, $-P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-P(=O)(OR^{230})(OR^{230})$, and $-P(=O)(SR^{230})(SR^{230})$;

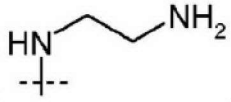
R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl;

R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl; and

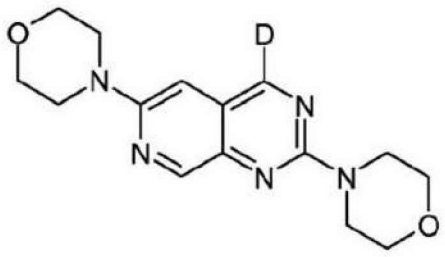
n at each occurrence is independently chosen from 0, 1, and 2;

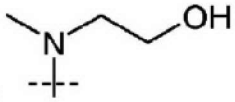
with the proviso that the compound is not

(a)

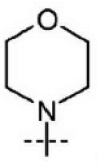
in which D is H or 

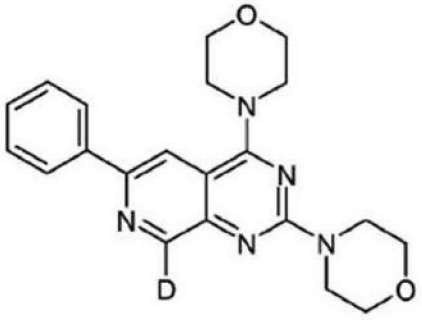
, or a salt form thereof;

(b) 

in which D is 

or

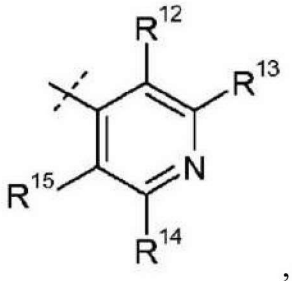

, or a salt form thereof; or

(c)  in which D is H or -CH_3, or a salt form thereof.

2. A compound as defined in claim 1, wherein X is chosen from 5-6 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $–NR^{24}R^{28}$.

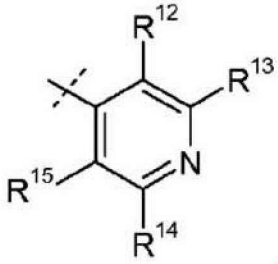
3. A compound as defined in claim 1, wherein X is chosen from morpholinyl optionally substituted by 1-6 R^{19}, piperidinyl optionally substituted by 1-6 R^{19}, piperazinyl optionally substituted by 1-6 R^{19}, and $–NR^{24}R^{28}$.

4. A compound as defined in any one of claims 1-3, wherein G is a group of formula


, and R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$ and $–S(=O)_2NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl

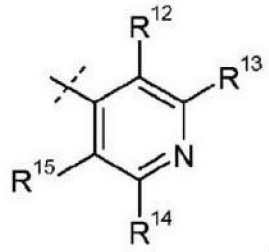
optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

5. A compound as defined in any one of claims 1-3, wherein G is a group of formula



, and R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, –$C(=O)R^{20}$, –$C(=O)OR^{20}$, –$C(=O)NR^{22}R^{23}$, –NO_2, –$NR^{22}R^{23}$, –$NR^{24}NR^{22}R^{23}$, –$NR^{24}OR^{26}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)OR^{21}$, –$NR^{24}C(=O)NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$OR^{20}$, –$OC(=O)R^{20}$, –$S(=O)_nR^{20}$, and –$S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

6. A compound as defined in any one of claims 1-3, wherein G is a group of formula



, and R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, –$NR^{22}R^{23}$, and –$NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

7. A compound as defined in any one of claims 1-3, wherein G is a group of formula

and, and R^{12}, R^{13}, R^{14} and R^{15} are H; or R^{12} and R^{13}, together with the atoms linking them, form a pyrrolyl ring.

8. A compound as defined in any one of claims 1-7, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

9. A compound as defined in any one of claims 1-8, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and a R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}.

10. A compound as defined in any one of claims 1-9, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

11. A compound as defined in any one of claims 1-10, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-OR^{70}$, and $-S(=O)_nR^{70}$.

12. A compound as defined in any one of claims 1-11, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{89}.

13. A compound as defined in any one of claims 1-11, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl.

14. A compound as defined in any one of claims 1-13, wherein R^{79} and R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl and phenyl.

15. A compound as defined in claim 1, wherein X is chosen from $-NHR^{28}$ and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

16. A compound as defined in any one of claims 1 or 7-15, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-O(C_{1-6}$alkyl); R^8 is H; and R^9 is H.

17. A compound chosen from:
1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;
N-(2-aminoethyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2R)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
(3R)-N-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
(3R)-N-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
N-[(2S)-2-amino-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(3S)-3-benzyl-1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]aminolpropan-2-ol;
(3S)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

(3R)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane;
(2S)-2,4-dibenzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine;
tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxylate;
tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane-1-carboxylate;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]thiomorpholine;
N,N-Dimethyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine;
N-[(2S)-2-amino-3-phenylpropyl]-N-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-one;
N-[(2S)-1-amino-3-phenylpropan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
(2R)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(3S)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane;
2-{4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}ethan-1-ol;
(3S)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol;
(3R)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol;
(3R)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(2S)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
methyl(2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-carboxylate;
methyl(2S,4S)-4-[(2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-amido]pyrrolidine-2-carboxylate;
[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl](methyl)amine;
N-[(3R)-oxolan-3-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;

(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine;
(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl]methanol;
N-[(2R,3R)-2-amino-3-fluoro-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
2-[(2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl]acetamide;
[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl]dimethylamine;
(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol;
1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3,5-cis-dimethylpiperazine;
(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine;
(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
3-(fluoromethyl)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
N-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidine-4-carboxamide;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide;
N-cyclohexyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide;
2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl}acetonitrile;
1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
(3S)-3-ethyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(3S)-3-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[2-(3-fluoropyridin-4-yl)-5-methoxypyrido[3,4-d]pyrimidin-4-yl]piperazine;
4-{4-[(8aR)-octahydropyrrolo[1,2-a]piperazin-2-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine;
1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
4-{4-[(3aS)-octahydro-1H-pyrrolo[3,2-c]pyridin-5-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine;
(3S)-3-benzyl-1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
3-phenyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine;
3-ethynyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine;
{1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]azetidin-3-yllmethanol;
(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidin-4-ol;
(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(4-fluorophenyl)[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl]methanol;
N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide;
N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-acetamide;
methyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrid[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine;
(2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1-methylpiperazine;
2-{[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amino}acetamide;
N-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)methanesulfonamide;
(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea;
3-ethyl-1-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea;
(3aR)-5-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-1H-[1,3]oxazolo[3,4-a]piperazin-1-one;
2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}acetonitrile;
N-{3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-8-yl]-phenyl}-methanesulfonamide;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-pyrazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-phenyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol;
3-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol;
N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(4-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(2-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(pyridin-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2,8-bis(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(4-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
2-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol;
N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(3-chlorophenyl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-[4-(4-chlorophenyl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(pyrimidin-5-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-aminophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-7-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(5-methylthiophen-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(dimethyl-1,2-oxazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(thiophen-3-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-1,3-benzodiazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-ethoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(1H-pyrazol-5-yl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-[5-(aminomethyl)furan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

(R)-3-Phenyl-N^1-(2-pyridin-4-yl-8-pyridin-2-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine;

N^4-((R)-2-Amino-3-phenyl-propyl)-N^8-phenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine;

4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(pyrimidin-2-yl)pyrido[3,4-d]pyrimidine-4,8-diamine;

4-N-[(2S)-2-amino-3-phenylpropyl]-8-N-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidine-4,8-diamine;

4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(1H-1,2,4-triazol-3-yl)pyrido[3,4-d]pyrimidine-4,8-diamine;

(R)-N^1-[8-(4-Methyl-piperazin-1-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine;

(R)-3-Phenyl-N^1-(8-phenylsulfanyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine;

N-[(2S)-2-amino-3-phenylpropyl]-8-phenoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(methylsulfanyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)-2-methylbut-3-yn-2-ol;

5-Chloro-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;

1-[5-bromo-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

1-[5,8-dichloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

5-Butyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;

1-[5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

N-[(2S)-2-amino-3-phenylpropyl]-5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

1-[5-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

1-[5-cyclopropyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

1-{5-[(benzyloxy)methyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl}piperazine;

5-Chloro-4-piperazin-1-yl-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;

5-chloro-N,N-dimethyl-4-(piperazin-1-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-amine;

5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
5-Methoxy-4-piperidin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid amide;
3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid phenylamide;
4-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid; [(S)-1-(4-chloro-phenyl)-3-hydroxy-propyl]-amide;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid methyl ester;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenylamide;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid benzylamide;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenethyl-amide;
4-Piperazin-1-yl-8-propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
8-Methyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-oxazol-2-yl)-amine;
(4,5-Dimethyl-oxazol-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(4-Cyclopropyl-thiazol-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
3-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;
(2-Fluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine;
4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-morpholin-4-yl-acetamide;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-piperidin-1-yl-acetamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-4-yl-amine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-benzamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-methyl-amine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
N-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl)-acetamide;
Cyclopropanecarboxylic acid [4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2,2-dimethyl-propionamide;
Tetrahydro-pyran-4-carboxylic acid [4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-thiazol-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-oxazol-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-oxazol-2-yl)-amine;
{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol;
1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-4-methyl-piperidin-4-ol;

{4-[4-((S)-3-Isopropyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

2-{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-ethanol;

N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-N',N'-dimethyl-benzene-1,4-diamine;

{5-Methoxy-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(2-Fluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{5-Methoxy-2-[2-(4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(4-Fluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{4-[5-Methoxy-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{(S)-4-(5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile;

{4-[4-((R)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

Cyclopropanecarboxylic acid {4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

{4-[4-((S)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[4-((S)-3-Cyclopropyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[4-((R)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,3,6-trifluoro-phenyl)-amine;

[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

{5-Methoxy-2-[2-(pyrazin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

Thiophene-2-carboxylic acid {4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

Cyclopentyl-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

Cyclohexyl-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{2[2-(Pyrazin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol;

2-{3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-R-pyrrolidin-1-yl}-acetamide;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine;

(2-Fluoro-phenyl)-{2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-5-yl}-amine;

4-{5-(4-Cyano-pyridin-2-ylamino)-2-[2-(4-cyano-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine;

{4-[5-Chloro-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

N-[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-difluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5–fluoro-pyridin-2-yl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;

5-[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;

{4-Piperazin-1-yl-2-[2-(2,3,6-trifluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-5-yl}-(2,3,6-trifluoro-phenyl)-amine;

(2,6-Difluoro-phenyl)-{2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-5-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,5-dimethyl-oxazol-2-yl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

1-{5-Cyclopropyl-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

{4-[5-Cyclopropyl-4-((S)-3-isopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine;

(4-{5-Cyclopropyl-4-[3-(1,1-difluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

{(S)-4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile;

Cyclopentyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

Cyclohexyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(tetrahydro-pyran-4-yl)-amine;

Cyclopentyl-{4-[5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

Adamantan-1-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

2-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide;

4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide;

4-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide;

{4-[(1S,4S)-4-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

Pyrazine-2-carboxylic acid {4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide;

3-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide;

2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide;

2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide;

2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;

2-(4-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;

2-(3-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{2-[2-(5-Phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(6-Morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
(2-{2-[6-(4-Methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;
2-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;
{2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide;
2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;
2-(3-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;
2-(4-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;
2-(4-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;
1-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile;
{5-Methoxy-2-[2-(5-phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
{5-Methoxy-2-[2-(6-morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
(5-Methoxy-2-{2-[6-(4-methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;
2-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;
{2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-Phenyl-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(4-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(2-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(3-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{2-[2-(4-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(4-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

6-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile;

2-[4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;

{2-[2-(4-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

6-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile;

{2-[2-(5-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(5-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-[2-(Pyrimidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-(3-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(4-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

(R)-Pyrrolidin-3-yl-{2-[2-(4-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

(R)-Pyrrolidin-3-yl-{2-[2-(5-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;
2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;
6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinonitrile;
{4-[5-Methoxy-4-(4-morpholin-4-yl-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;
2-(4-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
{2-[2-(5-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
{2-[2-(2-Methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
(2-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
{5-Methoxy-2-[2-(2-methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;
(5-Methoxy-2-{2-[4-(tetrahydro-pyran-4-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(tetrahydro-pyran-4-yl)-phenyl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-pyridin-2-yl)-amine;
(4-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(5-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine;
2-(4-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
2-(3-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide;
2-(3-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(3-trifluoromethyl-phenyl)-acetamide;
2-(4-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine;
{2-[2-(Pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl{-(R)-pyrrolidin-3-yl-amine;
{5-Methoxy-2-[2-(pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine;
2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinamide;
6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide;

(3-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine;
5-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;
{5-Methoxy-2-[2-(pyrimidin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-5-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-5-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine;
2-[4-(5-Methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;
2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,5-trimethoxy-phenyl)-amine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-phenyl-pyridin-3-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-3-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine;

N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-pyridin-3-yl-acetamide;

2-{4-[5-Methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

2-(3-Chloro-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-3-yl-acetamide;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-4-yl-acetamide;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methoxy-pyridin-2-yl)-amine;

2-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

2-(3-Cyano-phenyl)-N-{4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(3-Cyano-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

(6-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(R)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide;

(S)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide;

(R)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide;

(S)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide;

4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-pyridin-2-yl)-amine;

(3-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-piperazin-1-ylpyridin-3-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-methyl-4-(4-methyl-piperazin-1-yl)-phenyl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-piperidin-4-yl-1H-pyrazol-4-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-2-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl](5-methyl-pyridin-3-yl)-amine;
(5-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Fluoro-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
3-Fluoro-4-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;
4-Fluoro-3-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;
(2,6-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Fluoro-6-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-pyridin-3-yl)-amine;
(S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol;

2-{4-[4-((S)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;

(R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol;

2-{4-[4-((R)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine;

[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-1-pyrrolidin-2-ylmethyl-amine;

2-{4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol;

{1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol;

{(R)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol;

(R)-7-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one;

(±)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(±)-trans-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-one;

(2,3-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2,5-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine;

((R)-4-{2-[2-(2,6-Difluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl)-methanol;
3-Hydroxymethyl-1-[5-methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine;
(6-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine;
(2-Fluoro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Fluoro-3-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Fluoro-3-trifluoromethyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2,4-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl](2,3,4-trifluoro-phenyl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,5-trifluoro-phenyl)-amine;
(3S,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(3R,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;
3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-propionamide;
[4-(5-Methoxy-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;
{4-[4-(4,4-Difluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;
1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile;
{4-[4-(4-Fluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;
(3R,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;
(3S,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;
{(R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol;
{(S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol;
(meso)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azepane-4,5-diol;
1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;
1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;
((S)-1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol;
((S)-1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol;
2-(4-Cyano-phenyl)-N-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine;

(2-Chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

2-{4-[5-Cyclopropyl-4-(4-hydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine;

(±)-2-{4-[5-Cyclopropyl-4-cis-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-o-tolyl-amine;

2-{4-[5-Cyclopropyl-4-((3R,4S)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

2-{4-[5-Cyclopropyl-4-((3S,4R)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-N-(1-phenylpyrazol-4-yl)pyridin-2-amine;

(2,3-Dimethyl-2H-indazol-6-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[1-(2-Fluoro-phenyl)-1H-pyrazol-4-yl]-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-phenyl-1H-pyrazol-4-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dimethyl-2H-indazol-6-yl)-amine;
Phenyl-[4-(4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-pyridin-3-yl)-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-isoxazol-3-yl)-amine;
2-[2-(3-Piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol;
2-[2-(3-Piperazin-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol;
2-[2-(1-Piperidin-4-ylmethyl-1H-pyrazol-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol;
{5-Methoxy-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;
(5-Methoxy-2-{2-[4-(2-pyrrolidin-1-yl-ethoxy)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-methyl-amine;
{5-Methoxy-2-[2-(3-piperidin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;
[4-(5-Methoxy-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-dimethyl-phenyl)-amine;
5-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine;
Cyclopropyl-{4-[5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(R)-tetrahydro-furan-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,4-difluoro-cyclohexyl)-amine;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-trifluoromethyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-pyridin-3-yl)-amine;

(6-Chloro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxymethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(S)-tetrahydro-furan-3-yl-amine;

2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;

tert-Butyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-trifluoromethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-2-methyl-phenyl)-amine;

3-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-4-methyl-benzonitrile;

7-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-pyridin-2-yl)-amine;

(2-Chloro-6-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

3-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-4-fluoro-benzonitrile;

(4-tert-Butyl-2-chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

2-{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-ethyl)-amine;

2-{4-[5-Cyclopropyl-4-(3-oxo-tetrahydro-oxazolo[3,4-a]pyrazin-7-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-pyridin-3-yl)-amine;

{4-[5-Cyclopropyl-4-(2,5-diaza-bicyclo[4.1.0]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[5-Cyclopropyl-4-(2,5-diaza-bicyclo[4.1.0]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-dichloro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dimethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-dimethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dichloro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dichloro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridazin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(dimethyl-phosphinoyl)-phenyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(diethyl-phosphinoyl)-phenyl]-amine;

N^5-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-N^2,N^2-dimethyl-pyridine-2,5-diamine;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-2-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-5-trifluoromethyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-trifluoromethoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methanesulfonyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-3-methyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-isopropyl-2-methyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pent-deuterio-phenyl-amine;
1-{2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-phenyl}-ethanol;
(1R,2S)-2-Amino-cyclopentanecarboxylic acid [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;
1-{4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-cyclopropanol;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-6-yl-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-5-yl-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridazin-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-3-methoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-ethoxy-2,6-difluoro-phenyl)-amine;
(2-Chloro-3-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;
(2-Chloro-4-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-phenyl)-amine;
(2-Chloro-4-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-dimethyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-3-methyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-methyl-phenyl)-amine;
(2-Chloro-5-fluoro-phenyl)-[4-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Chloro-5-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Chloro-3-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
5-Cyclopropyl-2-(6,7-dimethoxy-quinolin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methoxy-phenyl)-amine;
N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamine;
N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-isobutyramide;
Cyclopropanecarboxylic acid [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclobutyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-ethyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((S)-1-phenyl-ethyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-3-methoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-4-methoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-2-methyl-phenyl)-amine;
(2-Chloro-5-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine;
(2-Chloro-5-trifluoromethyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4-difluoro-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-pyrazol-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-cyclohexyl)-amine;

(+/-)-(cis)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;
(4-Cyclopropyl-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-4-methyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-imidazol-4-yl)-amine;
2-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol;
(S)-3-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-propane-1,2-diol;
(R)-3-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-propane-1,2-diol;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-4-methyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4-dimethoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,5-trimethoxy-phenyl)-amine;
N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide;
N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-3,3,3-trifluoro-propionamide;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(1-methyl-4-oxo-4λ^5-[1,4]azaphosphinan-4-yl)-phenyl]-amine;
2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidine;
(2-Chloro-6-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(6-Chloro-2-fluoro-3-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(3-Chloro-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclopentyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-isopropyl-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-ethyl-phenyl)-amine;
2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(1-ethyl-4-oxo-4λ^5-[1,4]azaphosphinan-4-yl)-2-methoxy-phenyl]-amine;
N-(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-acetamide;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-3-methoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-5-methoxy-phenyl)-amine;
Cyclopropylmethyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-methyl-amine;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-fluoro-benzonitrile;
[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-cyclohexanol;

(2-Chloro-6-fluoro-3-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Chloro-3,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[5-Cyclopropyl-4-(2,2,3,3,5,5,6,6-octadeuterio-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-y]-phenyl-amine;

(4-Cyclopropyl-3-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acidamide;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(2,6-difluoro-phenyl)-acetamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-propyl-phenyl)-amine;

(4-Cyclopropyl-2-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(2,6-difluoro-phenyl)-amine;

(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(3-fluoro-phenyl)-ethyl]-amine;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine;

(3-Chloro-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-phenyl)-amine;
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(4-fluoro-phenyl)-ethyl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2,6-difluoro-phenyl)-ethyl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-phenyl-amine;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid isopropylamide;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid amide;
N-(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-acetamide;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-fluoro-ethyl)-amide;
N-{4-[5-Cyclopropyl-4-((S)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;
2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
(4-{5-Cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;
(4-{5-Cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(4-fluoro-phenyl)-amine;
(4-{5-Cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;
(4-{5-Cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(4-fluoro-phenyl)-amine;

Cyclopropanecarboxylic acid (4-{5-cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-amide;
Cyclopropanecarboxylic acid (4-{5-cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-amide;
(5-Cyclopropyl-2-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
1-{5-Cyclopropyl-4[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide;
1-{5-Cyclopropyl-4[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid methylamide;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-pyridin-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-pyridin-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclohexyl)-amine;
1-[2-(2-Cyclohexylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carboxylic acid isopropylamide;
(+/-)-(cis)-1-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;
(+/-)-(trans)-1-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;
(+/-)-2-{4-[5-Cyclopropyl-4-((trans)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylaminol-isonicotinonitrile;
(+/-)-(trans)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4d]pyrimidin-4-yl)-piperidine-3,4-diol;
1-[2-(2-Cyclopentylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carboxylicacid isopropylamide;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-pyridin-4-yl)-amine;
Biphenyl-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzoic acid;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-hydroxy-ethyl)-amide;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid dimethylamide;
4-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid amide;
1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-ol;
5-Cyclopropyl-2-(2-fluoro-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
{4-[4-(4-Amino-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;
{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-phenyl)-amine;
{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;
{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine;
{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;
(+/-)-(1RS,2RS,4SR)-Bicyclo[2.2.l]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[4-(4-Aminomethyl-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(S)-1-pyrrolidin-2-ylmethyl-amine;

[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

Bicyclo[1.1.1]pent-1-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-3-fluoro-pyridin-2-yl]-phenyl-amine;

[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

(+/-)-cis-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-cyclobutyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-1-phenyl-ethyl)-amine;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-3-carboxylic acid methylamide;

{4-[4-(3-Amino-pyrrolidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-phenyl}-acetic acid;

[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

3-{4-[5-Cyclopropyl-4-((3R,4S)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzonitrile;

Chroman-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

N-(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl)-acetamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-isopropyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-ethyl-2-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-isopropyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-ethyl-2-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine;

(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-ol;

[(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-methanol;

[(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-methanol;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid ethylamide;

(6-Cyclopropyl-2,4-difluoro-pyridin-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(6-Cyclopropyl-2-fluoro-pyridin-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidine-3-carboxylic acid methylamide;
(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-ol;
1-(3-{4-[5-Cyclopropyl-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylaminol-phenyl)-piperidin-4-ol;
1-{5-Cyclopropyl-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(1-methyl-1H-pyrazol-4-yl)-ethyl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-6-morpholin-4-yl-pyridin-3-yl)-amine;
1-{5-Cyclopropyl-2-[2-(1-piperidin-4-ylmethyl-1H-pyrazol-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;
4-((R)-3-Benzyloxymethyl-piperazin-1-yl)-2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidine;
(3-Cyclopropyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-(4-methyl-piperazin-1-yl)-methanone;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-dimethylamino-ethyl)-amide;
(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-ol;
(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-ol;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-methoxy-ethyl)-amide;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-3,5-difluoro-benzonitrile;

(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-piperazin-1-yl-methanone;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzamide;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl-amine;
1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-methylamino-ethyl)-amide;
6-{4-[5-Cyclopropyl-4-((cis)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-pyridine-2-carbonitrile;
6-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;
1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-3,3-difluoro-piperidine-4,4-diol;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-difluoro-pyridin-3-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine;
(3R,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;
(3R,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;
(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;
(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;
{4-[5-Cyclopropyl-4-(2-methylamino-ethoxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(piperidin-4-yloxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-pyrazol-4-ylmethyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenethyl-amine;

[4-(5-Cyclopropyl-4-pyrrolidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

[4-(4-Azetidin-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-6-methoxy-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-pyrrolidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine;

[4-(4-Azetidin-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine;

N-{4-[4-((R)-3-Benzyloxymethyl-piperazin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

N-{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

Cyclopropanecarboxylic acid {4-[5-cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,6-trifluoro-pyridin-2-yl)-amine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N'-methyl-ethane-1,2-diamine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N',N'-dimethyl-ethane-1,2-diamine;

1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-azetidin-3-ol;

1-{5-Cyclopropyl-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-azetidin-3-ol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-isopropyl-1H-pyrazol-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-ethyl-5-methyl-1H-pyrazol-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,6-trifluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

(R)-4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-2-carbonitrile;

{4-[5-Cyclopropyl-4-(1,2,3,6-tetrahydro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine;

{4-[5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3,4-diol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-cyclopropyl-1H-pyrazol-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine;

(1-Cyclopentyl-1H-pyrazol-4-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N,N',N'-trimethyl-ethane-1,2-diamine;

{4-[5-Cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,6-difluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3-fluoro-pyridin-2-yl)-amine;

(6-Chloro-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(3,6-difluoro-pyridin-2-yl)-ethyl]-amine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N',N'-dimethyl-butane-1,4-diamine;

[4-(4-Azepan-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

1-{5-Cyclopropyl-2-[2-(6-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

(R)-1-{5-Cyclopropyl-2-[2-(6-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-o1;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

{4-[5-Cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine;

((R)-1-Cyclopropyl-ethyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

((R)-1-Cyclohexyl-ethyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(5-Cyclopropyl-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

1-{4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-piperidin-1-yl}-2,2-dimethyl-propan-1-one;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methanesulfonyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2-fluoro-phenyl)-1H-pyrazol-4-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,6-difluoro-phenyl)-1H-pyrazol-4-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,4,6-trifluoro-phenyl)-1H-pyrazol-4-yl]-amine;
1-{5-Cyclopropyl-2-[2-(2-methyl-2,3-dihydro-1H-isoindo1-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-3,5-difluoro-benzamide;
(1S,2S,4R)-Bicyclo[2.2.l]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(1R,2R,4S)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;
{4-[5-Cyclopropyl-4-(2-dimethylamino-ethoxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine;
{4-[5-Cyclopropyl-4-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;
{4-[5-Cyclopropyl-4-(4,7-diaza-spiro[2.5]oct-7-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;
{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(7-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;
{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-methyl-1H-pyrazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

1-{5-Cyclopropyl-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

((R)-1-Cyclohexyl-ethyl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(5-trifluoromethyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3-fluoro-pyridin-2-yl)-amine;

-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-N-methyl-benzamide;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl-amine;

{4-[5-Cyclopropyl-4-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

6-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

4-((S)-3-Benzyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;

[2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

(S)-N^1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine;
5-Methoxy-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Methoxy-2-(2-phenoxymethyl-morpholin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[(R)-4-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-methanol;
5-Methoxy-2-morpholin-4-yl-4-((R)-3-phenoxymethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
[(S)-1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-yl]-phenyl-amine;
4-[(R)-3-(2-Fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;
5-Methoxy-4-((R)-3-methoxymethyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;
4-[(R)-3-(4-Fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;
(2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;
[2-Morpholin-4-yl-8-(2H-pyrazol-3-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;
N^4-((S)-2-Amino-3-phenyl-propyl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine;
(S)-N^1-(2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine;
5-Bromo-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
Synthesisof5-Cyclopropyl-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;
[(S)-4-(5-Cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-acetonitrile;
5-Methoxy-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Methoxy-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
2-(2-Benzyl-1H-pynolo[2,3-b]pyridin-4-yl)-5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
2-[2-(2-Fluoro-benzyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-methoxy-4-piperazin-1-yl

pyrido[3,4-d]pyrimidine;
2-(2-Ethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Methoxy-4-((R)-3-methoxymethyl-piperazin-1-yl)-2-(1H-pynolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
{(R)-4-[5-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol;
4-Piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
(R)-Pyrrolidin-3-yl-[2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;
5-Cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
8-Chloro-5-cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Isopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
[5-Cyclopropyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-((S)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{(S)-4-[5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile;
5-Cyclopropyl-4-piperazin-1-yl-2-(2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(2-cyclopropyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
4-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid ethylester;
5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol;
5-Cyclopropyl-2-(5-fluoro-1H-pyn-olo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-morpholin-4-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-piperazin-1-yl-2-(2-triduteriomethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
2-(2-tert-Butyl-5-chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-[2-(4-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-(5-fluoro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
(+/-)-(cis)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;
(+/-)-(trans)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyn-olo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

5-Cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-piperidin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;
1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;
5-Cyclopropyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile;
{1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol;
{1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol;
1-{5-Cyclopropyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;
5-Cyclopropyl-4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-4-thiomorpholin-4-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;
4-Azetidin-1-yl-5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-[1,4]diazepan-5-one;
(R)-1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-ol;

5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)spiro[1,3-dihydropyrrolo[2,3-b]pyridine-2,1'-cyclohexane];
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;
1-[5-Cyclopropyl-2-(9H-pyrido[2,3-b]indo1-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;
4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;or a salt form thereof.

18. A compound of formula (I) or a salt form thereof according to claim 1 wherein R^{12} and R^{13} are taken together to form C_{3-11} cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

19. A compound that is selected from:
2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-N,N-dimethyl-benzamide;
{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine;
(+/-)-cis-1-{5-Cyclopropyl-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-3,4-diol;
{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-((R)-1-cyclopropyl-ethyl)-amine;
{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-((R)-1-phenyl-ethyl)-amine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-{2-[1-(2-fluoro-phenyl)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridin-4-yl}-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

(5-Cyclobutyl-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

(4-Chloro-1-ethyl-1H-pyrazol-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-isopropyl-1H-pyrazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yll-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine;

{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-morpholin-4-yl-phenyl)-amine;

5-Cyclobutyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-pyrrolidin-3-yl-amine;

Azetidin-3-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5,8-difluoro-9H-pyrido[2,3-b]indole;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

Azetidin-3-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;

[4-Chloro-1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-8-fluoro-9H-pyrido[2,3-b]indole;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(7-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(S)-pyrrolidin-3-yl-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-7,8-difluoro-9H-pyrido[2,3-b]indole;

{4-[5-Cyclopropyl-4-((cis)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(2,2-dimethyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6,8-difluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-ethyl)-amine;

(4-Chloro-1-ethyl-1H-pyrazol-3-yl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

Benzooxazol-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

Benzothiazol-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-benzoimidazol-2-yl)-amine;

(5-Cyclopropyl-3,6-difluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Cyclopropyl-2-{2-[1-(4-fluoro-phenyl)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridin-4-yl}-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-naphthalen-2-yl-amine;

Biphenyl-3-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[5-Cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

{4-[5-Cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-methyl-1H-pyrazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-fluoro-4-(2-methyl-2H-pyrazol-3-yl)-phenyl]-amine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(R)-pyrrolidin-3-yl-amine;

Azepan-4-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-naphthalen-1-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-iso[D3-4]uinolin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-indazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(1-phenyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(tetrahydro-furan-2-yl)-ethyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2-fluoro-phenyl)-ethyl]-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

8-Chloro-5-cyclopropyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-2-yl-amine;

{4-[5-Cyclopropyl-4-((cis)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

2-(2-Chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-methoxymethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ylamino}-piperidin-2-one;

[5-Cyclopropyl-2-(1-methyl-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[D3-4]uinolin-2-yl-amine;

(±)-2-((endo)-2-Bicyclo[2.2.l]hept-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-methoxymethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-(1-methyl-piperidin-4-yl)-amine;

5-Cyclobutyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(1-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(1-methyl-piperidin-4-yl)-amine;

1-(4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ylamino}-piperidin-1-yl)-ethanone;

5-Cyclopropyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(3-Chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-(R)-pyrrolidin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-iso[D3-4]uinolin-1-yl-amine;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

8-Chloro-5-cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-exo-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]--7-oxa-bicyclo[2.2.1]hept-2-yl-amine;

(2,6-Difluoro-phenyl)-[4-(4-piperazin-1-yl-5-vinyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

1-[4-({5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidin-1-yl]-ethanone;

1-[4-({5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidin-1-yl]-ethanone;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(R)-indan-1-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(S)-indan-1-yl-amine;

[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-8-fluoro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

5-Cyclopropyl-8-fluoro-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(1-Cyclobutyl-piperidin-4-ylmethyl)-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

Benzo[1,2,5]oxadiazol-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Cyclopentyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-difluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ylmethyl-amine;

5-Cyclopropyl-2-[2-(2-methoxy-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(2-methoxy-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(1-Cyclobutyl-piperidin-4-yl)-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(tetrahydro-pyran-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-difluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(1-isopropyl-piperidin-4-yl)-methyl-amine;

Benzo[1,2,5]oxadiazol-5-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Bromo-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-8-chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-8-fluoro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Bromo-2-(2-tert-butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-exo-5-Cyclopropyl-2-[2-(7-oxa-bicyclo[2.2.1]hept-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-exo-5-Cyclobutyl-2-[2-(7-oxa-bicyclo[2.2.l]hept-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-[1-(2,2-difluoro-ethyl)-piperidin-4-yl]-methyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-indan-5-yl-amine;

(5-Cyclopropyl-3,6-difluoro-pyridin-2-yl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2,2-difluoro-2-phenyl-acetamide;

5-Cyclopropyl-2-[2-(1-fluoro-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[5-Cyclopropyl-4-(1-methyl-piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(1-methyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)-phenyl]-amine;

{4-[5-Cyclopropyl-4-(hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[5-Cyclopropyl-4-(hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-benzooxazol-5-yl)-amine;

5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(±)-endo-2-(2-Bicyclo[2.2.1]hept-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[8-Chloro-5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1,2,3,4-tetrahydro-naphthalen-2-yl)-amine;

{5-Cyclopropyl-2-[2-([D3-4]uinolin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-ylmethyl-amine;

(1S,2R)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

(1S,2S)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

(1R,2S)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

(1R,2R)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

5-Cyclobutyl-2-[2-(2,6-difluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(2,6-difluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
2-(2-Cyclobutyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-(2-cyclobutyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-3H-benzoimidazol-5-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-amine;
{2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
5-Cyclopropyl-2-(2-cyclohexyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-(2-cyclohexyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[3-Chloro-1-(5-trifluoromethyl-pyridin-2-yl)-1H-pyrazol-4-yl]-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-difluoro-piperidin-4-yl)-amine;
{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-difluoro-piperidin-4-yl)-amine;
{5-Cyclobutyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
trans-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-1-ol;
(R)-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-phenyl-ethanol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-naphthalen-2-yl-ethyl)-amine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2-fluoro-phenyl)-ethyl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethoxy-phenyl)-amine;
{5-Cyclobutyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
(S)-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-phenyl-ethanol;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-naphthalen-1-yl-ethyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2-difluoro-2-phenyl-ethyl)-amine;
{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-ylmethyl-amine;
{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(tetrahydro-pyran-4-yl)-amine;
{8-Chloro-5-cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
{8-Chloro-5-cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
(5-Chloro-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(tetrahydro-pyran-4-yl)-amine;
(4-{5-Cyclopropyl-4-[3-(tetrahydro-pyran-4-yl)-pyrrolidin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(3,5-difluoro-pyridin-2-yl)-amine;
{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;
{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-dimethyl-indan-1-yl)-amine;
[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;
5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-[2-(1-phenyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-piperazin-1-yl-2-[2-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;
{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3-fluoro-piperidin-4-yl)-amine;
[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;
[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;
[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5,8-dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridazin-3-yl)-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

(2,6-Difluoro-phenyl)-[4-(4-piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(3,5-Difluoro-pyridin-2-yl)-[4-(4-piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(4-Piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

5-Cyclopropyl-2-(2,2-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[4-(3-Amino-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole;

6-Chloro-4-(5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[5-Cyclopropyl-4-(3-methylamino-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;
N-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N'-methyl-benzene-1,4-diamine;
5-Cyclopropyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole;
2-(3-Chloro-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(tetrahydro-pyran-4-yl)-amine;
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-3,3-dimethyl-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one;
or a salt thereof.

20. A compound selected from:
4-({8-Chloro-2-[2-(5-chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidinedi-trifluoroacetate;
4-{8-Chloro-2-[2-(5-chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-piperazinedi-trifluoroacetate;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-pyridin-2-yl-ethyl)-amine;
2-(2-Cyclopentyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-(2-cyclopentyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-[2-(3,3-difluoro-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-[2-(3,3-difluoro-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-propyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2-methoxy-phenyl)-ethyl]-amine;

4-{2-[2-(5-Chloro-3-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclobutyl-pyrido[3,4-d]pyrimidin-4-yl}-piperazine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-quinolin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-phenoxy-ethyl)-amine;

4-({2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridn-4-yl]-5-cyclobutyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidine;

((R)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl);

5-Cyclobutyl-2-(3-methoxy-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2,2-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

4-{[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino)-piperidine;

{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

5-cyclobutyl-2-(6-fluoro-9H-pyrido[2,3-b]indol-4-yl)-N-methyl-N-(4-piperidyl)pyrido[3,4-d]pyrimidin-4-amine;

{5-Cyclopropyl-2-[2-((R)-1-phenyl-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

[5-Cyclobutyl-2-(7-fluoro-9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(4-trifluoromethoxy-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(3-methyl-3H-benzimidazol-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
((S)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl);
((R)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl)-methyl;
[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;
{5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethoxy-phenyl)-amine;
4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6-fluoro-9H-pyrido[2,3-b]indole;
4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-7-fluoro-9H-pyrido[2,3-b]indole;
((S)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl)-methyl;
4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-9H-pyrido[2,3-b]indole;
4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3-methyl-piperidine;
{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
1-(5-cyclopropyl-2-spiro[1,3-dihydropyrrolo[2,3-b]pyridine-2,1'-cyclohexane]-4-yl-pyrido[3,4-d]pyrimidin-4-yl)piperidin-3-amine;
4-({2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3,3-dimethyl-piperidine;
(5-Cyclopropyl-2-{2-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(1-cyclopropyl-piperidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
(1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-4-fluoro-piperidin-3-yl);
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-phenyl-amine;
5-Cyclopropyl-2-(3-phenyl-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
(±)-3,4-trans-4-{[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-1-methyl-pyrrolidin-3-ol;
(±)-3,4-trans-4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-1-methyl-pyrrolidin-3-ol;
(±)-3,4-trans-4-({5-Cyclopropyl-2-[2-((R)-1-phenyl-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-1-methyl-pyrrolidin-3-ol;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-(2,6-difluoro-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-(3,5-difluoro-pyridin-2-yl)-amine;
2-[2-(2-tert-Butyl-thiazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
{5-Cyclopropyl-2-[2-(2-phenoxy-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
2-(3-Bromo-pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-trifluoromethoxy-phenyl)-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-4-trifluoromethoxy-phenyl)-amine;
(±)-{5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3-methoxy-cyclohexane;

2-(3-Bromo-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

N*1*-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-ethane-1,2-diamine;

(±)-{5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;

N(1)-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-ethane-1,2-diamine;

{4-[5-Cyclopropyl-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;

(S)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

4-[5-Cyclobutyl-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;

4-[5-Cyclobutyl-7-oxy-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5,6,7,8-tetrahydro-cyclopenta[4,5]pyrrolo[2,3-b]pyridine;

{4-[4-((S)-3-Amino-piperidin-1-yl)-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[4-((S)-3-Amino-piperidin-1-yl)-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

5-Cyclopropyl-4-((S)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-((S)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;
5-Cyclopropyl-2-[3-(3-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-[3-(4-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclopropyl-2-[3-(2-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;
(±)-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;
(±)-(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;
(±)-(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;
5-cyclopropyl-2-[2-[(1R,2S,4S)-norbornan-2-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-cyclopropyl-2[2-[(1S,2R,4R)-norbornan-2-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[5-Cyclopropyl-2-(3-phenyl-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;
[2-(3-Bromo-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

(±)-3,4-trans-4-{[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-pyrrolidin-3-ol;

(±)-(3,4-trans)-4-{[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-pyrrolidin-3-ol;

1-[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-cyclobutanol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-trifluoromethoxy-phenyl)-amine;

(S)-1-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

(R)-1-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

4-(5-Cyclobutyl-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

N-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-cyclohexane-1,3-diamine;

N-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-cyclohexane-1,3-diamine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-((S)-2-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

(±)-(3,4-trans)-4-({2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-pyrrolidin-3-ol;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((R)-3-trifluoromethyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;compoundwithtrifluoro-acetic acid;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethoxy-phenyl)-amine;

(±)-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

(±)-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

(±)-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

(±)-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-3-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]ipyrimidine;

5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-5-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-6-yl-amine;

(±)-(3,4-trans)-4-({5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-pyrrolidin-3-ol;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-2-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

(S)-1-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine;

(S)-1-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine;

5-Cyclobutyl-2-[2-(2-methyl-tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(2-methyl-tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-cyclobutanol;

1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-3-phenyl-urea;

5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

(±)-{5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

(5-Aza-spiro[2.5]oct-8-yl)-{5-cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

{2-[2-(4-Chloro-phenylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

2-(3-Chloro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3,4-trans)-4-methoxy-pyrrolidin-3-yl)-amine;

(±)-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3,4-trans)-4-methoxy-pyrrolidin-3-yl)-amine;
[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3R,4S)-3-methoxy-piperidin-4-yl)-amine;
[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3R,4S)-3-methoxy-piperidin-4-yl)-amine;
[5-Cyclopropyl-2-(2-p-tolylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;
5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-2-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-2-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;
{5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;
{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;
(5-Aza-spiro[2.5]oct-8-yl)-{5-cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;
{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;
{5-Cyclobutyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;
5-Cyclobutyl-2-[2-(1-fluoromethyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
3-[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-tetrahydro-furan-3-ol;
{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;
5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-3,4-dihydro-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

(S)-1-[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

5-Cyclopropyl-4-(2,6-diaza-spiro[3.3]hept-2-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

4-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-2-carboxylic acid;

{5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-oxetan-3-yl-phenyl)-amine;

5-cyclobutyl-N-methyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-N-(4-piperidyl)pyrido[3,4-d]pyrimidin-4-amine;

5-Cyclopropyl-4-(octahydro-pyrrolo[3,2-c]pyridin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(S)-1-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

2-[3-(2-Chloro-phenyl)-pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-piperazin-1-yl-2-(3-o-tolyl-pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

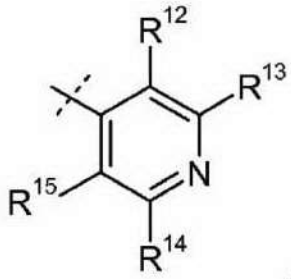
5-Cyclopropyl-2-[3-(2-methoxy-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(S)-2-Amino-6-[5-cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-hexanoic acid;
5-Cyclopropyl-4-((R)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-((R)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
{5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
{2-[2-(4-Chloro-phenylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
5-Cyclobutyl-4-((S)-2-methyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-4-((R)-2-methyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine;
2-(3-Bromo-pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-[3-(2-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
5-Cyclobutyl-2-(3-phenyl-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
[5-Cyclopropyl-2-(2-p-tolylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6-trifluoromethoxy-9H-pyrido[2,3-b]indole;
[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;
[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-benzamide;
[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;
[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;
5-Cyclobutyl-2-(2-phenylsulfanyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-benzenesulfonamide;
5-Cyclopropyl-2-(3-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-((3R,4R)-4-methoxy-pyrrolidin-3-yl)-amine;
{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-((3R,4R)-4-methoxy-pyrrolidin-3-yl)-amine;
5-Cyclobutyl-4-piperazin-1-yl-2-(1H-pyrazolo[3,4-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;
4-[5-Cyclobutyl-4-(octahydro-pyrrolo[3,2-c]pyridin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;
N-{4-[5-Cyclopropyl-4-(methyl-piperidin-4-yl-amino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzenesulfonamide;
5-Cyclopropyl-2-[2-(2-methoxy-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-3,4-dihydro-pyrido[3,4-d]pyrimidine;
(S)-1-{5-Cyclopropyl-2-[2-(2-methoxy-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine;
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

2-(2-Benzenesulfonyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;
or a salt thereof.

21. A compound as defined in claim 1, wherein G is a group of formula



; X is chosen from 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, $-OR^{28}$, $-S(=O)_nR^{28}$ and $-NR^{24}R^{28}$; R^7, R^8, R^9 R^{12}, R^{13}, R^{14} and R^{15} are independently chosen from H,C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, halogen, and$-OR^{20}$; or any of R^{12} and R^{13} or R^{14} and R^{15} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

22. A compound as defined in claim 21 where R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, halogen, –CN,$-C(=O)OR^{30}$, $-NR^{32}R^{33}$, $-OR^{30}$, =O, $-S(=O)_nR^{30}$, where n is 0, 1, or 2.

23. A compound as defined in claim 1 wherein G is a group of formula

; and R^7 is C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19} and R^8 and R^9 are H.

24. A pharmaceutical composition comprising a compound of Formula (I) according to any one of claims 1-23 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable excipient.

25. A method of treating an aPKC-dependent disorder or condition in a subject comprising: administering to a subject in recognized need thereof a compound of Formula (I) according to any one of claims 1-23 or a pharmaceutically acceptable salt thereof.

26. Use of a compound of Formula (I) according to any one of claims 1-23 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatemnet of an aPKC-dependent disorder or condition.

27. A method according to claim 25 or a use according to claim 26 wherein the aPKC-dependent disorder or condition is cancer.

CANCER RESEARCH TECHNOLOGY LIMITED

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