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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 May 2016 (26.05.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/081668 A1

(51) International Patent Classification:
C07D 487/04 (2006.01) *A61P 9/00* (2006.01)
A61K 31/519 (2006.01)

(21) International Application Number:
PCT/US2015/061442

(22) International Filing Date:
19 November 2015 (19.11.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/082,686 21 November 2014 (21.11.2014) US
62/144,697 8 April 2015 (08.04.2015) US

(71) Applicant: **MERCK SHARP & DOHME CORP.** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(72) Inventors; and
(71) Applicants *(for US only)*: **BERGER, Raphaelle** [FR/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **DONG, Guizhen** [US/US]; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US). **RAGHAVAN, Subharekha** [US/US]; 2000 Galloping Hill Road, Kenilworth, New Jersey 07033 (US). **YANG, Zhiqiang** [US/US]; 2000 Galloping Hill Road, Kenilworth, New Jersey 07033 (US).

(74) Common Representative: **MERCK SHARP & DOHME CORP.**; 126 East Lincoln Avenue, Rahway, New Jersey 07065-0907 (US).

(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, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, 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, ST, 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).

Declarations under Rule 4.17:

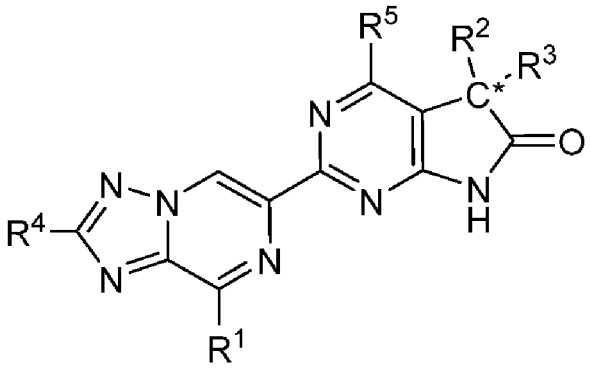
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

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

(54) **Title**: TRIAZOLO-PYRAZINYL DERIVATIVES USEFUL AS SOLUBLE GUANYLATE CYCLASE ACTIVATORS



I

(57) **Abstract**: A compound of Formula (I) or a pharmaceutically acceptable salt thereof, are capable of modulating the body's production of cyclic guanosine monophosphate ("cGMP") and are generally suitable for the therapy and prophylaxis of diseases which are associated with a disturbed cGMP balance. The invention furthermore relates to processes for preparing compounds of Formula (I), or a pharmaceutically acceptable salt thereof, for their use in the therapy and prophylaxis of the abovementioned diseases and for preparing pharmaceuticals for this purpose, and to pharmaceutical compositions which comprise compounds of Formula (I) or a pharmaceutically acceptable salt thereof.

WO 2016/081668 A1

TITLE OF THE INVENTION

TRIAZOLO-PYRAZINYL DERIVATIVES USEFUL AS SOLUBLE GUANYLATE CYCLASE ACTIVATORS

BACKGROUND OF THE INVENTION

Cyclic GMP (cGMP) is an important intracellular messenger which triggers a multitude of different effects via the modulation of cGMP-dependent protein kinases, phosphodiesterases and ion channels. Examples are the relaxation of smooth muscles, the inhibition of thrombocyte activation and the inhibition of the proliferation of smooth-muscle cells and of leukocyte adhesion. cGMP is produced by particulate and soluble guanylate cyclases as a response to a number of extracellular and intracellular stimuli. In the case of the particulate guanylate cyclases, stimulation is essentially effected by peptidic messengers, such as the atrial natriuretic peptide or the cerebral natriuretic peptide. The soluble guanylate cyclases ("sGC"), which are cytosolic heterodimeric heme proteins, in contrast, are essentially regulated by a family of low-molecular-weight factors which are formed enzymatically. The most important stimulant is nitrogen monoxide ("NO") or a closely related species. The function of other factors such as carbon monoxide or the hydroxyl radical is still largely unclear. The binding of NO to the heme with formation of a penta-coordinate heme-nitrosyl complex is proposed as the mechanism of the activation by NO. The associated release of the histidine which is bound in the basal state to the iron converts the enzyme into the active conformation.

Active soluble guanylate cyclases are each composed of an α and a β subunit. Several subunit subtypes have been described which differ from one another with respect to sequence, tissue-specific distribution and expression in different development stages. The subtypes α_1 and β_1 are mainly expressed in brain and lung, while β_2 is found in particular in liver and kidney. The subtype α_2 was shown to be present in human fetal brain. The subunits referred to as α_3 and β_3 were isolated from human brain and are homologous to α_1 and β_1. More recent works indicate an α_{2i} subunit which contains an insert in the catalytic domain. All subunits show great homologies in the region of the catalytic domain. The enzymes presumably contain one heme per heterodimer, which is bound via β_1-Cys-78 and/or β_1-His-105 and is part of the regulatory center.

Under pathologic conditions, the formation of guanylate-cyclase-activating factors can be reduced, or their degradation may be promoted owing to the increased occurrence of free radicals. The resulting reduced activation of the sGC leads, via a weakening of the

respective cGMP-mediated cellular response, for example to an increase of the blood pressure, to platelet activation or to increased cell proliferation and cell adhesion. As a consequence, formation of endothelial dysfunction, atherosclerosis, hypertension, stable or unstable angina pectoris, thrombosis, myocardial infarction, strokes or erectile dysfunction results. Pharmacological stimulation of sGC offers a possibility to normalize cGMP production and therefore may make possible the treatment and/or prevention of such disorders.

For the pharmacological stimulation of the sGC, use has been made of compounds whose activity is based on an intermediate NO release, for example organic nitrates. The drawback of this treatment is the development of tolerance and a reduction of activity, and the higher dosage which is required because of this.

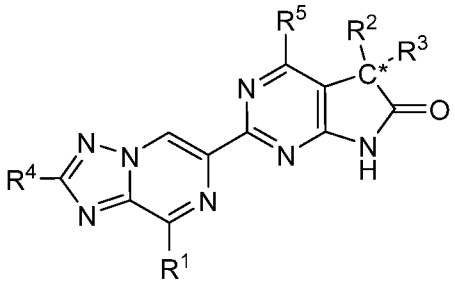
Various sGC stimulators which do not act via NO release were described by Vesely in a series of publications. However, the compounds, most of which are hormones, plant hormones, vitamins or natural compounds such as, for example, lizard poisons, predominantly only have weak effects on the cGMP formation in cell lysates. D. L. Vesely, Eur. J. Clin. Invest., vol.15, 1985, p. 258; D. L. Vesely, Biochem. Biophys. Res. Comm., vol. 88, 1979, p.1244. A stimulation of heme-free guanylate cyclase by protoporphyrin IX was demonstrated by Ignarro et al., Adv. Pharmacol., vol. 26, 1994, p. 35. Pettibone et al., Eur. J. Pharmacol., vol. 116, 1985 p. 307, described an antihypertensive action of diphenyliodonium hexafluorophosphate and attributed this to a stimulation of sGC. According to Yu et al., Brit. J. Pharmacol, vol. 114, 1995, p.1587, isoliquiritigenin, which has a relaxing action on isolated rat aortas, also activates sGC. Ko et al., Blood vol. 84, 1994, p. 4226, Yu et al., Biochem. J. vol. 306, 1995, p. 787, and Wu et al., Brit. J. Pharmacol. vol. 116, 1995, p. 1973, demonstrated a sGC-stimulating activity of 1-benzyl-3-(5-hydroxymethyl-2-furyl)indazole and demonstrated an antiproliferative and thrombocyte-inhibiting action. Pyrazoles and fused pyrazoles which exhibit a sGC-stimulating activity are described in European Patent No. 908,456 and German Patent Application No. 19,744,027.

It has now been found that the compounds of the present invention effect a strong activation of soluble guanylate cyclase and are therefore may be suitable for the therapy and prophylaxis of disorders which are associated with a low cGMP level.

SUMMARY OF THE INVENTION

The present invention relates to compounds which activate soluble guanylate cyclase and are valuable pharmaceutically active compounds for the therapy and prophylaxis of

diseases, for example for cardiovascular diseases such as hypertension, heart failure, pulmonary hypertension, angina pectoris, diabetes, cardiac insufficiency, thrombosis, chronic kidney disease, fibrosis or atherosclerosis. The compounds of Formula **I**

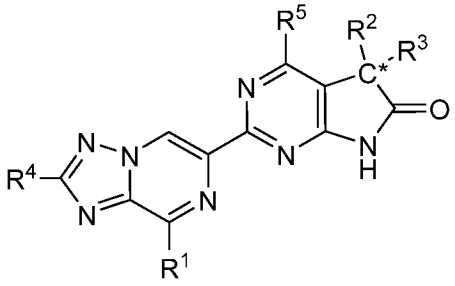


I

are capable of modulating the body's production of cyclic guanosine monophosphate ("cGMP") and may be suitable for the therapy and prophylaxis of diseases which are associated with a disturbed cGMP balance. The invention furthermore relates to processes for preparing compounds of Formula **I**, to the use of such compounds for the therapy and prophylaxis of the above mentioned diseases and for preparing pharmaceuticals for this purpose, and to pharmaceutical compositions which comprise compounds of Formula **I**.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to compounds having structural Formula **I**:



I

or a pharmaceutically acceptable salt thereof wherein:

C* indicates a potential chiral carbon atom;

R^1 is

(1) hydrogen,

(2) (C_{1-6})alkyl,

(3) halo(C_{1-6})alkyl,

(4) (C_{1-6})alkyl-O-,

(5) halo(C_{1-6})alkyl-O-,

(6) (C_{1-6})alkyl-NH-,

(7) halo(C_{1-6})alkyl-NH-,

(8) -(C_{1-3})alkyl-(C_{3-7})cycloalkyl,

(9) -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7,

(10) aryl unsubstituted or substituted by one, two, or three R^7,

(11) (C_{3-7})cycloalkyl, or

(12) -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7;

R^2 is

(1) (C_{1-3})alkyl, or

(2) (C_{3-7})cycloalkyl;

R^3 is

(1) aryl unsubstituted or substituted by one, two, or three R^6,

(2) five- or six-membered heteroaryl containing one, two or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted one, two, or three R^6,

(3) (C_{1-3})alkyl, or

(4) (C_{3-7})cycloalkyl;

R^4 is

(1) hydrogen,

(2) (C_{1-3})alkyl,

(3) halo(C_{1-3})alkyl, or

(4) (C_{3-7})cycloalkyl;

R^5 is

(1) hydrogen,

(2) hydroxy,

(3) -$N(R^{8a})(R^{8b})$,

(4) -COOH,

(5) -$C(O)NH_2$,

(6) (C_{1-3})alkyl,

(7) (C_{3-7})cycloalkyl, or

(8) four- to six-membered monocyclic heterocyclyl containing 1 N hetero atom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9;

each R^6 is independently

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl,

(3) (C_{1-3})alkoxy,

(4) halo(C_{1-3})alkoxy,

(5) (C_{3-7})cycloalkyl, unsubstituted or substituted by halo,

(6) halo,

(7) cyano,

(8) hydroxy,

(9) $-NH_2$,

(10) $-(C_{1-6})$alkyl-COOH, or

(11) $-(C_{1-6})$alkyl-COO(C_{1-4})alkyl;

each R^7 is independently

(1) (C_{1-3})alkoxy,

(2) halo,

(3) hydroxy, or

(4) (C_{1-3})alkyl;

R^{8a} and R^{8b} are independently

(1) hydrogen,

(2) (C_{1-3})alkyl, or

(3) (C_{3-7})cycloalkyl; and

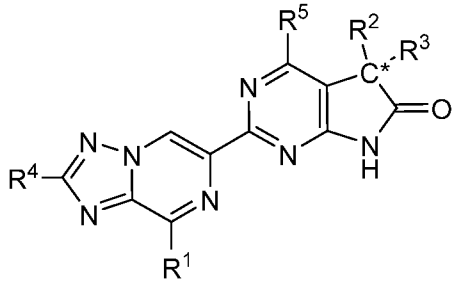
R^9 is

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl, or

(3) hydroxy.

In one embodiment, the present invention is directed to compounds having structural Formula **I**:



I

or a pharmaceutically acceptable salt thereof wherein:

C* indicates a potential chiral carbon atom;

R^1 is

(1) hydrogen,

(2) (C_{1-6})alkyl,

(3) halo(C_{1-6})alkyl,

(4) (C_{1-6})alkyl-O-,

(5) halo(C_{1-6})alkyl-O-,

(6) (C_{1-6})alkyl-NH-,

(7) halo(C_{1-6})alkyl-NH-,

(8) -(C_{1-3})alkyl-(C_{3-7})cycloalkyl,

(9) -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7,

(10) aryl unsubstituted or substituted by one, two, or three R^7,

(11) (C_{3-7})cycloalkyl, or

(12) -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7;

R^2 is

(1) (C_{1-3})alkyl, or

(2) (C_{3-7})cycloalkyl;

R^3 is

(1) aryl unsubstituted or substituted by one, two, or three R^6, or

(2) five- or six-membered heteroaryl containing one, two or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted one, two, or three R^6;

R^4 is

(1) hydrogen,

(2) (C_{1-3})alkyl,

(3) halo(C_{1-3})alkyl, or

(4) (C_{3-7})cycloalkyl;

R^5 is

(1) hydrogen,

(2) hydroxy,

(3) $-N(R^{8a})(R^{8b})$,

(4) -COOH,

(5) $-C(O)NH_2$,

(6) (C_{1-3})alkyl,

(7) (C_{3-7})cycloalkyl, or

(8) four- to six-membered monocyclic heterocyclyl containing 1 N hetero atom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9;

each R^6 is independently

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl,

(3) (C_{1-3})alkoxy,

(4) halo(C_{1-3})alkoxy,

(5) (C_{3-7})cycloalkyl, unsubstituted or substituted by halo,

(6) halo,

(7) cyano,

(8) hydroxy,

(9) $-NH_2$,

(10) $-(C_{1-6})$alkyl-COOH, or

(11) $-(C_{1-6})$alkyl-COO(C_{1-4})alkyl;

each R^7 is independently

(1) (C_{1-3})alkoxy,

(2) halo,

(3) hydroxy, or

(4) (C_{1-3})alkyl;

R^{8a} and R^{8b} are independently

(1) hydrogen,

(2) (C_{1-3})alkyl, or

(3) (C_{3-7})cycloalkyl; and

R^9 is

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl, or

(3) hydroxy.

In one embodiment, R^1 is hydrogen, (C_{1-6})alkyl, halo(C_{1-6})alkyl, (C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7; R^2 is (C_{1-3})alkyl or (C_{3-7})cycloalkyl; R^3 is aryl unsubstituted or substituted by one, two, or three R^6, or five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted one, two, or three R^6; R^4 is hydrogen or (C_{1-3})alkyl; R^5 is hydrogen, $-NH_2$, hydroxy, or $C(O)NH_2$; each R^6 (C_{1-3})alkyl, halo(C_{1-3})alkyl, (C_{1-3})alkoxy, halo, hydroxy, (C_{3-7})cycloalkyl, unsubstituted or substituted by halo or cyano; and R^7 is (C_{1-3})alkoxy, halo, or hydroxy.

In one embodiment, R^1 is hydrogen, (C_{1-6})alkyl, halo(C_{1-6})alkyl, or $-(C_{1-3})$alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one embodiment, R^1 is (C_{1-6})alkyl or halo(C_{1-6})alkyl.

In one embodiment, R^1 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, or $-(C_{1-3})$alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7.

In one embodiment, R^1 is hydrogen. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is (C_{1-6})alkyl. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is halo(C_{1-6})alkyl. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is (C_{1-6})alkyl-O-. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is halo(C_{1-6})alkyl-O-. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is (C_{1-6})alkyl-NH-. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is halo(C_{1-6})alkyl-NH-. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

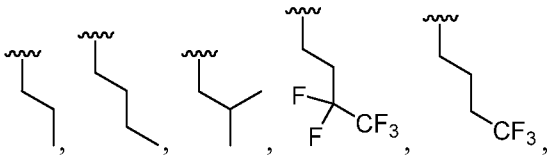
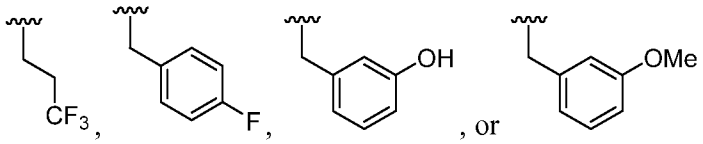
In one embodiment, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two,

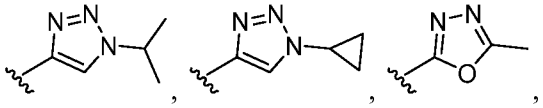
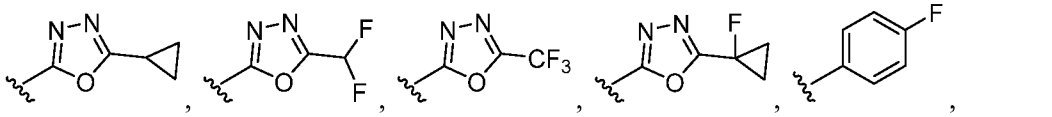
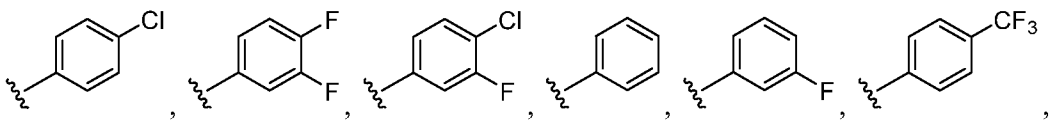
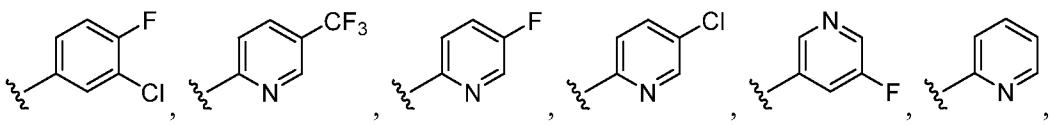
or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

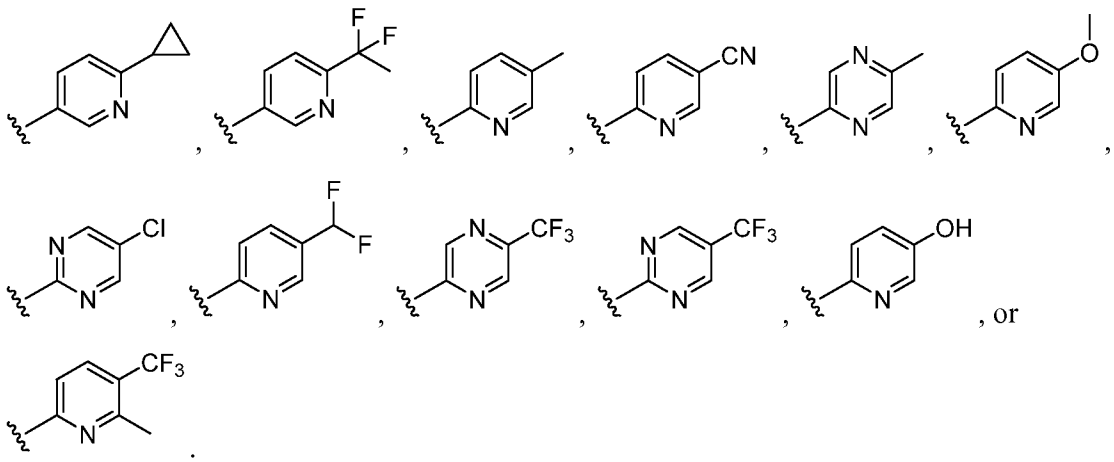
In one embodiment, R^1 is (C_{3-7})cycloalkyl. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is $-(C_{1-3})$alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one class of this embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6. In one class of this embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one embodiment, R^1 is hydrogen,  ,  , or .

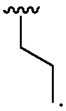
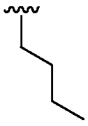
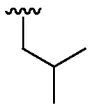
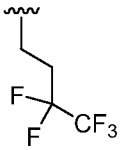
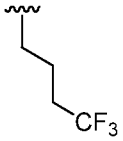
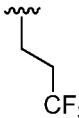
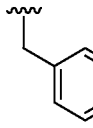
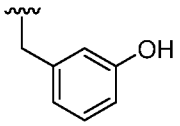
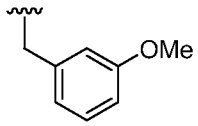
In one class of this embodiment, R^2 is methyl or cyclopropyl.

In one subclass of this class, R^3 is  ,  ,  ,  .



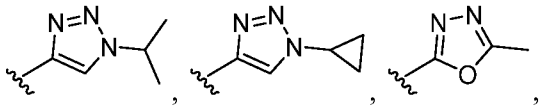
In one sub-subclass of this subclass, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2.

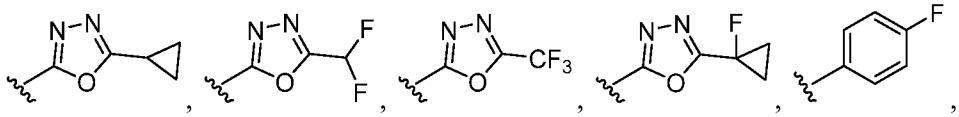
In one sub-sub-subclass of this sub-subclass, R^4 is hydrogen or methyl.

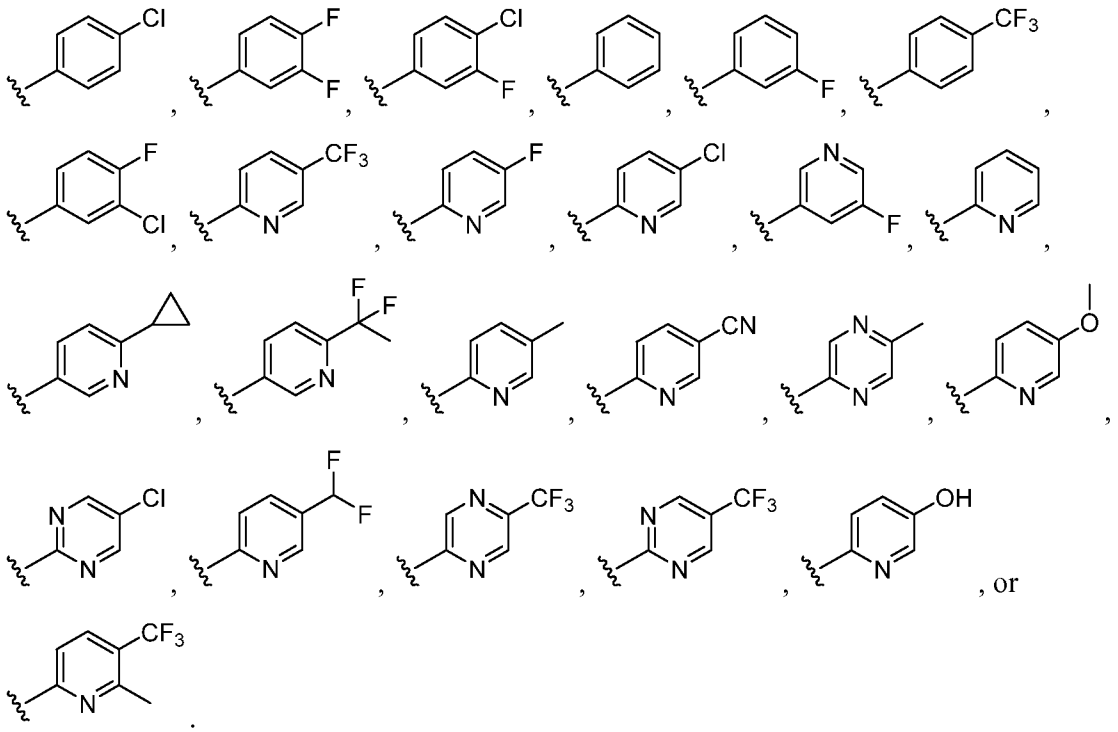
In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is . In one class of this embodiment, R^1 is  . In one class of this embodiment, R^1 is  .

In one embodiment R^2 is (C_{1-3})alkyl. In one class of this embodiment, R^2 is methyl.

In one embodiment R^2 is (C_{3-7})cycloalkyl. In one class of this embodiment, R^2 is cyclopropyl.

In one embodiment, R^3 is 





, or

.

In one embodiment, R^3 is aryl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^5 is $N(R^{8a})(R^{8b})$.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from

N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is hydroxy.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is hydrogen.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is COOH or -C(O)NH_2.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In

one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is (C_{1-3})alkyl.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is four- or six-membered monocyclic heterocyclyl containing 1 N heteroatom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from

N, O, and S heteroatoms, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one embodiment, R^3 is phenyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^5 is $-N(R^{8a})(R^{8b})$.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S heteroatoms, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is hydroxy.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-6})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from N, O, and S heteroatoms, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is hydrogen.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from

the group N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is COOH or $-C(O)NH_2$.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is (C_{1-3})alkyl.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is $-(C_{1-3})$alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one,

two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is four- to six-membered monocyclic heterocyclyl containing 1 N heteroatom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one embodiment, R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^5 is -$N(R^{8a})(R^{8b})$.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is hydroxy.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is hydrogen.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is COOH or -$C(O)NH_2$.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is (C_{1-3})alkyl.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from

the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^5 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is hydrogen. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is halo(C_{1-6})alkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-(C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is aryl unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{3-7})cycloalkyl. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one subclass of this class, R^1 is (C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7. In one sub-subclass of this subclass, R^2 is (C_{1-3})alkyl. In one sub-subclass of this subclass, R^2 is (C_{3-7})cycloalkyl.

In one embodiment, R^4 is (C_{1-3})alkyl. In one class of this embodiment, R^4 is methyl. In one embodiment, R^4 is halo(C_{1-3})alkyl. In one embodiment, R^4 is hydrogen. In one embodiment, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is -$N(R^{8a})(R^{8b})$.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{3-7})cycloalkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is hydroxyl.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{3-7})cycloalkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is hydrogen.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{3-7})cycloalkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is COOH or $-C(O)NH_2$.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is (C_{1-3})alkyl.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{3-7})cycloalkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{3-7})cycloalkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^5 is four- to six-membered monocyclic heterocyclyl containing 1 N heteroatom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9.

In one class of this embodiment, R^2 is (C_{1-3})alkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one class of this embodiment, R^2 is (C_{3-7})cycloalkyl. In one subclass of this class, R^4 is (C_{1-3})alkyl. In one subclass of this class, R^4 is hydrogen. In one subclass of this class, R^4 is (C_{3-7})cycloalkyl.

In one embodiment, R^6 is chloro, fluoro, hydroxy, trifluoromethyl, difluoromethyl, 1,1-difluoroethyl, cyano, methyl, isopropyl, methoxy, cyclopropyl, or fluoro-cyclopropyl.

In one embodiment, R^7 is fluoro, hydroxy, or methoxy. In one embodiment, R^7 is halo. In one class of this embodiment, R^7 is fluoro. In one embodiment, R^7 is hydroxy. In one embodiment, R^7 is (C_{1-3})alkoxy. In one class of this embodiment, R^7 is methoxy.

In one embodiment, R^3 is phenyl, pyridinyl, triazolyl, pyrazinyl, pyrimidinyl, or oxadiazolyl, each unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

In one subclass of this class, R^5 is hydroxy or $-NH_2$, hydrogen, or $-C(O)NH_2$. In one subclass of this class, R^5 is hydroxy or $-NH_2$. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is $-NH_2$. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is $-C(O)NH_2$.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or $-NH_2$, hydrogen, or $-C(O)NH_2$. In one subclass of this class, R^5 is hydroxy or $-NH_2$. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is $-NH_2$. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is $-C(O)NH_2$.

In one embodiment, R^3 is phenyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

In one subclass of this class, R^5 is hydroxy or $-NH_2$, hydrogen, or $-C(O)NH_2$. In one subclass of this class, R^5 is hydroxy or $-NH_2$. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is $-NH_2$. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is $-C(O)NH_2$.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one embodiment, R^3 is pyridinyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one embodiment, R^3 is triazolyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one embodiment, R^3 is pyrazinyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In

one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one embodiment, R^3 is pyrimidinyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one embodiment, R^3 is is oxadiazolyl unsubstituted or substituted by one, two, or three R^6.

In one class of this embodiment, R^2 is methyl.

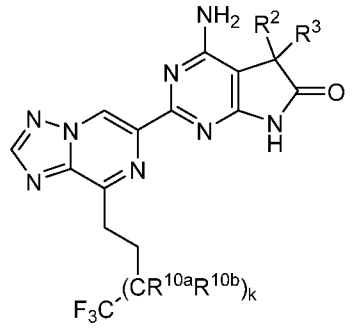
In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one class of this embodiment, R^2 is cyclopropyl.

In one subclass of this class, R^5 is hydroxy or -NH_2, hydrogen, or –C(O)NH_2. In one subclass of this class, R^5 is hydroxy or -NH_2. In one subclass of this class, R^5 is hydroxy. In one subclass of this class, R^5 is -NH_2. In one subclass of this class, R^5 is hydrogen. In one subclass of this class, R^5 is –C(O)NH_2.

In one embodiment, R^2 is methyl or cycloalkyl. In one class of this embodiment, R^2 is methyl. In one class of this embodiment, R^2 is cycloalkyl. In one subclass of this class, R^2 is cyclopropyl.

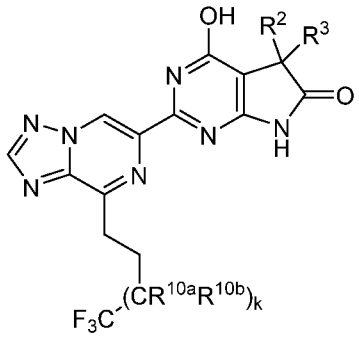
In one embodiment, the invention relates to compounds of Formula **I-a**:



I-a

or a pharmaceutically acceptable salt thereof, wherein k is 0 or 1; R^{10a} and R^{10b} are independently hydrogen or fluoro; and R^2, and R^3 are as previously defined.

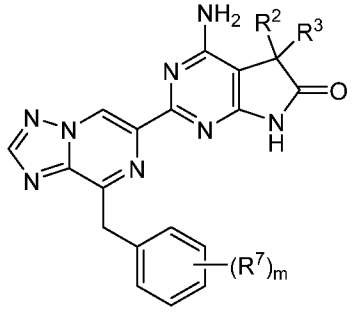
In one embodiment, the invention relates to compounds of Formula **I-b**:



I-b

or a pharmaceutically acceptable salt thereof, wherein k is 0 or 1; R^{10a} and R^{10b} are independently hydrogen or fluoro; and R^2, R^3, R^4 and R^5 are as previously defined.

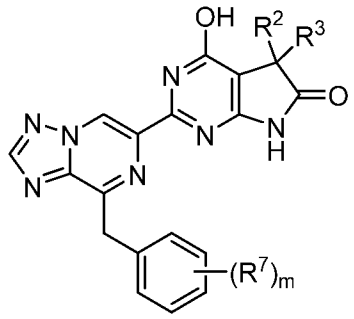
In one embodiment, the invention relates to compounds of Formula **I-c**:



I-c

or a pharmaceutically acceptable salt thereof, wherein m is 0, 1, 2, or 3; and R^2, R^3, and R^7 are as previously defined.

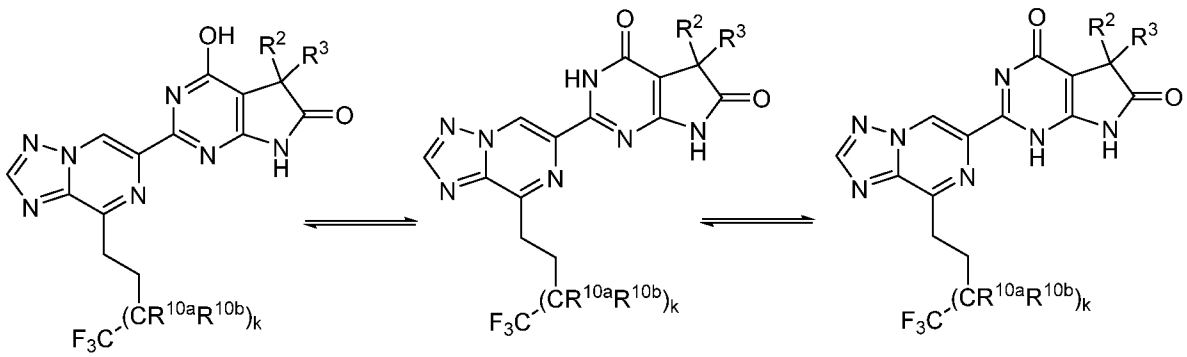
In one embodiment, the invention relates to compounds of Formula **I-d**:



I-d

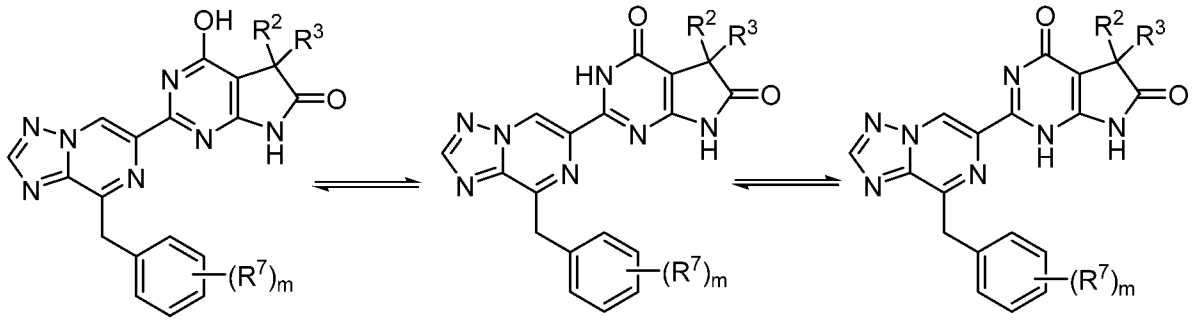
or a pharmaceutically acceptable salt thereof, wherein m is 0, 1, 2, or 3; and R^2, R^3, and R^7 are as previously defined.

As will be apparent to those of skill in the art, compounds of Formula **I-b** and **I-d** can exist in alternative tautomeric forms, with the ratio between the tautomeric forms varying depending on conditions. For instance, the tautomeric forms of the compound of Formula **I-b** are shown below.



I-b **I-b′** **I-b′′**

The tautomeric forms of the compound of Formula **I-d** are shown below.

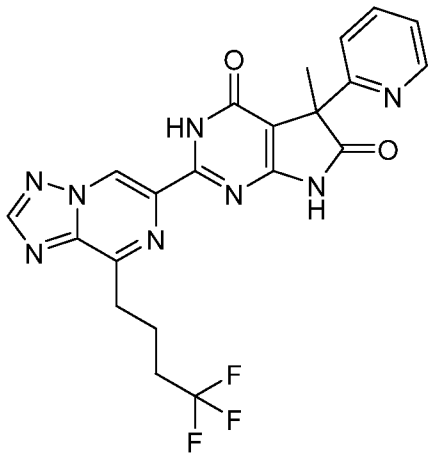


I-d **I-d′** **I-d′′**

In one embodiment of this invention are compounds of Formula **I**, wherein the compounds exist as *S* and *R* enantiomers with respect to C*. In one class of this embodiment,

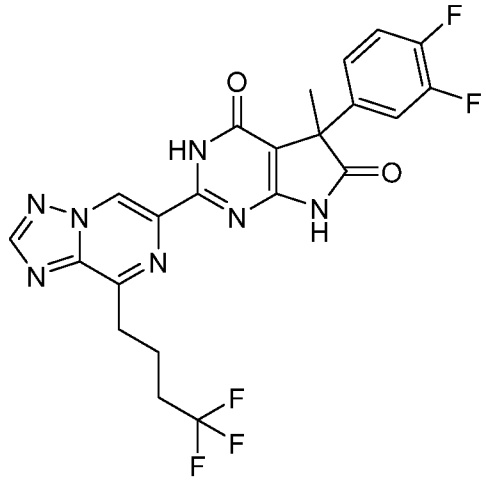
the compounds of Formula **I** exist as an *S* enantiomer with respect to C*. In one class of this embodiment, the componds of Formula **I** exist as *R* enantiomer with respect to C*.

In one embodiment of this invention includes the following compounds:



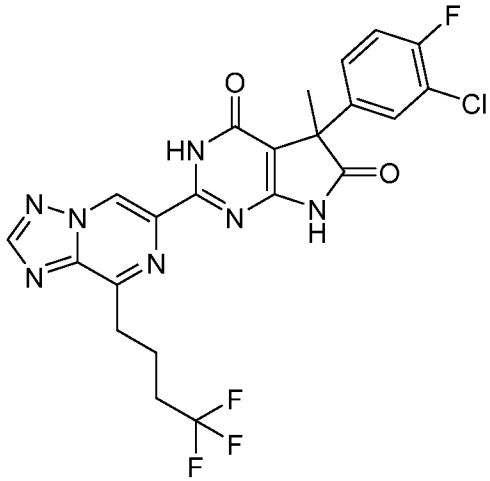
145B

5-methyl-5-(pyridin-2-yl)-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



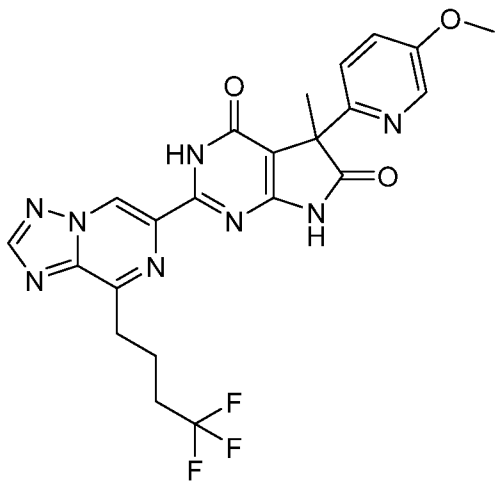
146B

5-(3,4-difluorophenyl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



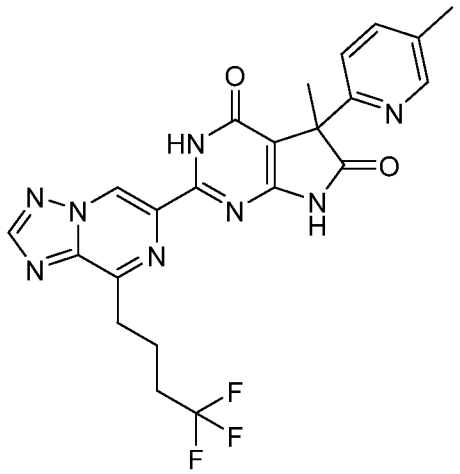
147B

5-(3-chloro-4-fluorophenyl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



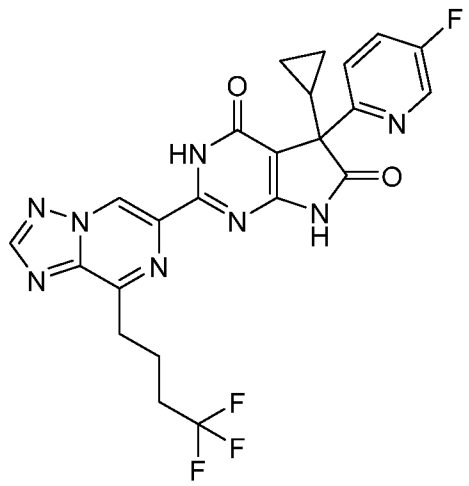
148A

5-(5-methoxypyridin-2-yl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



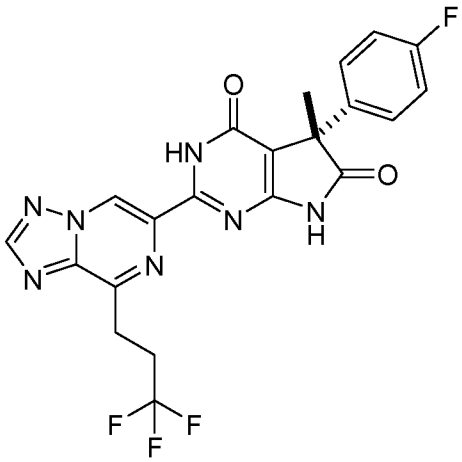
149B

5-methyl-5-(5-methylpyridin-2-yl)-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



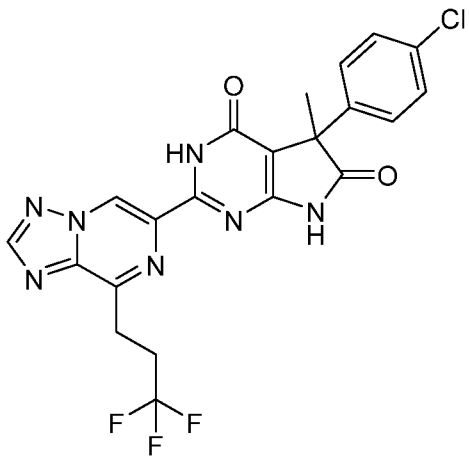
150A

5-cyclopropyl-5-(5-fluoropyridin-2-yl)-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



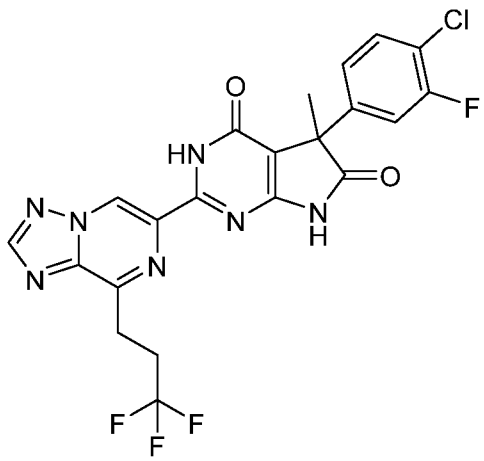
151A

(5*S*)-5-(4-fluorophenyl)-5-methyl-2-[8-(3,3,3-trifluoropropyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



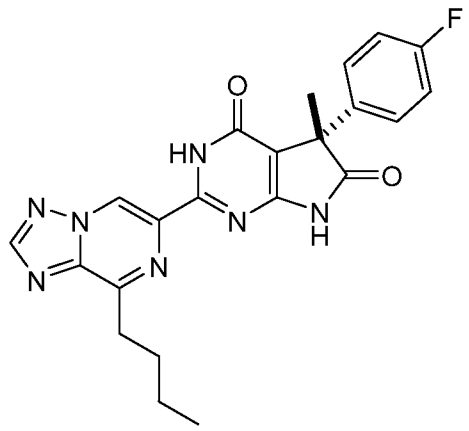
152A

5-(4-chlorophenyl)-5-methyl-2-[8-(3,3,3-trifluoropropyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



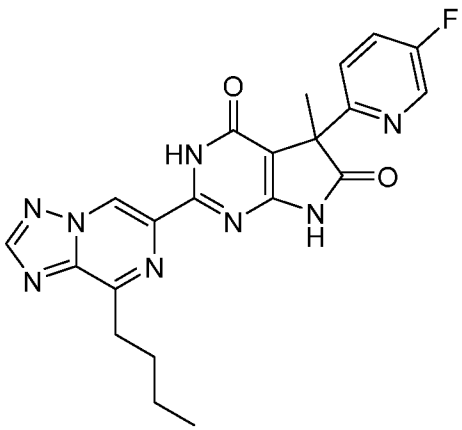
153B

5-(4-chloro-3-fluorophenyl)-5-methyl-2-[8-(3,3,3-trifluoropropyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



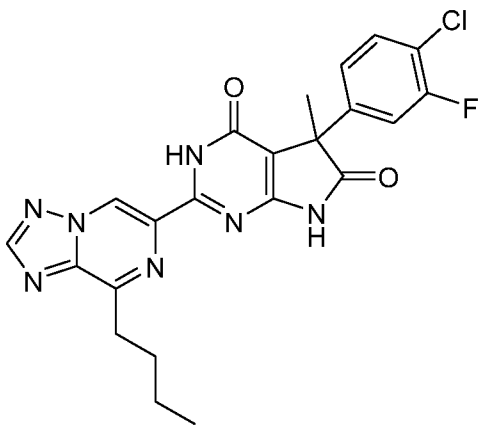
154A

(5*S*)-2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(4-fluorophenyl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



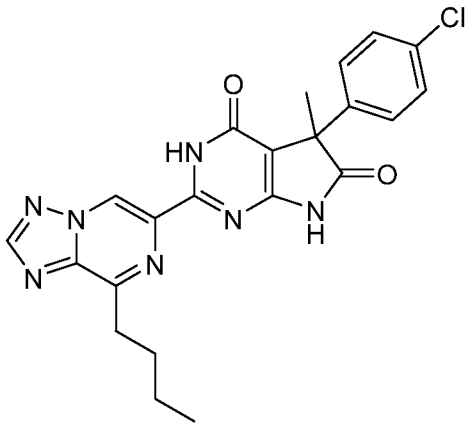
155B

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(5-fluoropyridin-2-yl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



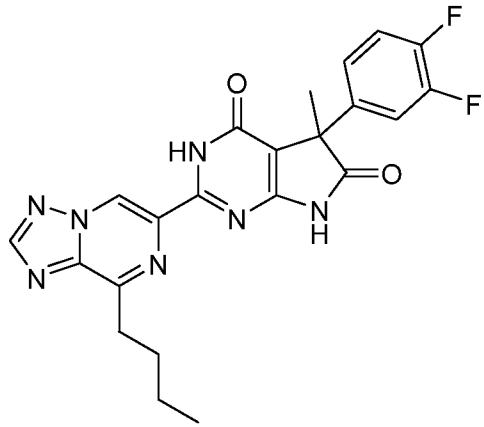
156B

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(4-chloro-3-fluorophenyl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



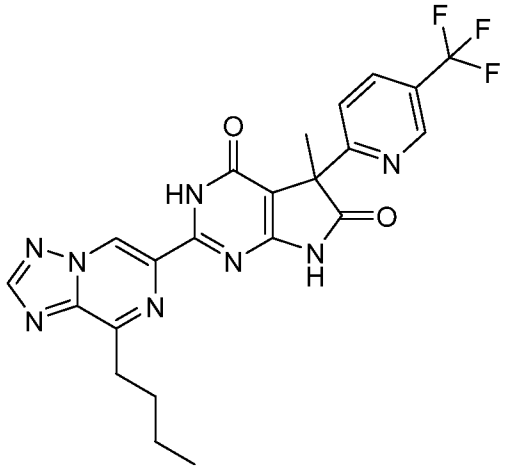
157A

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(4-chlorophenyl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



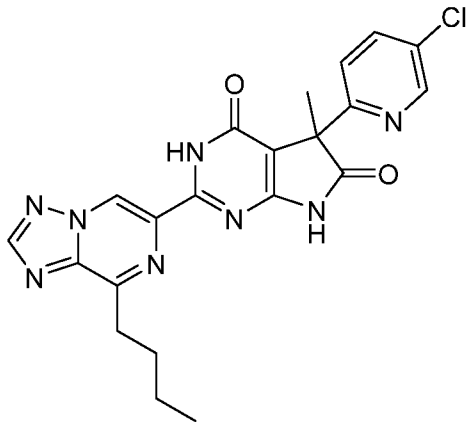
158B

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(3,4-difluorophenyl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



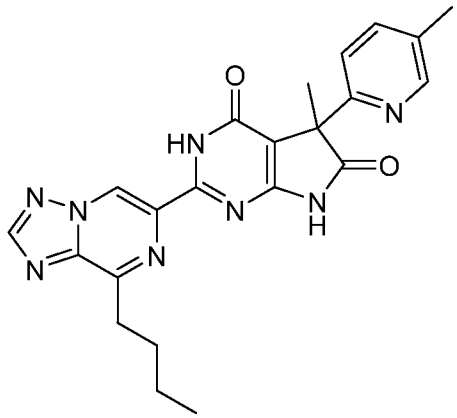
159B

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



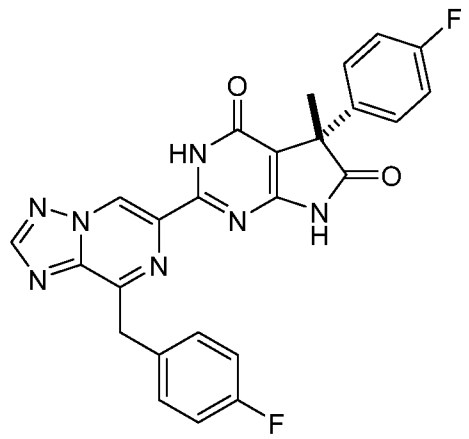
160A

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(5-chloropyridin-2-yl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



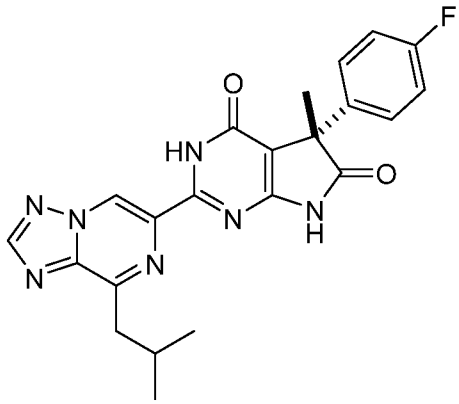
161B

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-methyl-5-(5-methylpyridin-2-yl)-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



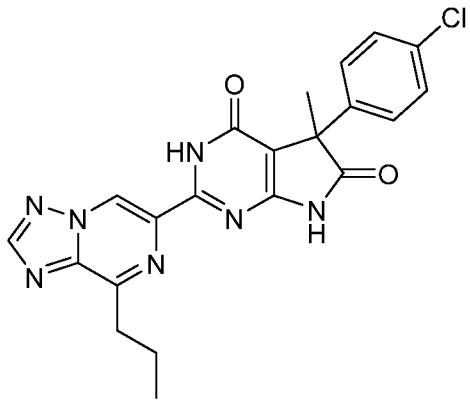
162B

(5*S*)-2-[8-(4-fluorobenzyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(4-fluorophenyl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



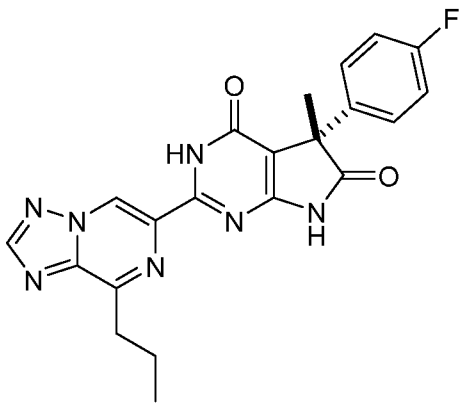
163A

(5*S*)-5-(4-fluorophenyl)-2-[8-isobutyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



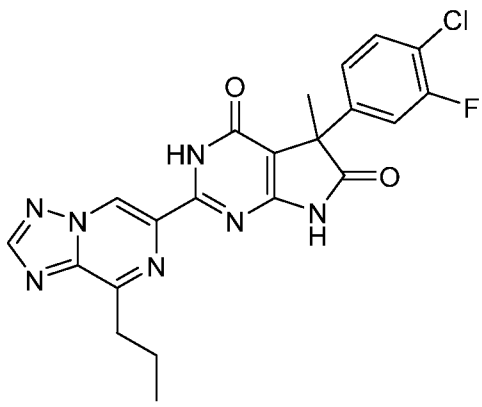
164A

5-(4-chlorophenyl)-5-methyl-2-[8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



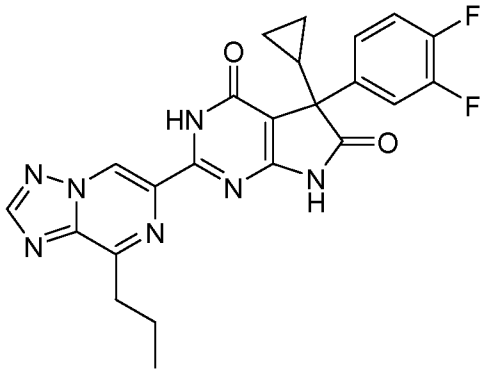
165A

(5*S*)-5-(4-fluorophenyl)-5-methyl-2-[8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



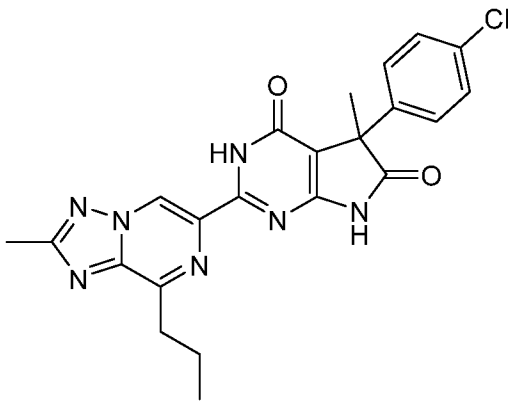
166B

5-(4-chloro-3-fluorophenyl)-5-methyl-2-[8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



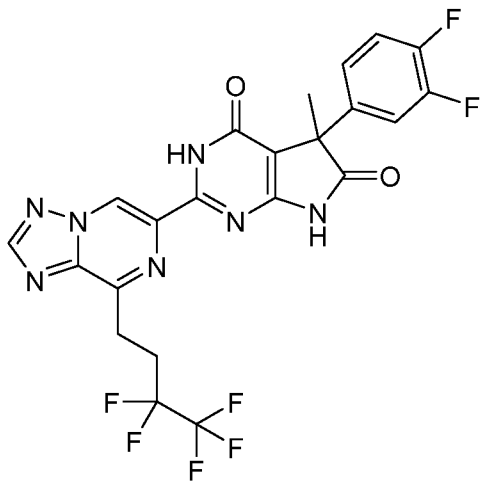
167A

5-cyclopropyl-5-(3,4-difluorophenyl)-2-[8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

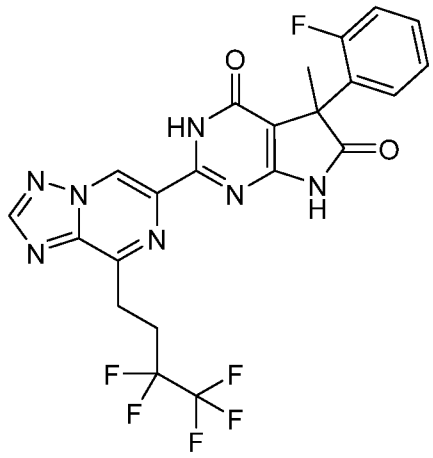


168A

5-(4-chlorophenyl)-5-methyl-2-[2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,



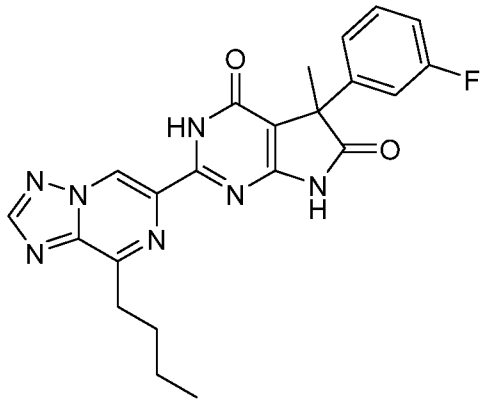
, or

169B

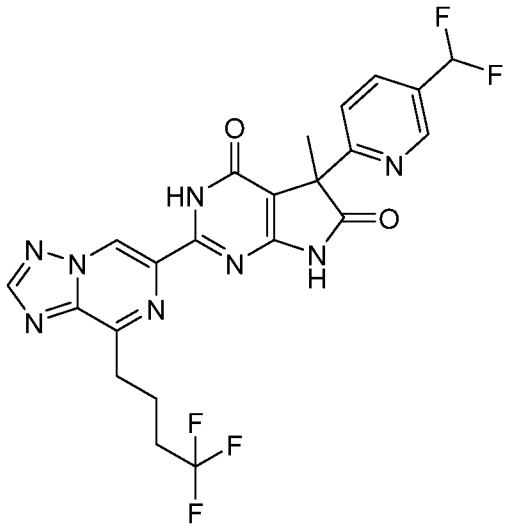
5-(3,4-difluorophenyl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

170A

5-(2-fluorophenyl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



;

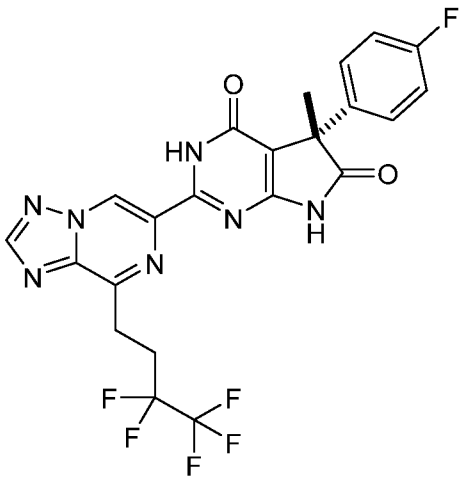


171A

2-[8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(3-fluorophenyl)-5-methyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

181A

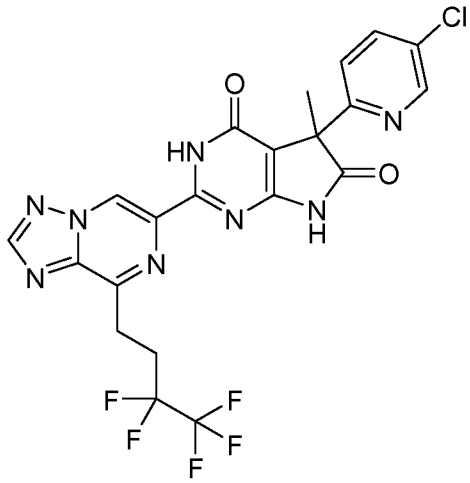
5-(5-(difluoromethyl)pyridin-2-yl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



119A

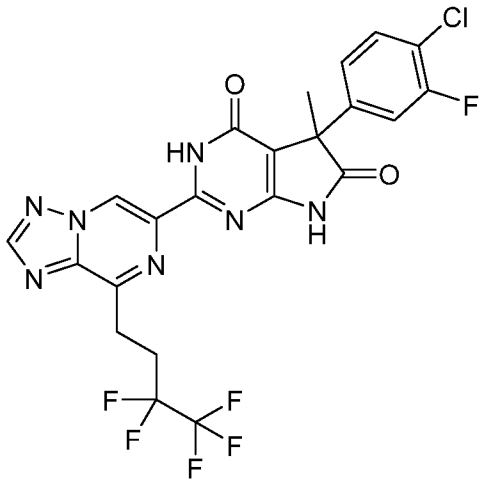
(5*S*)-5-(4-fluorophenyl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



120A

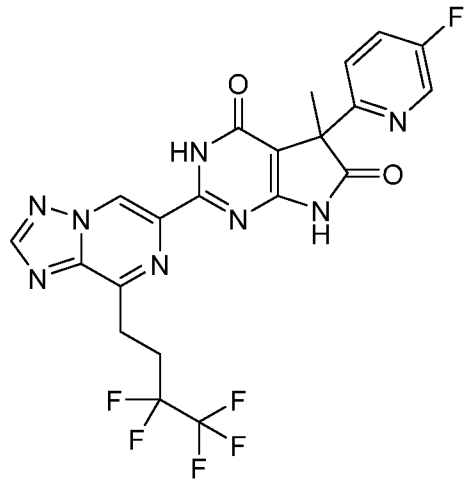
5-(5-chloropyridin-2-yl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-a]pyrazin-6-yl]-5,7-dihydro-1H-pyrrolo[2,3-d]pyrimidine-4,6-dione



121B

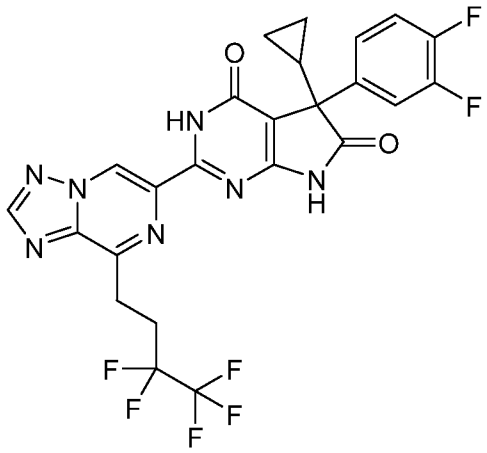
5-(4-chloro-3-fluorophenyl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



122B

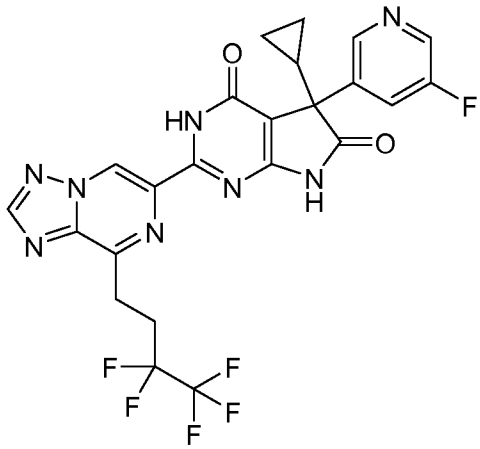
5-(5-fluoropyridin-2-yl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,

123A

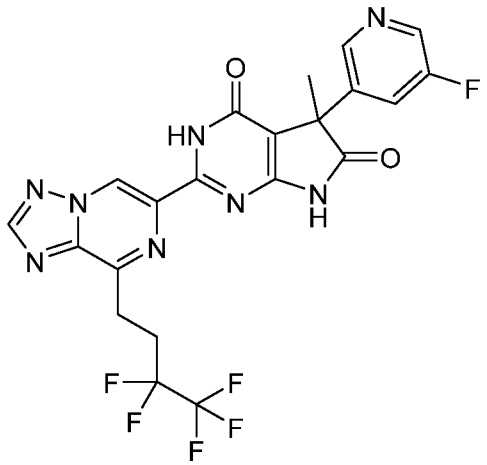
5-cyclopropyl-5-(3,4-difluorophenyl)-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,

124B

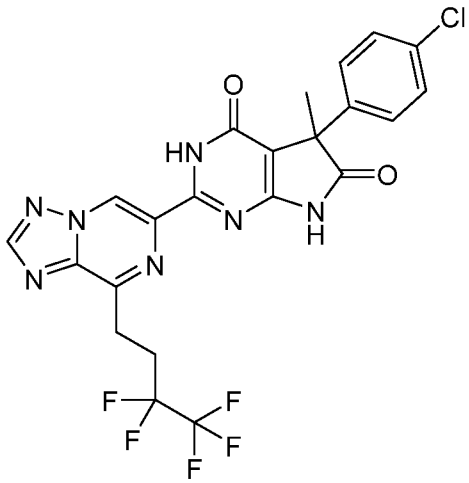
5-cyclopropyl-5-(5-fluoropyridin-3-yl)-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,

125A

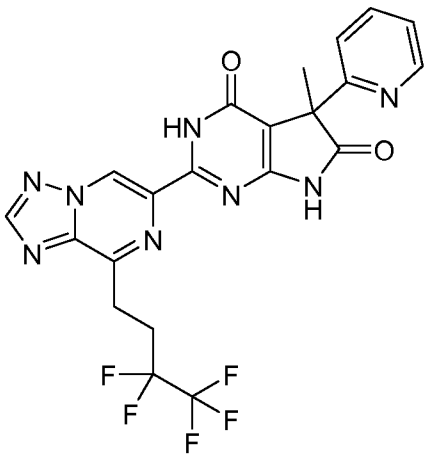
5-(5-fluoropyridin-3-yl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,

126A

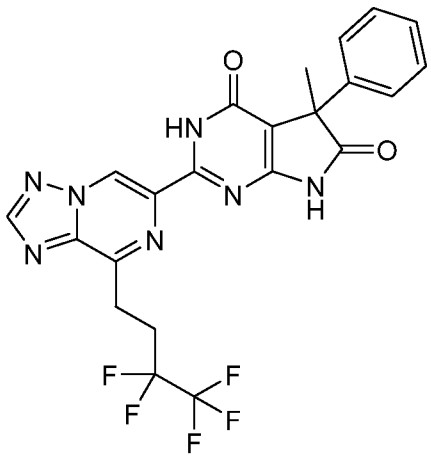
5-(4-chlorophenyl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



127B

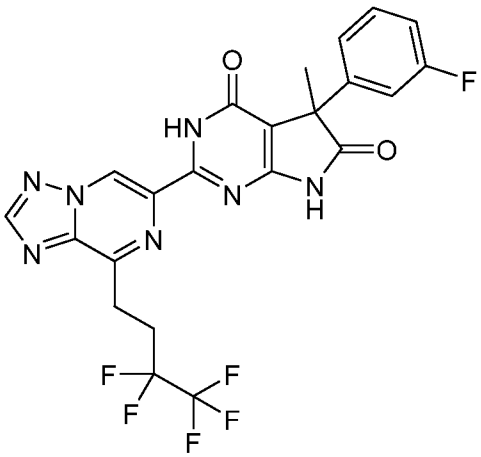
5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(pyridin-2-yl)-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



128B

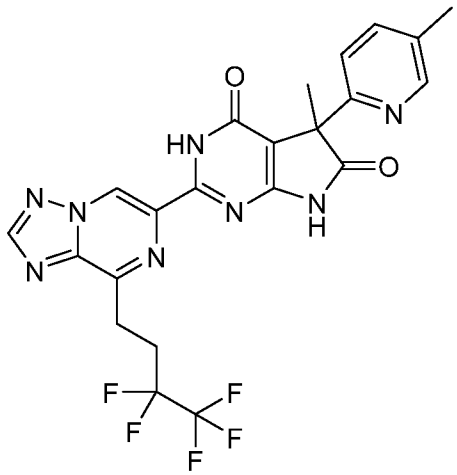
5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-phenyl-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



129B

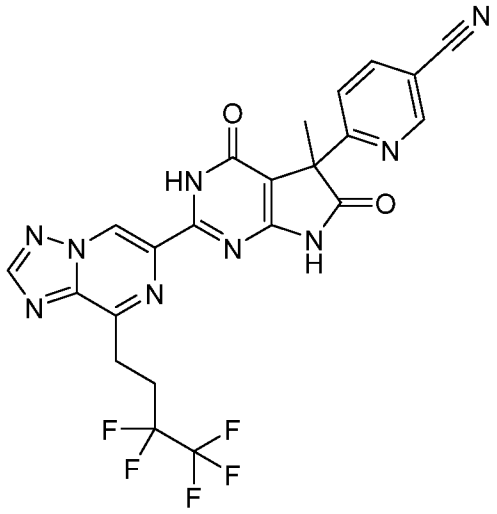
5-(3-fluorophenyl)-5-methyl-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



130B

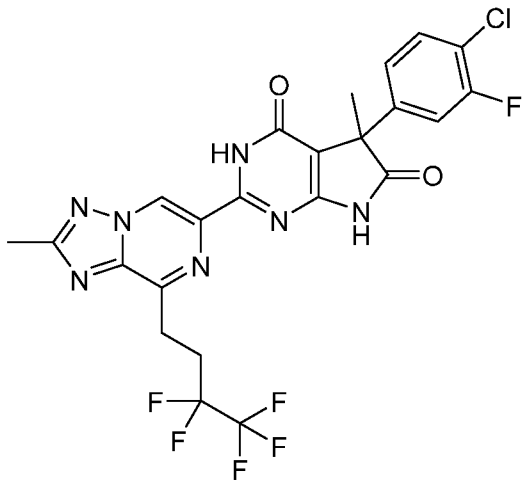
5-methyl-5-(5-methylpyridin-2-yl)-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,

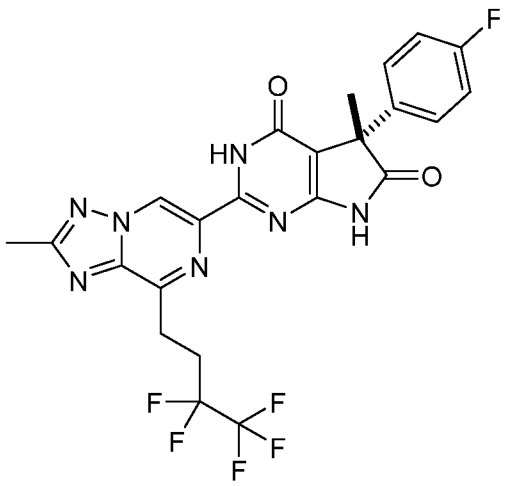
131A

6-(5-methyl-4,6-dioxo-2-[8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-4,5,6,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)nicotinonitrile



132B

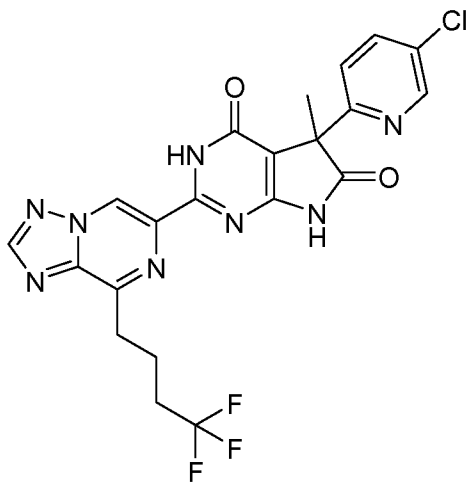
5-(4-chloro-3-fluorophenyl)-5-methyl-2-[2-methyl-8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



,

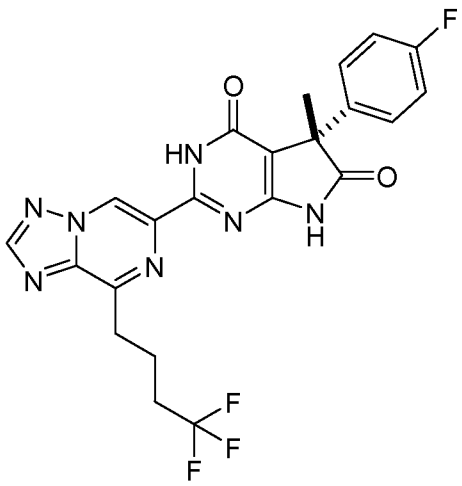
133B

(5*S*)-5-(4-fluorophenyl)-5-methyl-2-[2-methyl-8-(3,3,4,4,4-pentafluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



134A

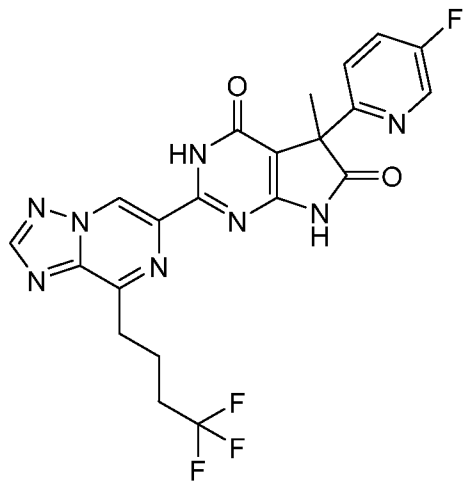
5-(5-chloropyridin-2-yl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



135A

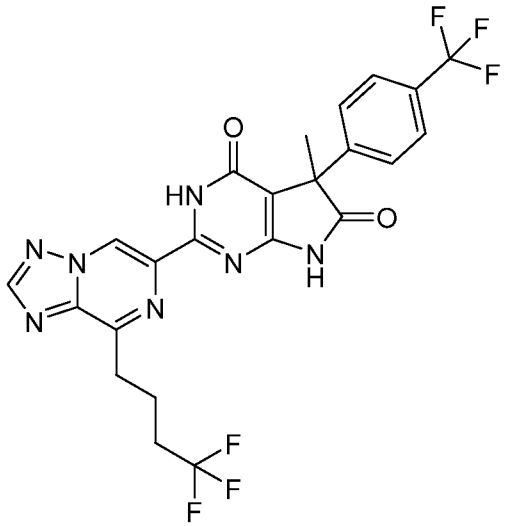
(5*S*)-5-(4-fluorophenyl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



136B

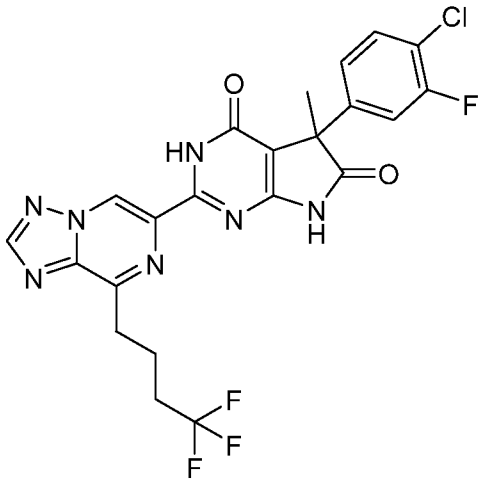
5-(5-fluoropyridin-2-yl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



137B

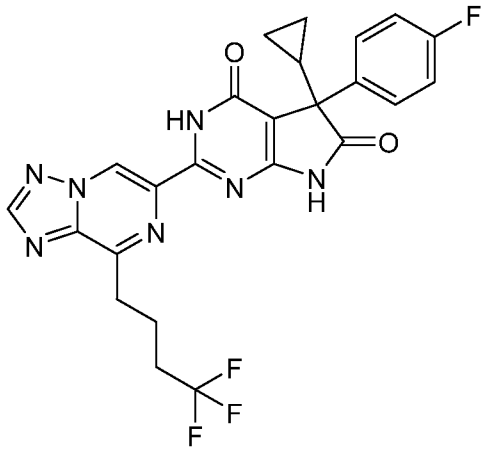
5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(4-(trifluoromethyl)phenyl)-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



138B

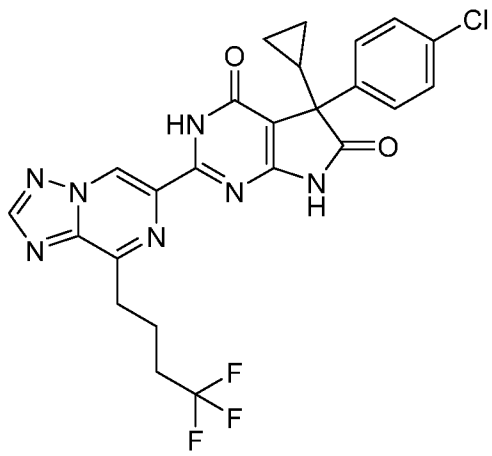
5-(4-chloro-3-fluorophenyl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



139B

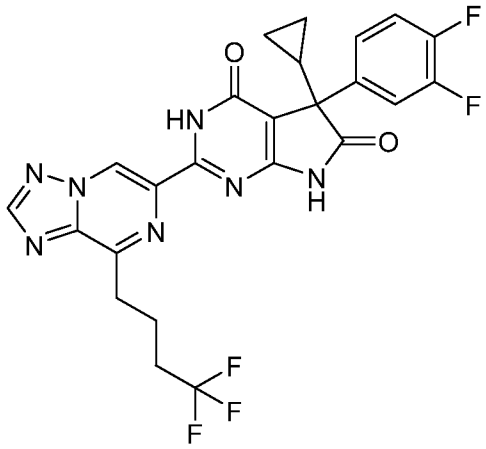
5-cyclopropyl-5-(4-fluorophenyl)-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-a]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



140B

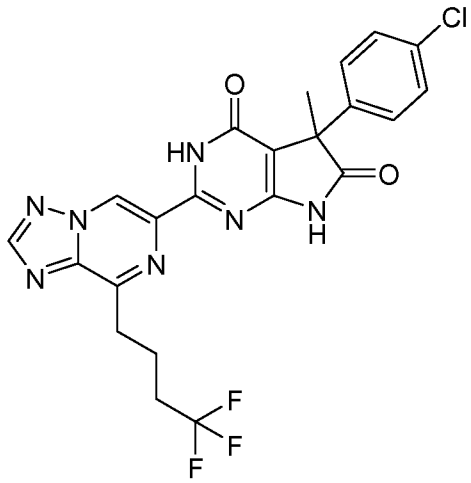
5-(4-chlorophenyl)-5-cyclopropyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



141A

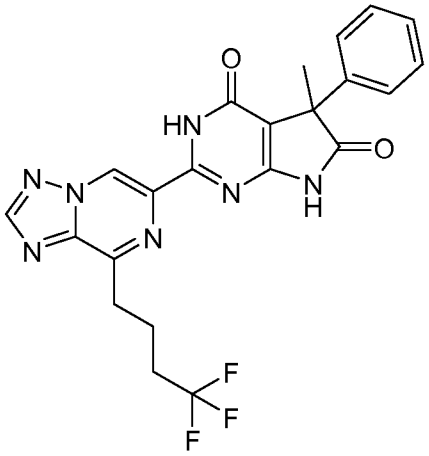
5-cyclopropyl-5-(3,4-difluorophenyl)-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



142A

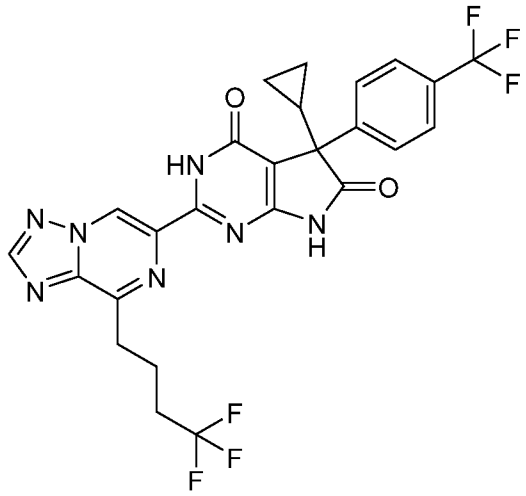
5-(4-chlorophenyl)-5-methyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione



143A

5-methyl-5-phenyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

,



144A

5-cyclopropyl-2-[8-(4,4,4-trifluorobutyl)[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl]-5-(4-(trifluoromethyl)phenyl)-5,7-dihydro-1*H*-pyrrolo[2,3-*d*]pyrimidine-4,6-dione

or a pharmaceutically acceptable salt thereof.

All structural Formulas, embodiments and classes thereof described herein include the pharmaceutically acceptable salts of the compounds defined therein. Reference to the compounds of structural Formula **I** includes the compounds of other generic structural Formulas and embodiments that fall within the scope of Formula **I**, including but not limited to Formula **Ia** to **I-d**.

"Alkyl", as well as other groups having the prefix "alk", such as alkoxy, and the like, means carbon chains which may be linear or branched, or combinations thereof, containing the indicated number of carbon atoms. If no number is specified, 1-6 carbon atoms are intended for linear and 3-7 carbon atoms for branched alkyl groups. Examples of alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, sec- and *tert*-butyl, pentyl, hexyl, heptyl, octyl, nonyl and the like.

"Alkoxy" and “alkyl-O-“ are used interchangeably and refer to an alkyl group linked to oxygen.

“Alkyl-NH-“ refers to an alkyl group linked to an NH group. Examples of alkyl-NH- include methyl-amino or methyl-NH- and ethyl-amino or ethyl-NH-.

"Aryl" means phenyl or naphthyl.

"Haloalkyl" include mono- substituted as well as multiple halo substituted alkyl groups, up to perhalo substituted alkyl. For example, halomethyl, 1,1-difluoroethyl, trifluoromethyl or 1,1,1,2,2-pentafluorobutyl are included.

"Haloalkoxy" and "haloalkyl-O" are used interchangeably and refer to halo substituted alkyl groups or "haloalkyl" linked through the oxygen atom. Haloalkoxy include mono- substituted as well as multiple halo substituted alkoxy groups, up to perhalo substituted alkoxy. For example, trifluoromethoxy is included.

"Cycloalkyl" means a saturated cyclic hydrocarbon radical having the number of carbon atoms designated if no number of atoms is specified, 3-7 carbon atoms are intended, forming 1-3 carbocyclic rings that are fused. "Cycloalkyl" also includes monocyclic rings fused to an aryl group in which the point of attachment is on the non-aromatic portion. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, tetrahydronaphthyl, decahydronaphthyl, indanyl and the like.

"Cycloalkoxy" and "cycloalkyl-O" are used interchangeably and refer to a cycloalkyl group, as defined above, linked to oxygen.

"Heterocyclyl" "heterocycle" or "heterocyclic" refers to nonaromatic cyclic ring structures in which one or more atoms in the ring, the heteroatom(s), is an element other than carbon. Heteroatoms are typically O, S or N atoms. Examples of heterocyclyl groups include: piperidine, piperazinyl, morpholinyl, pyrrolidinyl, tetrahydrofuranyl, azetidinyl, oxiranyl, or aziridinyl, and the like.

"Heteroaryl" refers to an aromatic cyclic ring structures in which one or more atoms in the ring, the heteroatom(s), is an element other than carbon. Heteroatoms are typically O, S, or N atoms. Examples of heteroaromatic groups include: pyridinyl, pyrimidinyl, pyrrolyl, pyridazinyl, isoxazolyl, indolyl, or imidazolyl.

"Halogen" (or "halo") unless otherwise indicated, includes fluorine (fluoro), chlorine (chloro), bromine (bromo) and iodine (iodo). In one embodiment, halo is fluoro (-F) or chloro (-Cl).

When any variable (e.g., R^1, R^2, etc.) occurs more than one time in any constituent or in Formula **I** or other generic formulas herein, its definition on each occurrence is independent of its definition at every other occurrence. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. In choosing compounds of the present invention, one of ordinary skill in the art will recognize that the various substituents, i.e., R^1, R^2, etc., are to be chosen in conformity with well-known

principles of chemical structure connectivity and stability. Unless expressly stated to the contrary, substitution by a named substituent is permitted on any atom in a ring (e.g., aryl, a heteroaryl ring, or a saturated heterocyclic ring) provided such ring substitution is chemically allowed and results in a stable compound. A "stable" compound is a compound which can be prepared and isolated and whose structure and properties remain or can be caused to remain essentially unchanged for a period of time sufficient to allow use of the compound for the purposes described herein (e.g., therapeutic or prophylactic administration to a subject).

The term "substituted" shall be deemed to include multiple degrees of substitution by a named substituent. Where multiple substituent moieties are disclosed or claimed, the substituted compound can be independently substituted by one or more of the disclosed or claimed substituent moieties, singly or plurally. By independently substituted, it is meant that the (two or more) substituents can be the same or different.

Unless expressly depicted or described otherwise, variables depicted in a structural formula with a "floating" bond, such as R^7 in Formulas **I-c** and **I-d**, are permitted on any available carbon atom in the ring to which the variable is attached. When a moiety is noted as being "optionally substituted" in Formulas **I** to **Id** or any embodiment thereof, it means that Formula **I** or the embodiment thereof encompasses compounds that contain the noted substituent (or substituents) on the moiety and also compounds that do not contain the noted substituent (or substituents) on the moiety.

Compounds of structural Formulas **I** to **I-d** may contain one or more asymmetric centers and can thus occur as racemates and racemic mixtures, single enantiomers, diastereoisomeric mixtures and individual diastereoisomers. Centers of asymmetry that are present in the compounds of Formula **I** can all independently of one another have S configuration or R configuration. The compounds of this invention include all possible enantiomers and diastereomers and mixtures of two or more stereoisomers, for example mixtures of enantiomers and/or diastereomers, in all ratios. Thus, enantiomers are a subject of the invention in enantiomerically pure form, both as levorotatory and as dextrorotatory antipodes, in the form of racemates and in the form of mixtures of the two enantiomers in all ratios. In the case of a cis/trans isomerism the invention includes both the cis form and the trans form as well as mixtures of these forms in all ratios. The present invention is meant to comprehend all such stereo-isomeric forms of the compounds of structural Formulas **I** to **I-d**.

Compounds of structural Formulas **I** to **I-d** may be separated into their individual diastereoisomers by, for example, fractional crystallization from a suitable solvent, for example methanol or ethyl acetate or a mixture thereof, or via chiral chromatography using

an optically active stationary phase. Absolute stereochemistry may be determined by X-ray crystallography of crystalline products or crystalline intermediates which are derivatized, if necessary, with a reagent containing an asymmetric center of known absolute configuration. Alternatively, any stereoisomer or isomers of a compound of Formulas **I** to **I-d** may be obtained by stereospecific synthesis using optically pure starting materials or reagents of known absolute configuration.

If desired, racemic mixtures of the compounds may be separated so that the individual enantiomers are isolated. The separation can be carried out by methods well known in the art, such as the coupling of a racemic mixture of compounds to an enantiomerically pure compound to form a diastereoisomeric mixture, followed by separation of the individual diastereoisomers by standard methods, such as fractional crystallization or chromatography. The coupling reaction is often the formation of salts using an enantiomerically pure acid or base. The diasteromeric derivatives may then be converted to the pure enantiomers by cleavage of the added chiral residue. The racemic mixture of the compounds can also be separated directly by chromatographic methods utilizing chiral stationary phases, which methods are well known in the art.

For compounds of Formulas **I** to **I-d** described herein which contain olefinic double bonds, unless specified otherwise, they are meant to include both E and Z geometric isomers.

Some of the compounds described herein may exist as tautomers which have different points of attachment of hydrogen accompanied by one or more double bond shifts. For example, a ketone and its enol form are keto-enol tautomers. The individual tautomers as well as mixtures thereof are encompassed with compounds of Formulas **I** to **I-d** of the present invention.

In the compounds of structural Formulas **I** to **I-d**, the atoms may exhibit their natural isotopic abundances, or one or more of the atoms may be artificially enriched in a particular isotope having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number predominately found in nature. The present invention as described and claimed herein is meant to include all suitable isotopic variations of the compounds of structural Formulas **I** to **I-d** and embodiments thereof. For example, different isotopic forms of hydrogen (H) include protium (^{1}H) and deuterium (^{2}H, also denoted herein as D). Protium is the predominant hydrogen isotope found in nature. Enriching for deuterium may afford certain therapeutic advantages, such as increasing *in vivo* half-life or reducing dosage requirements, or may provide a compound useful as a standard for characterization of biological samples. Isotopically-enriched compounds within structural Formulas **I** to **I-d**, can

be prepared without undue experimentation by conventional techniques well known to those skilled in the art or by processes analogous to those described in the Schemes and Examples herein using appropriate isotopically-enriched reagents and/or intermediates.

The term "pharmaceutically acceptable salts" refers to salts prepared from pharmaceutically acceptable non-toxic bases or acids. When the compound of the present invention is acidic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic bases, including inorganic bases and organic bases. Salts derived from such inorganic bases include aluminum, ammonium, calcium, copper (ic and ous), ferric, ferrous, lithium, magnesium, manganese (ic and ous), potassium, sodium, zinc and the like salts. Preferred are the ammonium, calcium, magnesium, potassium and sodium salts. Salts prepared from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines derived from both naturally occurring and synthetic sources. Pharmaceutically acceptable organic non-toxic bases from which salts can be formed include, for example, arginine, betaine, caffeine, choline, N,N'-dibenzyl-ethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethylmorpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, dicyclohexylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine and the like.

When the compound of the present invention is basic, its corresponding salt can be conveniently prepared from pharmaceutically acceptable non-toxic inorganic and organic acids. Such acids include, for example, acetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid and the like. Preferred are citric, hydrobromic, hydrochloric, maleic, phosphoric, sulfuric, and tartaric acids. If the compounds of Formulas **I** to **I-d** simultaneously contain acidic and basic groups in the molecule the invention also includes, in addition to the salt forms mentioned, inner salts or betaines (zwitterions). Salts can be obtained from the compounds of Formulas **I** to **I-d** by customary methods which are known to the person skilled in the art, for example by combination with an organic or inorganic acid or base in a solvent or dispersant, or by anion exchange or cation exchange from other salts. The present invention also includes all salts of the compounds of Formula **I** which, owing to low physiological compatibility, are not directly suitable for use in pharmaceuticals but which can be used, for example, as

intermediates for chemical reactions or for the preparation of pharmaceutically acceptable salts.

Furthermore, compounds of the present invention may exist in amorphous form and/or one or more crystalline forms, and as such all amorphous and crystalline forms and mixtures thereof of the compounds of Formula **I**, including the Examples, are intended to be included within the scope of the present invention. In addition, some of the compounds of the instant invention may form solvates with water (i.e., a hydrate) or common organic solvents such as but not limited to ethyl acetate. Such solvates and hydrates, particularly the pharmaceutically acceptable solvates and hydrates, of the instant compounds are likewise encompassed within the scope of this invention, along with un-solvated and anhydrous forms.

Any pharmaceutically acceptable pro-drug modification of a compound of this invention which results in conversion in vivo to a compound within the scope of this invention is also within the scope of this invention. For example, esters can optionally be made by esterification of an available carboxylic acid (-COOH) group or by formation of an ester on an available hydroxy group in a compound. Similarly, labile amides can be made. Pharmaceutically acceptable esters or amides of the compounds of this invention may be prepared to act as pro-drugs which can be hydrolyzed back to an acid (or $-COO^-$ depending on the pH of the fluid or tissue where conversion takes place) or hydroxy form particularly in vivo and as such are encompassed within the scope of this invention. Included are those esters and acyl groups known in the art for modifying the solubility or hydrolysis characteristics for use as sustained-release or prodrug formulations. Also, in the case of a carboxylic acid (-COOH) or alcohol group being present in the compounds of the present invention, pharmaceutically acceptable esters of carboxylic acid derivatives, such as methyl, ethyl, or pivaloyloxymethyl, or acyl derivatives of alcohols, such as *O*-acetyl, *O*-pivaloyl, *O*-benzoyl, and *O*-aminoacyl, can be employed.

The present invention also relates to processes for the preparation of the compounds of Formulas **I** to **I-d** which are described in the following and by which the compounds of the invention are obtainable.

The compounds of Formulas **I** to **I-d** according to the invention effect an increase of cGMP concentration via the activation of the soluble guanylate cyclase (sGC), and they therefore bay be useful agents for the therapy and prophylaxis of disorders which are associated with a low or decreased cGMP level or which are caused thereby, or for whose therapy or prophylaxis an increase of the present cGMP level is desired. The activation of the

sGC by the compounds of Formulas **I** to **I-d** can be examined, for example, in the activity assay described herein.

The terms "therapeutically effective (or efficacious) amount" and similar descriptions such as "an amount efficacious for treatment" are intended to mean that amount of a pharmaceutical drug that will elicit the biological or medical response of a tissue, a system, animal or human that is being sought by a researcher, veterinarian, medical doctor or other clinician. The terms "prophylactically effective (or efficacious) amount" and similar descriptions such as "an amount efficacious for prevention" are intended to mean that amount of a pharmaceutical drug that will prevent or reduce the risk of occurrence of the biological or medical event that is sought to be prevented in a tissue, a system, animal or human by a researcher, veterinarian, medical doctor or other clinician. As an example, the dosage a patient receives can be selected so as to achieve the desired reduction in blood pressure; the dosage a patient receives may also be titrated over time in order to reach a target blood pressure. The dosage regimen utilizing a compound of the instant invention is selected in accordance with a variety of factors including type, species, age, weight, sex and medical condition of the patient; the severity of the condition to be treated; the potency of the compound chosen to be administered; the route of administration; and the renal and hepatic function of the patient. A consideration of these factors is well within the purview of the ordinarily skilled clinician for the purpose of determining the therapeutically effective or prophylactically effective dosage amount needed to prevent, counter, or arrest the progress of the condition. It is understood that a specific daily dosage amount can simultaneously be both a therapeutically effective amount, e.g., for treatment of hypertension, and a prophylactically effective amount, e.g., for prevention of myocardial infarction.

Disorders and pathological conditions which are associated with a low cGMP level or in which an increase of the cGMP level is desired and for whose therapy and prophylaxis it is possible to use compounds of Formulas **I** to **I-d** are, for example, cardiovascular diseases, such as endothelial dysfunction, diastolic dysfunction, atherosclerosis, hypertension, heart failure, pulmonary hypertension, which includes pulmonary arterial hypertension (PAH), stable and unstable angina pectoris, thromboses, restenoses, myocardial infarction, strokes, cardiac insufficiency, fibrosis or pulmonary hypertonia, or, for example, erectile dysfunction, asthma bronchiale, chronic kidney insufficiency and diabetes. Compounds of Formulas **I** to **I-d** can additionally be used in the therapy of cirrhosis of the liver and also for improving a restricted memory performance or ability to learn.

The compounds of Formulas **I** to **I-d** and their pharmaceutically acceptable salts can be administered to animals, preferably to mammals, and in particular to humans, as pharmaceuticals by themselves, in mixtures with one another or in the form of pharmaceutical compositions. The term "patient" includes animals, preferably mammals and especially humans, who use the instant active agents for the prevention or treatment of a medical condition. Administering of the drug to the patient includes both self-administration and administration to the patient by another person. The patient may be in need of, or desire, treatment for an existing disease or medical condition, or may be in need of or desire prophylactic treatment to prevent or reduce the risk of occurrence of said disease or medical condition. As used herein, a patient "in need" of treatment of an existing condition or of prophylactic treatment encompasses both a determination of need by a medical professional as well as the desire of a patient for such treatment.

Subjects of the present invention therefore also are the compounds of Formulas **I** to **I-d** and their pharmaceutically acceptable salts for use as pharmaceuticals, their use for activating soluble guanylate cyclase, for normalizing a disturbed cGMP balance and in particular their use in the therapy and prophylaxis of the above mentioned syndromes as well as their use for preparing medicaments for these purposes.

Furthermore, a subject of the present invention is pharmaceutical compositions which comprise as active component an effective dose of at least one compound of Formulas **I** to **I-d** and/or a pharmaceutically acceptable salt thereof and a customary pharmaceutically acceptable carrier, i.e., one or more pharmaceutically acceptable carrier substances and/or additives.

Thus, a subject of the invention is, for example, said compound and its pharmaceutically acceptable salts for use as a pharmaceutical, pharmaceutical compositions which comprise as active component an effective dose of said compound and/or a pharmaceutically acceptable salt thereof and a customary pharmaceutically acceptable carrier, and the uses of said compound and/or a pharmaceutically acceptable salt thereof in the therapy or prophylaxis of the abovementioned syndromes as well as their use for preparing medicaments for these purposes.

The pharmaceutical compositions according to the invention can be administered orally, for example in the form of pills, tablets, lacquered tablets, sugar-coated tablets, granules, hard and soft gelatin capsules, aqueous, alcoholic or oily solutions, syrups, emulsions or suspensions, or rectally, for example in the form of suppositories. Administration can also be carried out parenterally, for example subcutaneously,

intramuscularly or intravenously in the form of solutions for injection or infusion. Other suitable administration forms are, for example, percutaneous or topical administration, for example in the form of ointments, tinctures, sprays or transdermal therapeutic systems, or the inhalative administration in the form of nasal sprays or aerosol mixtures, or, for example, microcapsules, implants or rods. The preferred administration form depends, for example, on the disease to be treated and on its severity.

The amount of active compound of Formulas **I** to **I-d** and/or its pharmaceutically acceptable salts in the pharmaceutical composition normally is from 0.1 to 200 mg, preferably from 1 to 200 mg, per dose, but depending on the type of the pharmaceutical composition it can also be higher. The pharmaceutical compositions usually comprise 0.5 to 90 percent by weight of the compounds of Formulas **I** to **I-d** and/or their pharmaceutically acceptable salts. The preparation of the pharmaceutical compositions can be carried out in a manner known per se. For this purpose, one or more compounds of Formulas **I** to **I-d** and/or their pharmaceutically acceptable salts, together with one or more solid or liquid pharmaceutical carrier substances and/or additives (or auxiliary substances) and, if desired, in combination with other pharmaceutically active compounds having therapeutic or prophylactic action, are brought into a suitable administration form or dosage form which can then be used as a pharmaceutical in human or veterinary medicine.

For the production of pills, tablets, sugar-coated tablets and hard gelatin capsules, it is possible to use, for example, lactose, starch, for example maize starch, or starch derivatives, talc, stearic acid or its salts, etc. Carriers for soft gelatin capsules and suppositories are, for example, fats, waxes, semisolid and liquid polyols, natural or hardened oils, etc. Suitable carriers for the preparation of solutions, for example of solutions for injection, or of emulsions or syrups are, for example, water, physiologically acceptable sodium chloride solution, alcohols such as ethanol, glycerol, polyols, sucrose, invert sugar, glucose, mannitol, vegetable oils, etc. It is also possible to lyophilize the compounds of Formulas **I** to **I-d** and their pharmaceutically acceptable salts and to use the resulting lyophilisates, for example, for preparing preparations for injection or infusion. Suitable carriers for microcapsules, implants or rods are, for example, copolymers of glycolic acid and lactic acid.

Besides the active compounds and carriers, the pharmaceutical compositions can also contain customary additives, for example fillers, disintegrants, binders, lubricants, wetting agents, stabilizers, emulsifiers, dispersants, preservatives, sweeteners, colorants, flavorings, aromatizers, thickeners, diluents, buffer substances, solvents, solubilizers, agents for

achieving a depot effect, salts for altering the osmotic pressure, coating agents or antioxidants.

The dosage of the active compound of Formulas **I** to **I-d** and/or of a pharmaceutically acceptable salt thereof to be administered depends on the individual case and is, as is customary, to be adapted to the individual circumstances to achieve an optimum effect. Thus, it depends on the nature and the severity of the disorder to be treated, and also on the sex, age, weight and individual responsiveness of the human or animal to be treated, on the efficacy and duration of action of the compounds used, on whether the therapy is acute or chronic or prophylactic, or on whether other active compounds are administered in addition to compounds of Formulas **I** to **I-d**. In general, a daily dose of approximately 0.01 to 100 mg/kg, preferably 0.01 to 10 mg/kg, in particular 0.3 to 5 mg/kg (in each case mg per kg of bodyweight) is appropriate for administration to an adult weighing approximately 75 kg in order to obtain the desired results. The daily dose can be administered in a single dose or, in particular when larger amounts are administered, be divided into several, for example two, three or four individual doses. In some cases, depending on the individual response, it may be necessary to deviate upwards or downwards from the given daily dose. A single daily dose is preferred.

The compounds of Formulas **I** to **I-d** activate soluble guanylate cyclase. On account of this property, apart from use as pharmaceutically active compounds in human medicine and veterinary medicine, they can also be employed as a scientific tool or as an aid for biochemical investigations in which such an effect on soluble guanylate cyclase is intended, and also for diagnostic purposes, for example in the in vitro diagnosis of cell samples or tissue samples. The compounds of Formulas **I** to **I-d** and salts thereof can furthermore be employed, as already mentioned above, as intermediates for the preparation of other pharmaceutically active compounds.

One or more additional pharmacologically active agents may be administered in combination with a compound of Formulas **I** to **I-d**. An additional active agent (or agents) is intended to mean a pharmaceutically active agent (or agents) that is active in the body, including pro-drugs that convert to pharmaceutically active form after administration, which are different from the compound of Formulas **I** to **I-d**, and also includes free-acid, free-base and pharmaceutically acceptable salts of said additional active agents. Generally, any suitable additional active agent or agents, including but not limited to anti-hypertensive agents, anti-atherosclerotic agents such as a lipid modifying compound, anti-diabetic agents and/or anti-obesity agents may be used in any combination with the compound of Formulas **I** to **I-d** in a

single dosage formulation (a fixed dose drug combination), or may be administered to the patient in one or more separate dosage formulations which allows for concurrent or sequential administration of the active agents (co-administration of the separate active agents). Examples of additional active agents which may be employed include but are not limited to angiotensin converting enzyme inhibitors (e.g, alacepril, benazepril, captopril, ceronapril, cilazapril, delapril, enalapril, enalaprilat, fosinopril, imidapril, lisinopril, moveltipril, perindopril, quinapril, ramipril, spirapril, temocapril, or trandolapril), angiotensin II receptor antagonists (e.g., losartan i.e., COZAAR®, valsartan, candesartan, olmesartan, telmesartan and any of these drugs used in combination with hydrochlorothiazide such as HYZAAR®); neutral endopeptidase inhibitors (e.g., thiorphan and phosphoramidon), aldosterone antagonists, aldosterone synthase inhibitors, renin inhibitors (e.g. urea derivatives of di- and tri-peptides (See U.S. Pat. No. 5,116,835), amino acids and derivatives (U.S. Patents 5,095,119 and 5,104,869), amino acid chains linked by non-peptidic bonds (U.S. Patent 5,114,937), di- and tri-peptide derivatives (U.S. Patent 5,106,835), peptidyl amino diols (U.S. Patents 5,063,208 and 4,845,079) and peptidyl beta-aminoacyl aminodiol carbamates (U.S. Patent 5,089,471); also, a variety of other peptide analogs as disclosed in the following U.S. Patents 5,071,837; 5,064,965; 5,063,207; 5,036,054; 5,036,053; 5,034,512 and 4,894,437, and small molecule renin inhibitors (including diol sulfonamides and sulfinyls (U.S. Patent 5,098,924), N-morpholino derivatives (U.S. Patent 5,055,466), N-heterocyclic alcohols (U.S. Patent 4,885,292) and pyrolimidazolones (U.S. Patent 5,075,451); also, pepstatin derivatives (U.S. Patent 4,980,283) and fluoro- and chloro-derivatives of statone-containing peptides (U.S. Patent 5,066,643), enalkrein, RO 42-5892, A 65317, CP 80794, ES 1005, ES 8891, SQ 34017, aliskiren (2(S),4(S),5(S),7(S)-N-(2-carbamoyl-2-methylpropyl)-5-amino-4-hydroxy-2,7-diisopropyl-8-[4-methoxy-3-(3-methoxypropoxy)-phenyl]-octanamid hemifumarate) SPP600, SPP630 and SPP635), endothelin receptor antagonists, phosphodiesterase-5 inhibitors (e.g., sildenafil, tadalfil and vardenafil), vasodilators, calcium channel blockers (e.g., amlodipine, nifedipine, veraparmil, diltiazem, gallopamil, niludipine, nimodipins, nicardipine), potassium channel activators (e.g., nicorandil, pinacidil, cromakalim, minoxidil, aprilkalim, loprazolam), diuretics (e.g., hydrochlorothiazide), sympatholitics, beta-adrenergic blocking drugs (e.g., propranolol, atenolol, bisoprolol, carvedilol, metoprolol, or metoprolol tartate), alpha adrenergic blocking drugs (e.g., doxazocin, prazocin or alpha methyldopa) central alpha adrenergic agonists, peripheral vasodilators (e.g. hydralazine); lipid lowering agents e.g., HMG-CoA reductase inhibitors such as simvastatin and lovastatin which are marketed as ZOCOR® and MEVACOR® in

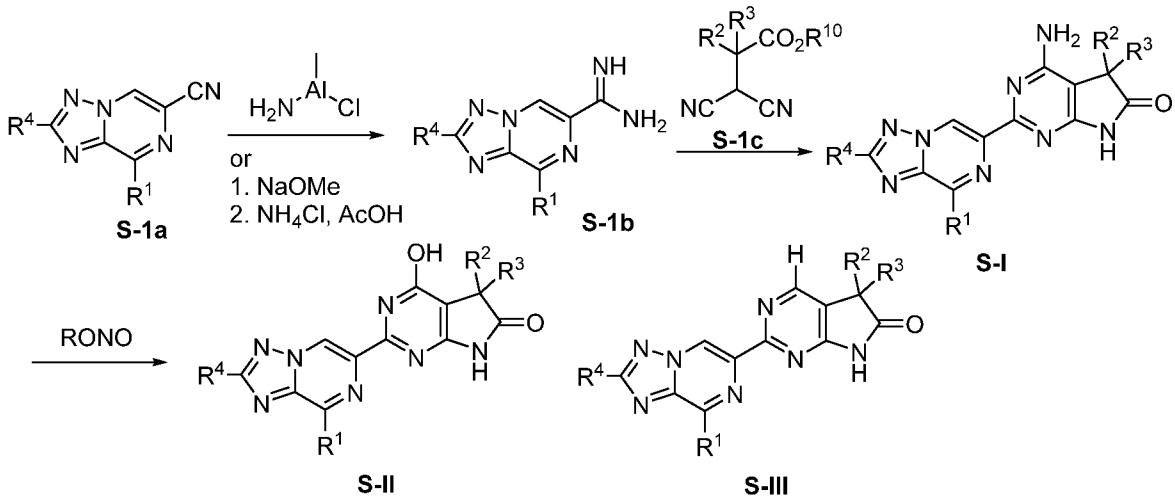
lactone pro-drug form and function as inhibitors after administration, and pharmaceutically acceptable salts of dihydroxy open ring acid HMG-CoA reductase inhibitors such as atorvastatin (particularly the calcium salt sold in LIPITOR®), rosuvastatin (particularly the calcium salt sold in CRESTOR®), pravastatin (particularly the sodium salt sold in PRAVACHOL®), and fluvastatin (particularly the sodium salt sold in LESCOL®); a cholesterol absorption inhibitor such as ezetimibe (ZETIA®) and ezetimibe in combination with any other lipid lowering agents such as the HMG-CoA reductase inhibitors noted above and particularly with simvastatin (VYTORIN®) or with atorvastatin calcium; niacin in immediate-release or controlled release forms, and/or with an HMG-CoA reductase inhibitor; niacin receptor agonists such as acipimox and acifran, as well as niacin receptor partial agonists; metabolic altering agents including insulin and insulin mimetics (e.g., insulin degludec, insulin glargine, insulin lispro), dipeptidyl peptidase-IV (DPP-4) inhibitors (e.g., sitagliptin, alogliptin, omarigliptin, linagliptin, vildagliptin); insulin sensitizers, including (i) PPARγ agonists, such as the glitazones (e.g. pioglitazone, AMG 131, MBX2044, mitoglitazone, lobeglitazone, IDR-105, rosiglitazone, and balaglitazone), and other PPAR ligands, including (1) PPARα/γ dual agonists (e.g., ZYH2, ZYH1, GFT505, chiglitazar, muraglitazar, aleglitazar, sodelglitazar, and naveglitazar); (2) PPARα agonists such as fenofibric acid derivatives (e.g., gemfibrozil, clofibrate, ciprofibrate, fenofibrate, bezafibrate), (3) selective PPARγ modulators (SPPARγM's), (e.g., such as those disclosed in WO 02/060388, WO 02/08188, WO 2004/019869, WO 2004/020409, WO 2004/020408, and WO 2004/066963); and (4) PPARγ partial agonists; (ii) biguanides, such as metformin and its pharmaceutically acceptable salts, in particular, metformin hydrochloride, and extended-release formulations thereof, such as Glumetza™, Fortamet™, and GlucophageXR™; and (iii) protein tyrosine phosphatase-1B (PTP-1B) inhibitors (e.g., ISIS-113715 and TTP814); insulin or insulin analogs (e.g., insulin detemir, insulin glulisine, insulin degludec, insulin glargine, insulin lispro and inhalable formulations of each); leptin and leptin derivatives and agonists; amylin and amylin analogs (e.g., pramlintide); sulfonylurea and non-sulfonylurea insulin secretagogues (e.g., tolbutamide, glyburide, glipizide, glimepiride, mitiglinide, meglitinides, nateglinide and repaglinide); α-glucosidase inhibitors (e.g., acarbose, voglibose and miglitol); glucagon receptor antagonists (e.g., MK-3577, MK-0893, LY-2409021 and KT6-971); incretin mimetics, such as GLP-1, GLP-1 analogs, derivatives, and mimetics; and GLP-1 receptor agonists (e.g., dulaglutide, semaglutide, albiglutide, exenatide, liraglutide, lixisenatide, taspoglutide, CJC-1131, and BIM-51077, including intranasal, transdermal, and once-weekly formulations thereof); LDL cholesterol lowering agents such as (i) HMG-CoA

reductase inhibitors (e.g., simvastatin, lovastatin, pravastatin, cerivastatin, fluvastatin, atorvastatin, and rosuvastatin), (ii) bile acid sequestering agents (e.g., colestilan, colestimide, colesevalam hydrochloride, colestipol, cholestyramine, and dialkylaminoalkyl derivatives of a cross-linked dextran), (iii) inhibitors of cholesterol absorption, (e.g., ezetimibe), and (iv) acyl CoA:cholesterol acyltransferase inhibitors, (e.g., avasimibe); HDL-raising drugs, (e.g., niacin and nicotinic acid receptor agonists, and extended-release versions thereof); antiobesity compounds; agents intended for use in inflammatory conditions, such as aspirin, non-steroidal anti-inflammatory drugs or NSAIDs, glucocorticoids, and selective cyclooxygenase-2 or COX-2 inhibitors; glucokinase activators (GKAs) (e.g., AZD6370); inhibitors of 11β-hydroxysteroid dehydrogenase type 1, (e.g., such as those disclosed in U.S. Patent No. 6,730,690, and LY-2523199); CETP inhibitors (e.g., anacetrapib, evacetrapib, and torcetrapib); inhibitors of fructose 1,6-bisphosphatase, (e.g., such as those disclosed in U.S. Patent Nos. 6,054,587; 6,110,903; 6,284,748; 6,399,782; and 6,489,476); inhibitors of acetyl CoA carboxylase-1 or 2 (ACC1 or ACC2); AMP-activated Protein Kinase (AMPK) activators; other agonists of the G-protein-coupled receptors: (i) GPR-109, (ii) GPR-119 (e.g., MBX2982 and PSN821), and (iii) GPR-40; SSTR3 antagonists (e.g., such as those disclosed in WO 2009/001836); neuromedin U receptor agonists (e.g., such as those disclosed in WO 2009/042053, including, but not limited to, neuromedin S (NMS)); SCD modulators; GPR-105 antagonists (e.g., such as those disclosed in WO 2009/000087); SGLT inhibitors (e.g., ASP1941, SGLT-3, empagliflozin, dapagliflozin, ertugliflozin, canagliflozin, BI-10773, PF-04971729, remogloflozin, TS-071, tofogliflozin, ipragliflozin, and LX-4211); inhibitors of acyl coenzyme A:diacylglycerol acyltransferase 1 and 2 (DGAT-1 and DGAT-2); inhibitors of fatty acid synthase; inhibitors of acyl coenzyme A:monoacylglycerol acyltransferase 1 and 2 (MGAT-1 and MGAT-2); agonists of the TGR5 receptor (also known as GPBAR1, BG37, GPCR19, GPR131, and M-BAR); ileal bile acid transporter inhibitors; PACAP, PACAP mimetics, and PACAP receptor 3 agonists; PPAR agonists; protein tyrosine phosphatase-1B (PTP-1B) inhibitors; IL-1b antibodies, (e.g., XOMA052 and canakinumab); and bromocriptine mesylate and rapid-release formulations thereof; or with other drugs beneficial for the prevention or the treatment of the above-mentioned diseases including nitroprusside and diazoxide the free-acid, free-base, and pharmaceutically acceptable salt forms of the above active agents where chemically possible.

The following examples are provided so that the invention might be more fully understood. Unless otherwise indicated, the starting materials are commercially available. They should not be construed as limiting the invention in any way.

Several methods for preparing the compounds of this invention are described in the following Schemes and Examples. Starting materials and intermediates are purchased, made from known procedures, or as otherwise illustrated. Some frequently applied routes to the compounds of Formula **S-I** are also described by the Schemes as follows. In some cases the order of carrying out the steps of reaction schemes may be varied to facilitate the reaction or to avoid unwanted reaction products. The "R" and "X" groups in the Schemes correspond to the variables defined in Formula **S-I** at the same positions on the structures.

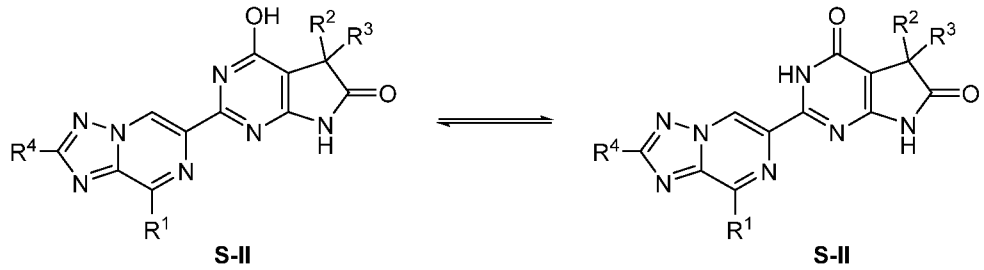
SCHEME **1**



Compounds of Formula **S-I**, **S-II** and **S-III** can be prepared according to the sequence as depicted in Scheme 1. Conversion of the triazolo[1,5-*a*]pyrazine nitrile **S-1a** to the amidine intermediate **S-1b** can be accomplished with a reagent such as amino(chloro)methylaluminum, prepared from trimethylaluminum and NH_4Cl, in a non-polar solvent such as toluene at elevated temperature as described by Garigipati, R. S. et al Tetrahedron Letters **1990**, *31*, 1969. The nitrile **S-1a** can also be converted to the amidine **S-1b** by using NaOMe in MeOH to form the imidate, which can then be transformed to the amidine **S-1b** using NH_4Cl and acetic acid as described by Pinner, A. et al, Ber. Dtsch. Chem. Ges. **1877**, *10*, 1889. Treatment of the amidine **S-1b** with a suitable malononitrile intermediate **S-1c** in an alcoholic solvent, such as *t*-BuOH, and a suitable base such as $NaHCO_3$, $KHCO_3$, or Na_2CO_3 at elevated temperature provides compounds of Formula **S-I**. The reactions leading to compounds of Formula **S-I** in Scheme **1** may also be carried out using the corresponding methyl, ethyl, or propyl esters (R^{10}) of compound **S-1c**. Treatment of compounds of Formula **S-I** with a suitable diazotizing reagent such as *tert*-butyl nitrite, isopentyl nitrite, or sodium nitrite in a solvent such as 1,2-DCE, DMA, DMF, MeCN, or THF

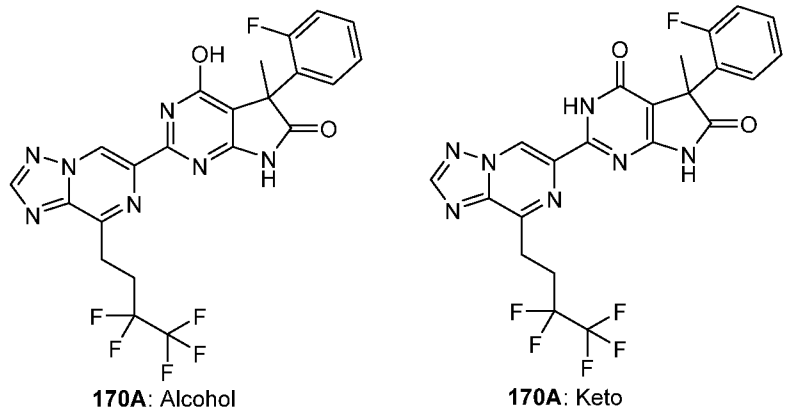
at elevated temperature provides compounds with Formula **S-II** and **S-III**. The ratio of **S-II** and **S-III** varies depending on the structure of Formula **S-I** and water content in the reaction.

Figure **1**

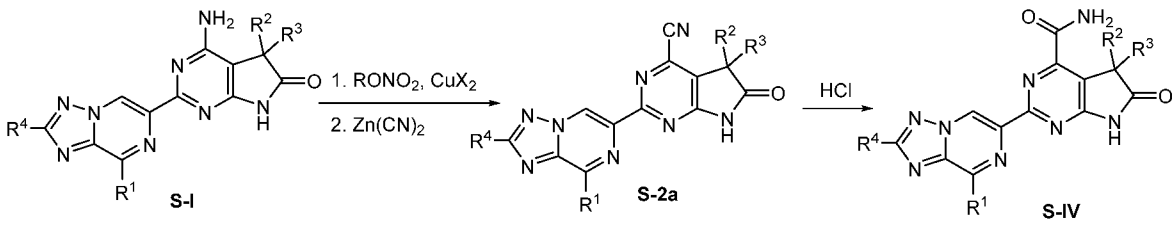


Compounds of Formula **S-II** can be drawn in both tautomeric forms as shown in Figure **1**. Although the compounds are drawn in the alcohol form throughout, the compounds can also be drawn in the keto form. For example, Example **170A** is drawn in the alcohol form. However, Example **170A** could have been drawn in the keto form.

Figure **2**



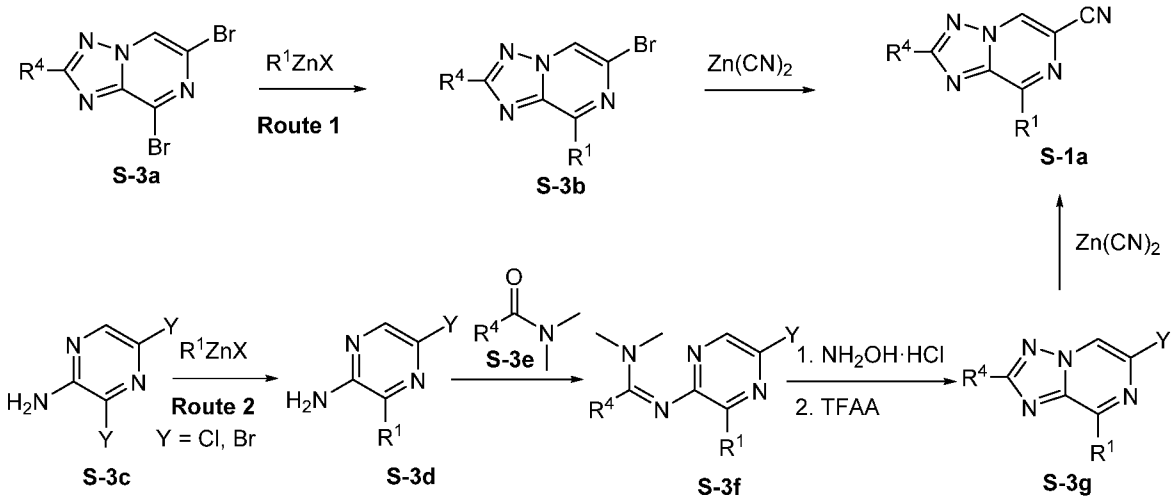
SCHEME **2**



Compounds of Formula **S-IV**, can be prepared according to the sequence as depicted in Scheme **2**. Treatment of compounds of Formula **S-I** with a suitable diazotizing reagent such as *tert*-butyl nitrite, in presence of a copper (II) salt such as $CuCl_2$ or $CuBr_2$ can afford halogenated intermediate which can be transformed into the nitrile intermediate **S-2a** using

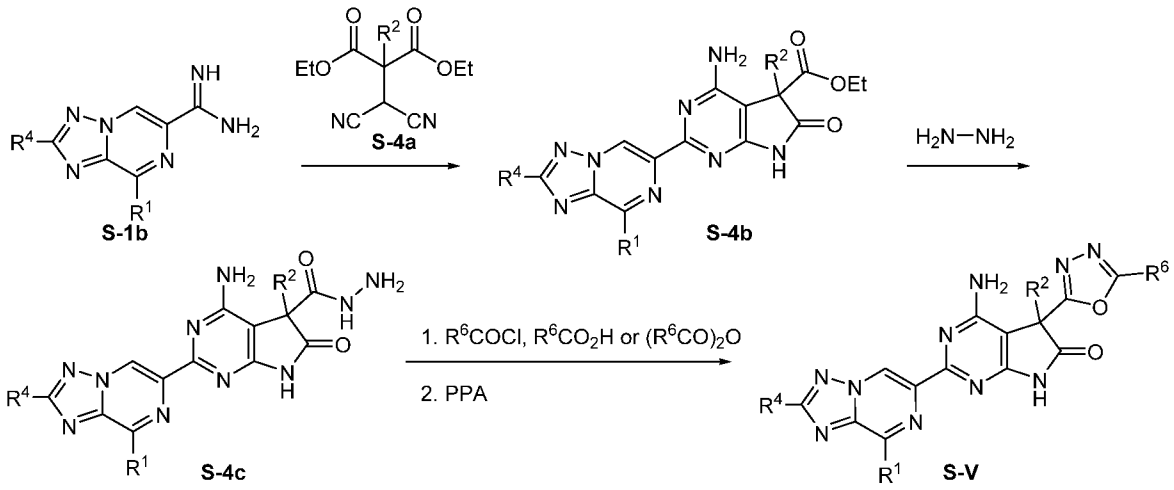
$Zn(CN)_2$ and a palladium catalyst such as $Pd(dppf)Cl_2$ at an elevated temperature. Compounds of Formula **S-IV** can be obtained by the treatment of compound **S-2a** with an aq. HCl solution.

SCHEME **3**



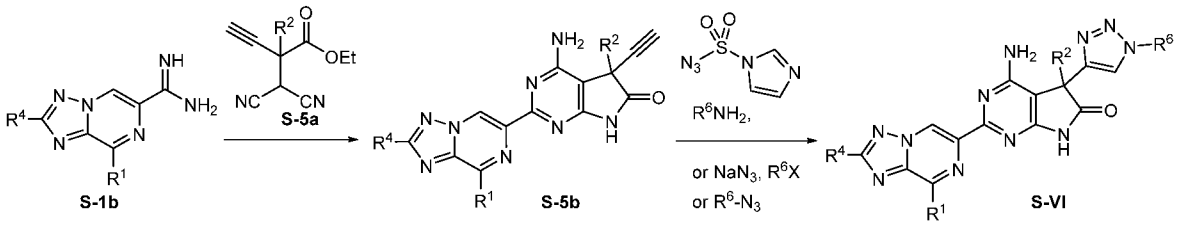
The nitrile intermediate **S-1a** can be prepared by two different routes as depicted in Scheme **3**. In the first route 6,8-dibromo-[1,2,4]triazolo[1,5-*a*]pyrazine **S-3a** can be selectively coupled to an alkylzinc reagent, R^1ZnX, using a palladium catalyst such as $Pd(PPh_3)_2Cl_2$ to give compound **S-3b**, which can be transformed into the nitrile intermediate **S-1a** using $Zn(CN)_2$ and a palladium catalyst such as $Pd(dppf)Cl_2$ at an elevated temperature. Alternatively, nitrile intermediate **S-1a** can be obtained from 3,5-dihalopyrazin-2-amine **S-3c** such as 3,5-dichloropyrazin-2-amine or 3,5-dibromopyrazin-2-amine, via route 2. Treatment of **S-3c** with an alkylzinc reagent, R_1ZnX, using a palladium catalyst such as $Pd(PPh_3)_2Cl_2$ affords **S-3d**, which can be tranformed into compound **S-3f** by condensation with amide **S-3e**. Treatment of compound **S-3f** with hydroxylamine hydrochloride followed by trifluoroacetic anhydride (TFAA) affords the triazolo[1,5-*a*]pyrazine **S-3g**. Compound **S-3g** can be transformed into the nitrile intermediate **S-1a** using $Zn(CN)_2$ and a palladium catalyst such as $Pd(dppf)Cl_2$ at an elevated temperature.

SCHEME **4**



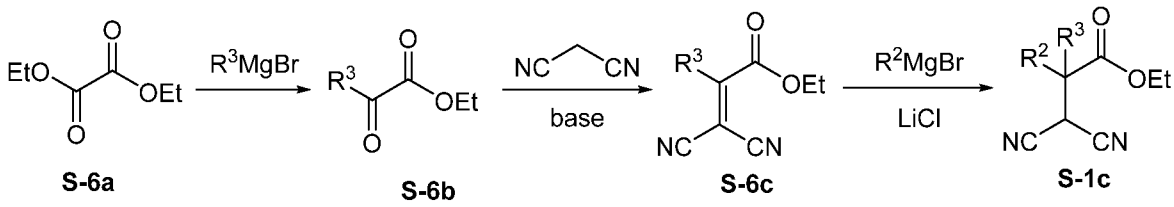
In one embodiment of the present invention, compounds with Formula **S-V** may be prepared by the sequence depicted in Scheme **4**. The amidine intermediate **S-1b** from Scheme **1** can be cyclized with a suitable diester-malononitrile intermediate (**S-4a**) to afford compound **S-4b**. Treatment of the ester intermediate **S-4b** with hydrazine affords the acyl hydrazide intermediate **S-4c**, which can be acylated with a suitable acylating reagent bearing the desired R^6 substitution and subsequently can be cyclized in the presence of a suitable condensing reagent such as polyphosphoric acid (PPA) to form a 1,3,4-oxadiazole Formula **S-V**.

SCHEME 5



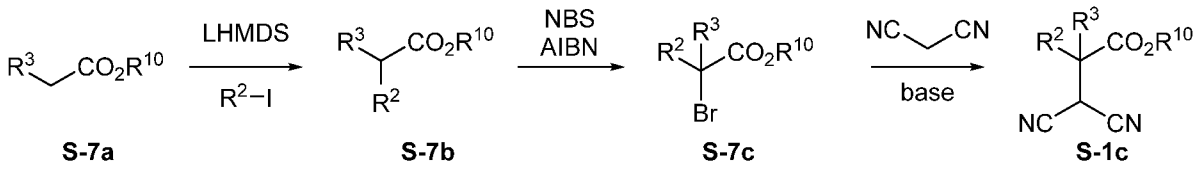
In one embodiment of the present invention, compounds with Formula **S-VI** may be prepared by the sequence outlined in Scheme **5**. The amidine intermediate **S-1b** from Scheme **1** can be treated with a suitable malononitrile reagent **S-5a** under similar conditions described for Scheme **1** to afford the alkyne intermediate **S-5b**. The alkyne intermediate **S-5b** can be further transformed into 1,2,3-triazoles with Formula **S-VI** by treatment with a suitable alkyl azide that is either commercially available or formed *in situ* from sodium azide and an alkyl bromide or an alkyl amine and imidazole-1-sulfonyl azide hydrochloride in the presence of a suitable copper source such as copper(II) sulfate.

SCHEME **6**



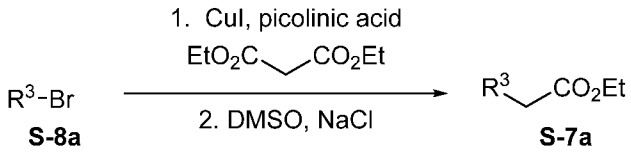
The preparation of compound **S-1c** is outlined in Scheme **6**. Treatment of diethyl oxalate with a suitable aryl magnesium bromide (with or without LiCl additive) or the lithiate of heteroaryl reagents derived via metal-halogen exchange in a suitable solvent such as THF affords compound **S-6b**. Treatment of compound **S-6b** with malononitrile and a suitable base such as piperidine in a solvent such as EtOH at elevated temperature affords compound **S-6c**. Compound **S-6c**, upon treatment with a suitable alkyl magnesium bromide (with or without LiCl additive) in a solvent such as THF affords compound **S-1c**.

SCHEME **7**



In addition to the method described in Scheme **6**, intermediates **S-1c**, may also be prepared as shown in Scheme **7**. Deprotonation of ester **S-7a** using a suitable base such as LiHMDS, NaHMDS, NaH or LDA in a solvent such as THF or DMF followed by treatment with an alkyl iodide affords the intermediate **S-7b**. Treatment of intermediate **S-7b** with a suitable brominating reagent such as NBS and AIBN in a solvent such as carbon tetrachloride at refluxing temperatures affords intermediate **S-7c**. Intermediate **S-7c** can be transformed to compound **S-1c** by reaction with malononitrile in the presence of a suitable base such as NaH, *t*-BuOK, K_2CO_3 or DBU in a solvent such as THF or DMF at RT or at elevated temperatures. The synthetic sequence depicted in Scheme **7** can be used to prepare the corresponding methyl, ethyl or propyl esters (R^{10}) of compound **S-1c**.

SCHEME **8**



The ester **S-7a** can be prepared according to Scheme **8** from the corresponding carboxylic acid by one skilled in the art. The ester **S-7a** may also be prepared by the α-arylation/heteroarylation of esters as described by Buchwald, S. L. et al Organic Letters **2009**, *11*, 1773; or by Shen, H. C. et al Organic Letters **2006**, *8*, 1447. Commercially available aryl bromides **S-8a** can be converted to compound **S-7a** (depicted as the ethyl ester) by the reaction with diethyl malonate in the presence of a suitable catalyst system such as CuI and picolinic acid, followed by decarboxylation at elevated temperatures.

Compounds of the present invention possess an asymmetric center at the carbon bearing the R^2/R^3 substituent which can be either *R* or *S* configuration. These enantiomeric mixtures may be separated or resolved to single enantiomers using methods familiar to those skilled in the art. For example, compounds of the present invention may be resolved to the pure isomers by using chiral SFC chromatography. Racemic material can be resolved to enantiomerically pure compounds whenever possible and at any step in the route. Characterization data may be of the chiral or racemic material.

The independent synthesis of diastereomers and enantiomers or their chromatographic separations may be achieved using methods familiar to those skilled in the art and by appropriate modification of the methodology disclosed herein. Their absolute stereochemistry may be determined by X-ray crystallography of crystalline products or crystalline intermediates which are derivatized, if necessary, with a reagent containing an asymmetric center of known absolute stereochemistry, or by vibrational circular dichroism (VCD) spectroscopy.

Throughout the synthetic schemes and examples, abbreviations and acronyms may be used with the following meanings unless otherwise indicated:

AcOH = acetic acid; AIBN = 2,2'-azobisisobutyronitrile; Anhydr. = Anhydrous; Aq. = aqueous; bp, b.p. = boiling point; br s = broad singlet; Bu = butyl; *t*-Bu = *tert*-butyl; BuLi = butyllithium; *t*BuOH, *tert*-BuOH = t*ert*-butanol; *t*BuOK = potassium *tert*-butoxide; $CDCl_3$ = deuterated chloroform; CD_3OD = Tetradeuteromethanol; CELITE = diatomaceous earth; CF_3 = trifluoromethyl; cGMP = cyclic guanosine monophosphate; conc, conc. = concentrated, concentrate, concentrates; DBU = 1,8-Diazabicyclo[4.3.0]undec-7-ene; DCM = dichloromethane; 1,2- DCE, DCE = 1,2-dichloroethane; DIEA = diisopropylethylamine; DMA, DMAC = *N,N*-dimethylacetamide; DMF = *N,N*-dimethylformamide; DMF-DMA = *N,N*-Dimethylformamide dimethyl acetal; DMSO = dimethylsulfoxide; dppf = 1,1'-bis(diphenylphosphino)ferrocene; EAB = egg albumin; EBSS = Earle's balanced salt solution; equiv, eq. = equivalent(s); Et = ethyl; Et_3N = triethylamine; EtOAc = ethyl acetate;

EtOH = ethanol; GTP = guanosine triphosphate; h, hr = hour; HATU = 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate; HCl = hydrogen chloride; HOBt = Hydroxybenzotriazole; HPLC = High pressure liquid chromatography; Int. = intermediate; *i*Pr = isopropyl; IPA, *i*-PrOH = Isopropanol; LCMS, LC/MS = liquid chromatography-mass spectrometry; LDA = lithium diisopropylamide; LiHMDS, LHMDS = lithium bis(trimethylsilyl)amide; min, min. = minute; M = Molar; Me = methyl; MeCN = acetonitrile; MeI = methyl iodide; MeOH = methanol; mp, m.p. = melting point; mpk = milligrams per kilogram; N = Normal; N_2 = nitrogen; NaOMe = sodium methoxide; NCS = *N*-chloro succinimide; NMP = *N*-methylpyrrolidone; NBS = *N*-bromo succinimide; NaHMDS = sodium bis(trimethylsilyl)amide; NMR = nuclear magnetic resonance; N.D. = not determined; PDA = photodiode array; $Pd(dppf)Cl_2$ = dichloro((1,1'-bis(diphenylphosphino)ferrocene) palladium (II); $Pd(PPh_3)_2Cl_2$ = dichlorobis(triphenylphosphine)palladium(II) or bis(triphenylphosphine) palladium (II) chloride; $Pd_2(dba)_3$ = tris(dibenzylideneacetone)dipalladium (0); Ph = phenyl; PPA = polyphosphoric acid; Pr = propyl; psig = pounds per square inch gauge; PTFE = polytetrafluoroethylene; PTLC, prep TLC = preparative thin layer chromatography; PyBOP = (benzotriazol-1-yloxy) tripyrrolidinophosphonium hexafluorophosphate; rac = racemic; rt = retention time; RP-HPLC = reverse phase HPLC; RT = room temperature; sat., sat'd = saturated; SFC = supercritical fluid chromatography; sGC = soluble guanylate cyclase; TFA = trifluoroacetic acid; TFAA = trifluoroacetic anhydride; TLC = thin layer chromatography; THF = tetrahydrofuran; VCD = vibrational circular dichroism; v, v/v = volume, volume to volume; w, w/w = weight, weight to weight.

The following examples are provided to more fully illustrate the present invention, and shall not be construed as limiting the scope in any manner. Unless stated otherwise, the following conditions were employed. All operations were carried out at room or ambient temperature (RT), that is, at a temperature in the range 18-25°C. Reactions are generally done using commercially available anhydrous solvents under an inert atmosphere, either nitrogen or argon. Microwave reactions were done using a BIOTAGE Initiator™ or CEM EXPLORER® system. Evaporation of solvent was carried out using a rotary evaporator under reduced pressure (4.5-30 mmHg) with a bath temperature of up to 50°C. The course of reactions was followed by thin layer chromatography (TLC) and/or tandem high performance liquid chromatography (HPLC) followed by electron spray mass spectroscopy (MS), herein termed LCMS, and any reaction times are given for illustration only. The structure of all final compounds was assured by at least one of the following techniques: MS or proton nuclear

magnetic resonance (^{1}H NMR) spectrometry, and the purity was assured by at least one of the following techniques: TLC or HPLC. ^{1}H NMR spectra were recorded on either a Varian Unity or a Varian Inova instrument at 300, 400, 500 or 600 MHz using the indicated solvent. When line-listed, NMR data are in the form of delta values for major diagnostic protons, given in parts per million (ppm) relative to residual solvent peaks (multiplicity and number of hydrogens). Conventional abbreviations used for signal shape are: s. singlet; d. doublet (apparent); t. triplet (apparent); m. multiplet; br. broad; etc. MS data were recorded on a Waters Micromass unit, interfaced with a Hewlett-Packard (AGILENT 1100) HPLC instrument, and operating on MASSLYNX/OpenLynx software. Electrospray ionization was used with positive (ES+) or negative ion (ES-) detection; and diode array detection. Purification of compounds by preparative reverse phase HPLC was performed on a GILSON system using a YMC-Pack Pro C18 column (150 x 20 mm i.d.) eluting at 20 mL/min with a water/acetonitrile (0.1% TFA) gradient (typically 5% acetonitrile to 95% acetonitrile) using a SUNFIRE Prep C18 OBD 5μM column (100 x 30 mm i.d.) eluting at 50 mL/min with a water/acetonitrile (0.1% TFA) gradient. Purification of compounds by preparative thin layer chromatography (PTLC) was conducted on 20 x 20 cm glass plates coated with silica gel, commercially available from Analtech; or E. Merck. Flash column chromatography was carried out on a glass silica gel column using Kieselgel 60, 0.063-0.200 mm (SiO_2), or on a BIOTAGE SiO_2 cartridge system using the BIOTAGE Horizon and BIOTAGE SP-1 systems; or a Teledyne Isco SiO_2 cartridge using the COMBIFLASH Rf system. Chemical symbols have their usual meanings, and the following abbreviations have also been used: h or hr (hours), min (minutes), v (volume), w (weight), b.p. (boiling point), m.p. (melting point), L (litre(s)), mL (millilitres), g (gram(s)), mg (milligrams(s)), mol (moles), mmol (millimoles), eq or equiv (equivalent(s)), μM (micromolar), nM (nanomolar), ca (circa/about).

The following are representative procedures for the preparation of intermediates used to prepare the final products described in the Examples that follow thereafter. These examples are provided for the purpose of further illustration only and are not intended to be limitations on the disclosed invention.

It is understood that a chiral center in a compound may exist in the "S" or "R" stereo-configurations, or as a mixture of both. In some of the examples for intermediate compounds and final compounds, such compounds having a racemic chiral center were separated into individual stereoisomers, for example, referred to as isomer A (or enantiomer A or the like), which refers to the observed faster eluting isomer, and isomer B (or enantiomer B or the like), which refers to the observed slower eluting isomer, and each such isomer may be noted in the

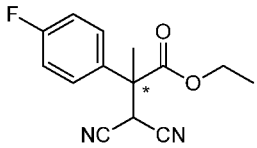
example as either the fast or slow eluting isomer. When a single "A" or "B" isomer intermediate is used to prepare a downstream compound, the downstream compound may take the "A" or "B" designation that corresponds to the previously used intermediate.

Any Intermediates described below may be referred to herein by their number preceded by "**I-**." For illustration, the racemic parent title compound would be referred to as Intermediate **39** (**I-39**, or rac **I-39**), and the separated stereoisomers are noted as Intermediates **39A** and **39B** (or **I-39A** and **I-39B**). In some examples, compounds having a chiral center were derived synthetically from a single isomer intermediate; e.g., Example **63** was made using stereoisomer **I-2A**. Absolute stereochemistry (*R* or *S*) of each of the separated isomers was not determined, unless specifically described. An asterisk (*) may be used in a chemical structure drawing that indicates the location of a chiral center.

Absolute stereochemistry of separate stereoisomers in the Examples and Intermediates was not determined unless stated otherwise in an Example or Intermediate synthesis.

INTERMEDIATE **1**, **1A and 1B** and the S and R isomers

Ethyl 3,3-dicyano-2-(4-fluorophenyl)-2-methylpropanoate



Step A- Ethyl 2-(4-fluorophenyl)-2-oxoacetate: Into a flask was placed a solution of diethyl oxalate (28.5 g, 195 mmol) in THF (300 mL) which was cooled at -78°C. 4-fluorophenylmagnesium bromide (150 mL, 1.0 M in THF) was added dropwise, and the resulting solution was stirred for 1.5 h with warming to RT. The reaction was quenched by the addition of sat. aq. NH_4Cl. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (1%) to afford the title compound.

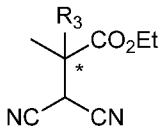
Step B- Ethyl 3,3-dicyano-2-(4-fluorophenyl)acrylate: Into a flask was placed the intermediate from Step A (28.0 g, 143 mmol), malononitrile (37.7 g, 571 mmol), piperidine (2.5 mL), and EtOH (125 mL). The resulting solution was stirred at reflux for 16 h. Upon completion, the resulting mixture was conc. *in vacuo*. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (10%) to afford the title compound.

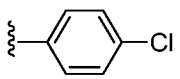
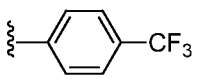
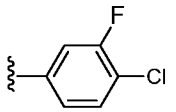
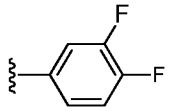
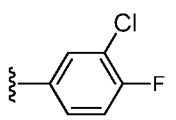
Step C-Ethyl 3,3-dicyano-2-(4-fluorophenyl)-2-methylpropanoate: Into a flask was placed the intermediate from Step B (3.0 g, 12 mmol), THF (50 mL), and lithium chloride (1.0 g,

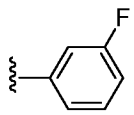
23.6 mmol) which was cooled at 0°C. Subsequently, methylmagnesium bromide (7 mL) was added dropwise, and the resulting solution was stirred for 1 h at 0°C. The reaction was then quenched by the addition of water. The resulting solution was extracted with EtOAc (2X). The organic layers were combined, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (25%) to afford the racemic title compound **I-1**. The racemic material was resolved using chiral SFC (OJ column) to afford isomers **I-1A** (faster eluting) and **I-1B** (slower eluting) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40-7.33 (2H, m), 7.17-7.09 (2H, m), 4.45 (1H, s), 4.30 (2H, q, *J*=7.2 Hz), 1.99 (3H, s), 1.26 (3H, t, *J*=7.2 Hz).

Using a similar procedure to that described in Intermediate **1**, the following compounds in Table **1** were prepared using either commercial starting reagents or from compounds known in the literature.

Table 1

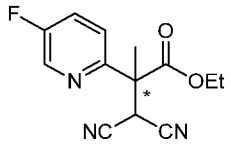


Int	Chiral Resolution Column	R_3	m/z (M+H) or ^{1}H NMR
I-2A and **2B**	CHIRALCEL OJ		275 $[M-1]^-$
I-3A and **3B**	CHIRALPAK IA		^{1}H NMR (400 MHz, DMSO-d_6): δ 7.89 (2H, d, *J*=8.4 Hz), 7.67 (2H, d, *J*=8.4 Hz) 5.83 (1H, s), 4.28 (2H, q, *J*=7.2 Hz), 1.89 (3H, s), 1.19 (3H, t, *J*=7.2 Hz)
I-4A and **B**	CHIRALPAK AD		293 $[M-1]^-$
I-5A and **B**	CHIRALPAK AD		^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.12 (3H, m), 4.46 (1H, s), 4.31 (2H, q, *J*=7.2 Hz), 1.99 (3H, s), 1.28 (3H, t, *J*=7.2 Hz)
I-6A and **B**	PHENOMENEX LUX 5U CELLULOSE-3		293 $[M-1]^-$

I-7A and **B**	CHIRALPAK IA		^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (1 H, td, *J* = 8.11, 5.97 Hz), 7.07-7.16 (3 H, m), 4.49 (1 H, s), 3.82 (3 H, s), 2.00 (3 H, s).

INTERMEDIATE **8**, **8A** and **8B**

Ethyl 3,3-dicyano-2-(5-fluoropyridin-2-yl)-2-methylpropanoate and S and R isomers thereof



Step A- Diethyl 2-(5-fluoropyridin-2-yl)malonate: Into a flask was placed 2-bromo-5-fluoropyridine (20.0 g, 114 mmol), 1,3-diethyl propanedioate (54.5 g, 340 mmol), picolinic acid (5.6 g, 45 mmol), Cs_2CO_3 (143 g, 438 mmol), CuI (4.3 g, 23 mmol), and 1,4-dioxane (500 mL). The resulting solution was stirred for 12 h at 100°C. The mixture was quenched by the addition of water (300 mL). The resulting solution was extracted with EtOAc (2X), the organic layers combined and dried over anhydr. Na_2SO_4, and conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using EtOAc:petroleum ether (0-20%) to afford the title compound.

Step B- Ethyl 2-(5-fluoropyridin-2-yl)acetate: Into a flask was placed the intermediate from Step A (46 g, crude), NaCl (20 g, 342 mmol), water (6 mL), and DMSO (90 mL). The mixture was stirred for 3 h at 180°C. Upon completion, the resulting solution was diluted with EtOAc, washed with water (5X) and the organic layer was dried over anhydr. Na_2SO_4 and conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using EtOAc:petroleum ether (0-20%) to afford the title compound.

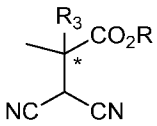
Step C- Ethyl 2-(5-fluoropyridin-2-yl)propanoate: Into a flask was placed THF (200 mL) and LiHMDS (45 mL, 1.0 M). This was followed by dropwise addition of the intermediate from Step B (7.5 g, 41 mmol) with stirring at 0°C. After stirring the resulting solution for 1 h, a solution of iodomethane (5.8 g, 41 mmol) in THF (10 mL) was added dropwise. The resulting solution was stirred for 3 h at 0°C. The reaction was then quenched by the addition of water. The resulting mixture was extracted with EtOAc (3X), the organic layers combined and dried over anhydr. Na_2SO_4, and conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using EtOAc:petroleum ether (0-20%) to afford the title compound.

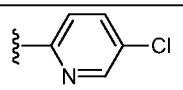
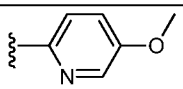
Step D- Ethyl 2-bromo-2-(5-fluoropyridin-2-yl)propanoate: Into a flask was added the intermediate from Step C (1 g, 5 mmol) and THF (50 mL). This was followed by the addition of LiHMDS (5 mL, 1.0 M) dropwise with stirring at –78°C. The resulting solution was stirred for 30 min at –78°C before NBS (1.2 g, 7.1 mmol) in THF (10 mL) was added, and the solution was warmed to RT and stirred for 1h. The reaction was then quenched by the addition of water. The resulting solution was extracted with EtOAc (3X) and the organic layers combined and dried over anhydr. Na_2SO_4. The solid was filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using EtOAc:petroleum ether (0-10%) to afford the title compound.

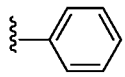
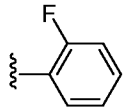
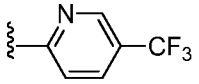
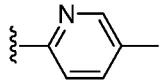
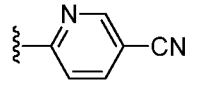
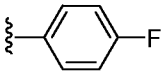
Step E- Ethyl 3,3-dicyano-2-(5-fluoropyridin-2-yl)-2-methylpropanoate: Into a flask was placed DMF (20 mL) and sodium hydride (260 mg, 6.50 mmol, 60%). This was followed by the addition of malononitrile (460 mg, 6.96 mmol) with stirring at 0°C. The resulting solution was stirred for 30 min at 0°C. To this was added the intermediate from Step D (950 mg, 3.44 mmol) in DMF dropwise with stirring at 0°C. The resulting solution was stirred for 1 h at RT. Upon completion, the resulting solution was quenched with water, and extracted with EtOAc. The organic layer was dried over anhydr. Na_2SO_4 and conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using EtOAc:petroleum ether (0-20%). The racemic material was resolved using a chiral SFC (IA column) to afford isomers **I-8A** (faster eluting) and **I-8B** (slower eluting) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45-8.44 (1H, dd, J=0.9, 2.4 Hz), 7.57-7.47 (2H, m), 5.17 (1H, s), 4.29-4.19 (2H, m), 2.00 (3H, s), 1.27-1.22 (3H, t, J=6.9 Hz).

Using a similar procedure for the preparation of Intermediate **8**, the following intermediates in Table **2** were prepared.

Table 2

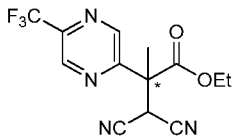


Int.	Chiral Resolution Column	R_3	R	m/z (M+H) or ^{1}H NMR
I-9A and **9B**	CHIRALPAK IA		Et	278.2
I-10A and **10B**	CHIRALPAK AD-H		Et	274.0

Int.	Chiral Resolution Column	R_3	R	m/z (M+H) or ^{1}H NMR
I-11A and **11B**	CHIRALPAK AD		Me	^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44-7.42 (3H, m), 7.38-7.36 (2H, m), 4.50 (1H, s), 3.80 (3H, s), 2.00 (3H, s).
I-12A and **12B**	CHIRALCEL OJ		Et	259 $[M - 1]^-$
I-13A and **13B**	CHIRALPAK IA		Et	312.0
I-14A and **14B**	CHIRALPAK IA		Et	258
I-15A and **15B**	CHIRALPAK AS		Et	269.1
I-16A and **16B**	PHENO LUX CELLULOSE-2		Me	247.1

INTERMEDIATE **17**, **17A** and **17B** and the S and R isomers thereof

Ethyl 3,3-dicyano-2-methyl-2-(5-(trifluoromethyl)pyrimidin-2-yl)



Step A-Diethyl 2-(5-iodopyrazin-2-yl)malonate: To a flask was added 2-bromo-5-iodopyrazine (3.0 g, 10.53 mmol), diethyl malonate (3.5 g, 22.11 mmol), potassium carbonate (3.0 g, 21.59 mmol), and DMSO (20 mL). The resulting mixture was stirred for 16 h at 80°C, then cooled to RT and quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (10-20%) to afford the title compound.

Step B- Diethyl 2-(5-(trifluoromethyl)pyrazin-2-yl)malonate: To a flask, under an inert atmosphere of nitrogen, was added copper(I) iodide (6.15 g, 32.3 mmol), potassium fluoride (1.75 g, 30.1 mmol) (dried *in vacuo* at 200°C for 30 min), trimethyl(trifluoromethyl)silane

(3.45 g, 24.3 mmol), and *N*-methyl-2-pyrrolidinone (80 mL). The mixture was heated to 50°C over 30 min and stirred for 5 min before diethyl 2-(5-iodopyrazin-2-yl)malonate (7.3 g, 14.0 mmol) in *N*-methyl-2-pyrrolidinone (10 mL) was added. The resulting mixture was stirred for 6 h at 50°C. The reaction mixture was cooled to RT and quenched by the addition of NH_4OH (10%). The mixture was extracted with EtOAc (3X). The organic layer was washed with NH_4OH (10%) and brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-20%) to afford the title compound.

Step C- Synthesis of ethyl 2-(5-(trifluoromethyl)pyrazin-2-yl)acetate: To a flask, under an inert atmosphere of nitrogen, was added diethyl 2-(5-(trifluoromethyl)pyrazin-2-yl)malonate (3.8 g, 12.4 mmol), dimethyl sulfoxide (40 mL), water (0.34 mL, 18.6 mmol), and sodium chloride (1.09 mL, 18.6 mmol). The resulting mixture was stirred at 150°C for 1 h, then allowed to cool down to RT. The resulting mixture was diluted with EtOAc, the organic layer was washed with brine (2X), dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-20%). The crude product was applied onto a C18 column with water:acetonitrile (with 0.05% ammonium bicarbonate) (30-70%). The residue was extracted with EtOAc (3X). The organic layer was dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*, to afford the title compound.

Step D- Ethyl 2-(5-(trifluoromethyl)pyrazin-2-yl)propanoate: To a flask, under an inert atmosphere of nitrogen, was added ethyl 2-(5-(trifluoromethyl)pyrazin-2-yl)acetate (700 mg, 2.60 mmol) and THF (14 mL). The resulting mixture was cooled to 0°C, and bis(trimethylsilyl)amide (2.86 mL, 2.86 mmol) was added dropwise. The resulting mixture was stirred for 1 h at 0°C before MeI (0.16 mL, 2.60 mmol) was added dropwise. The resulting mixture was stirred for 1 h at 0°C then 3 h at RT. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-10%) to afford the title compound.

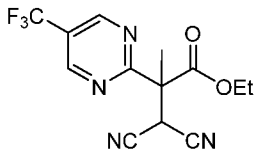
Step E- Ethyl 2-bromo-2-(5-(trifluoromethyl)pyrazin-2-yl)propanoate: To a flask, under an inert atmosphere of nitrogen, was added ethyl 2-(5-(trifluoromethyl)pyrazin-2-yl)propanoate (280 mg, 0.98 mmol) and THF (8 mL). The resulting mixture was cooled to 0°C and bis(trimethylsilyl)amide (1.47 mL, 1.47 mmol, 1.5 equiv) was added dropwise. The resulting mixture was stirred for 1 h at 0°C before 1-bromopyrrolidine-2,5-dione (262 mg,

1.47 mmol) in THF (4 mL) RT and stirred for 1 h. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-10%) to afford the title compound.

Step F- Ethyl 3,3-dicyano-2-methyl-2-(5-(trifluoromethyl)pyrazin-2-yl)propanoate: To a flask, under an inert atmosphere of nitrogen, was added ethyl 2-bromo-2-(5-(trifluoromethyl)pyrazin-2-yl)propanoate (270 mg, 0.83 mmol), malononitrile (109 mg, 1.65 mmol), potassium carbonate (114 mg, 0.83 mmol) and DMSO (13 mL). The resulting mixture was stirred for 2 h at RT. The reaction mixture was quenched by the addition of water, extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-20%) to afford the racemic title compound **I-19**. The racemic material was resolved using Chiral-Prep-HPLC (Chiralpak IA) to afford isomers **I-17A** (faster eluting) and **I-17B** (slower eluting). ^1H NMR (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 9.23 (s, 1H), 5.88 (s, 1H), 4.25 (q, J=7.2 Hz, 2H), 1.96 (s, 3H), 1.18 (t, J=7.2 Hz, 3H); m/z=311 $[M-1]^-$.

INTERMEDIATE **18**

Ethyl 3,3-dicyano-2-methyl-2-(5-(trifluoromethyl)pyrimidin-2-yl)propanoate



Step A-*N*-(3-(dimethylamino)-2-(trifluoromethyl)allylidene)-*N*-methylmethanaminium hexafluorophosphate(V): In a flask containing 3,3,3-trifluoropropanoic acid (7.4 g, 57.8 mmol) and DMF (37 mL) at 70°C phosphoryl trichloride (26.6 g, 173.4 mmol) was added dropwise over 1h. The resulting mixture was stirred at 70°C for 1.5 h before the mixture was cooled to RT. The reaction mixture and a 5 N solution of NaOH (100 mL) were added concurrently into a mixture of 60% hydrogen hexafluorophosphate(V) (15.5 g, 63.7 mmol), a 5 N NaOH (18.5 mL) and water (67 mL) at a temperature below 10°C. The resulting mixture was aged for 1 h, filtered and washed with water. The filter cake was dried *in vacuo* below 40°C to afford the title compound.

Step B- Ethyl 3-ethoxy-3-imino-2-methylpropanoate hydrochloride: In a flask containing ethyl 2-cyanopropanoate (10 g, 79 mmol) and EtOH (100 mL) at 0°C, was bubbled HCl (gas) for 30 min and the mixture was stirred at 0°C for 4 h. The reaction mixture was conc. *in*

vacuo at RT to afford the title compound.

Step C- Ethyl 3-amino-3-imino-2-methylpropanoate: In a flask containing ethyl 3-ethoxy-3-imino-2-methylpropanoate hydrochloride (7.0 g, 33.4 mmol) and EtOH (35 mL) at 0°C, was added a solution of ammonia in EtOH (22 mL, 3.34 N). The resulting mixture was stirred at 0°C for 3 h then stirred for 16 h at RT. The reaction mixture was conc. *in vacuo* at RT to afford the title compound.

Step D- Ethyl 2-(5-(trifluoromethyl)pyrimidin-2-yl)propanoate: In a flask containing ethyl 3-amino-3-imino-2-methylpropanoate (2.0 g, 13.87 mmol), *N*-(3-(dimethylamino)-2-(trifluoromethyl)allylidene)-*N*-methylmethanaminium hexafluorophosphate(V) (4.7 g, 13.8 mmol) and acetonitrile (40 mL) was added triethylamine (2.81 g, 27.7 mmol). The resulting mixture was stirred at RT for 16 h. The reaction mixture was diluted with EtOAc, washed with brine (2X), the organic layer was dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-10%) to afford the title compound.

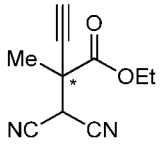
Step E- Ethyl 2-bromo-2-(5-(trifluoromethyl)pyrimidin-2-yl)propanoate: A flask, under an inert atmosphere of nitrogen, was charged with ethyl 2-(5-(trifluoromethyl)pyrimidin-2-yl)propanoate (1.0 g, 4.03 mmol) and THF (20 mL). To this was added lithium bis(trimethylsilyl)amide (4.83 mL, 4.83 mmol) dropwise at 0°C. The resulting mixture was stirred at RT for 30 min. Then the mixture was cooled to 0°C and a solution of 1-bromopyrrolidine-2,5-dione (1.0 g, 5.64 mmol) in THF (10 mL) was added in one portion. The resulting mixture was stirred at RT for 1 h. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine (2X), dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-10%) to afford the title compound.

Step F- Ethyl 3,3-dicyano-2-methyl-2-(5-(trifluoromethyl)pyrimidin-2-yl)propanoate: To a flask containing ethyl 2-bromo-2-(5-(trifluoromethyl)pyrimidin-2-yl)propanoate (500 mg, 1.53 mmol), malononitrile (202 mg, 3.06 mmol), and DMSO (15 mL) was added potassium carbonate (215 mg, 1.56 mmol) in portions at RT during 1 h. The resulting mixture was stirred for 2 h at RT then quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-20%) to afford the title compound.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.07 (s, 2H), 5.02 (s, 1H), 4.31 (q, *J*=7.2 Hz, 2H), 2.08 (s, 3H), 1.28 (d, *J*=7.2 Hz, 3H); *m/z* =311 $[M - 1]^-$.

INTERMEDIATE **19**, **19A** and **19B**

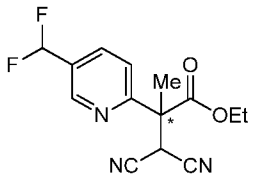
Ethyl-2-(dicyanomethyl))-2-methylbut-3-ynoate and the S and R isomers thereof



To a flask containing anhydr. LiCl (25.8 mg, 0.609 mmol) in THF (1 mL), was added a solution of ethynylmagnesium bromide (1.3 mL, 0.64 mmol, 0.5M in THF). The reaction was stirred at RT for 0.5 h. The resulting solution was then quickly added dropwise via syringe to a solution of ethyl 3,3-dicyano-2-methylprop-2-enoate (prepared according to Hagiware et. al. Synthesis **1974**, *9*, 669) (0.609 mL, 0.609 mmol, 1M solution in benzene) in THF (22.5 mL) at –10°C. The reaction was stirred for 10 min then quenched with sat. aq. NH_4Cl and diluted with water and EtOAc. The layers were separated and the organic layer was dried over anhydr. Na_2SO_4, and conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using an EtOAc:hexanes gradient to afford the racemic title product **I-19**. The racemic material was resolved using chiral SFC (OJ-H column) to afford isomers **I-19A** (faster eluting) and **I-19B** (slower eluting). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.34 (2H, q, *J*=7.2 Hz), 4.31 (1H, s), 2.66 (1H, s), 1.80 (3H, s), 1.35 (3H, t, *J*=7.1 Hz).

INTERMEDIATE **20**, **20A** and **20B**

Ethyl 3,3-dicyano-2-(5-(difluoromethyl)pyridin-2-yl)-2-methylpropanoate and the S and R isomers thereof

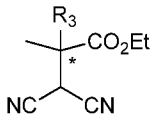


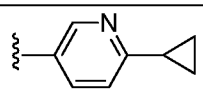
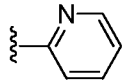
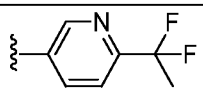
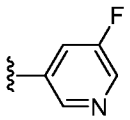
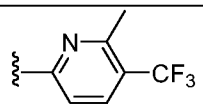
To a 3-necked flask, under an inert atmosphere of nitrogen, containing a solution of *n*-butyllithium (1.5 mL, 3.65 mmol) in toluene (25 mL), was added 2-bromo-5-(difluoromethyl)pyridine (760 mg, 3.65 mmol) in toluene (5 mL) dropwise at -78°C. After 30 min, ethyl 3,3-dicyano-2-methylprop-2-enoate (prepared according to Hagiware et. al. Synthesis **1974**, *9*, 669) (500 mg, 3.05 mmol) in THF (2 mL) was added in one portion at -78 °C. The reaction was stirred for 1 h at -78°C, then quenched with sat. aq. NH_4Cl and diluted with water and EtOAc. The layers were separated and the organic layer was dried over anhydr. Na_2SO_4, and conc. *in vacuo* to dryness. The residue was purified by silica gel

chromatography using an EtOAc/petroleum ether (10%-15%) gradient. The crude product was purified with C18 column with acetonitrile/water with 0.05% ammonium bicarbonate (30%-70%) to afford the racemic title product **20**. The racemic material was resolved using Chiral-Prep-HPLC (Chiralpak IA) to afford isomers **I-20A** (faster eluting) and **I-20B** (slower eluting). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.73 (s, 1H), 7.95 (d, *J*=8.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 6.74 (t, *J*=55.5 Hz, 1H), 5.21 (s, 1H), 4.24 (q, *J*=7.2 Hz, 2H), 2.03 (s, 3H), 1.25 (t, *J*=7.2 Hz, 3H); *m/z* =292 $[M-1]^-$.

Using a similar procedure described for the synthesis of intermediate **19** and **20**, the following compounds in Table **3** were prepared using either commercial starting reagents or from compounds known in the literature.

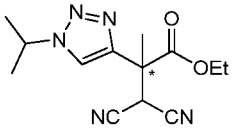
Table 3



Int.	Chiral Resolution Column	R_3	m/z (M+H)
I-21A and **21B**	CHIRALPAK AS		284
I-22A and **22B**	CHIRALPAK IA		243.9
I-23	Racemic		308
I-24A and **24B**	CHIRALPAK AD		262.2
I-25	Racemic		326.9

INTERMEDIATE **26**, **26A** and **26B**

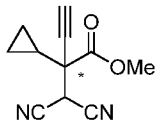
Ethyl 3,3-dicyano-2-(1-isopropyl-1H-1,2,3-triazol-4-yl)-2-methylpropanoate and the S and R isomers thereof



A flask, under an inert atmosphere of nitrogen, was charged with ethyl-2-(dicyanomethyl))-2-methylbut-3-ynoate **I-19** (2 g, 10.32 mmol), bromotris(triphenylphosphine)copper(I) (0.192 g, 0.206 mmol) and DMSO (20 mL). To this was added 2-azidopropane (1.27 mL, 12.3 mmol) and the reaction was stirred at 50°C for 18 h. The reaction mixture was diluted with EtOAc, and quenched by the addition of water. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine (2X), dried over anhydr. magnesium sulfate, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:hexane (0-50%) to afford the racemic title compound **I-26**. The racemic material was resolved using chiral SFC (CHIRALCEL ID) to afford isomers **I-26A** (faster eluting) and **I-26B** (slower eluting). ^{1}H NMR ($CHCl_3$, 400 MHz): δ 7.66 (1 H, s), 5.01 (1 H, s), 4.88-4.83 (1 H, m), 4.36-4.30 (2 H, m), 1.99 (3 H, s), 1.64 (6 H, d, J = 6.8 Hz), 1.34 (3 H, t, J = 7.1 Hz),). *m/z* =276.2 [M+H].

INTERMEDIATE **27**, **27A** and **27B** and the S and R isomers thereof

Methyl 2-cyclopropyl-2-(dicyanomethyl)but-3-ynoate



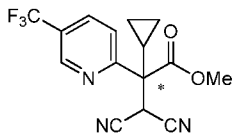
Step A- Methyl 3,3-dicyano-2-cyclopropylacrylate: A mixture of methyl 2-cyclopropyl-2-oxoacetate (prepared similarly to: Russian Chemical Bulletin **2007**, *56*, 1515-1521) (800 mg, 6.24 mmol) and malononitrile (516 mg, 7.80 mmol) was stirred for 2-3 min. A solution of beta-alanine (27.8 mg, 0.312 mmol) in water (540 µl) was added in small portions over ~5 min period. The reaction was cooled in an ice-bath and EtOH (350 µl) was added. The reaction was stirred at RT for 24 h. The reaction was diluted with water and extracted with ethyl ether. The ether layer was back extracted with water (2X). The organic layer was further diluted with EtOAc and dried over anhydr. Na_2SO_4. The combined organic layers were purified by silica gel column chromatography with EtOAc:hexanes (0-30%) to give the title compound.

Step B- Methyl 2-cyclopropyl-2-(dicyanomethyl)but-3-ynoate: To a flask containing anhydr. LiCl (144 mg, 3.41 mmol) in THF (2 mL) was added a solution of ethynylmagnesium bromide (6.8 mL, 3.41 mmol, 0.5 M in THF). The reaction was stirred at RT for 30 min. The resulting solution was cooled to –30°C. A solution of Methyl 3,3-dicyano-2-cyclopropylacrylate (0.500 g, 2.84 mmol) in THF (5 mL) was added. The reaction was stirred for 1 h in then raised to RT slowly. The mixture was quenched with sat. aq. NH_4Cl, and then diluted with water and EtOAc. The layers were separated and the organic

layer was dried over anhydr. Na_2SO_4 and conc. *in vacuo*. Purification by silica gel column chromatography with EtOAc:hexanes (0-30%) gave the racemic title compound **I-27**. The racemic material was resolved using chiral SFC (CHIRALCEL OJ-H) to afford isomers **I-27A** (faster eluting) and **I-27B** (slower eluting). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.41 (1 H, s), 3.93 (3 H, s), 2.63 (1 H, s), 1.31-1.24 (1 H, m), 1.03-0.96 (1 H, m), 0.92-0.79 (2 H, m), 0.77-0.67 (1 H, m).

INTERMEDIATE **28**, **28A** and **28B** and the S and R isomers thereof

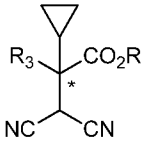
Methyl 3,3-dicyano-2-cyclopropyl-2-(5-(trifluoromethyl)pyridin-2-yl)propanoate

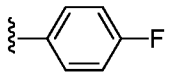
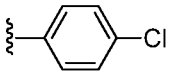
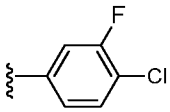
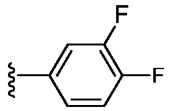
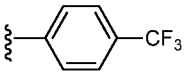
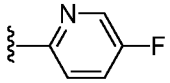
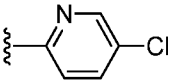
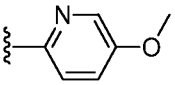
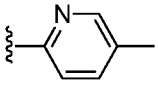
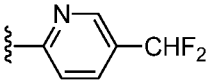
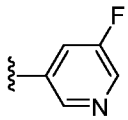
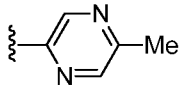
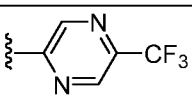


To a flask, under an inert atmosphere of nitrogen, was added toluene (300 mL) and *n*-butyl-lithium (14.8 mL, 36.9 mmol, 2.5M in hexane). 2-Bromo-5-(trifluoromethyl)pyridine (8.34 g, 36.9 mmol) in toluene (15 mL) was added dropwise with stirring at –78 °C. The resulting mixture was stirred for 45 min at –78 °C. To this was added Methyl 3,3-dicyano-2-cyclopropylacrylate (5 g, 28 mmol) in THF (20 mL). The resulting mixture was stirred for 0.5 h at –78°C. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-30%). The major component was further purified by RP-HPLC with acetonitrile:water (0.3% ammonium bicarbonate) to afford the racemic title compound **I-28**. The racemic material was resolved using chiral SFC (CHIRALPAK AD-H) to afford isomers **I-28A** (faster eluting) and **I-28B** (slower eluting). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.05 (dd, J=1.8, 8.4 Hz, 1H), 7.95 (d, J=8.4 Hz, 1H), 5.06 (s, 1H), 3.78 (s, 3H), 1.65-1.55 (m, 1H), 1.08-0.84 (m, 3H), 0.63-0.54 (m, 1H); m/z=322 $[M-1]^-$.

Using a similar procedure to that described in Intermediates **27** & **28**, the following compounds in Table **4** were prepared using either commercial starting reagents or from compounds known in the literature.

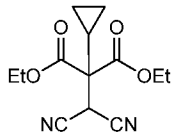
Table 4



Int.	Chiral Resolution Column	R_3	R	m/z (M+H)
I-29A and **29B**	CHIRALPAK AS		Et	285.0 $[M-1]^-$
I-30A and **30B**	CHIRALPAK IC		Et	301.2 $[M-1]^-$
I-31A and **21B**	CHIRALCEL OJ		Me	305 $[M-1]^-$
I-32A and **32B**	CHIRALCEL OJ		Me	289 $[M-1]^-$
I-33A and **33B**	CHIRALCEL OJ		Me	321 $[M-1]^-$
I-34A and **34B**	CHIRALCEL OJ		Me	274
I-35A and **35B**	CHIRALPAK AD		Me	290.1
I-36A and **36B**	CHIRALCEL OJ		Me	286
I-37	Racemic		Me	270.0
I-38	Racemic		Me	304 $[M-1]^-$
I-39A and **39B**	CHIRALPAK AD		Me	274.2
I-40	Racemic		Me	268.9 $[M-1]^-$
I-44	Racemic		Me	322.9 $[M-1]^-$

INTERMEDIATE **41**

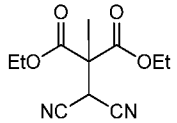
Diethyl 2-cyclopropyl-2-(dicyanomethyl)malonate



A THF (45.0 mL) solution of diethyl 2-(dicyanomethylene)malonate (prepared analogously to Sentman et. al. J. Org. Chem. **1982**, *47*, 4577) (4.50 mL, 4.50 mmol, 1M solution in benzene) was cooled to 0°C and cyclopropylmagnesium bromide (9.00 mL, 4.50 mmol) and lithium chloride (0.191 g, 4.50 mmol) were added. The reaction was stirred at 0 °C for 2 hours and then warmed to RT while stirring for an additional 2 h. The reaction was diluted with EtOAc and quenched with sat. NH_4Cl. The layers were separated and the organic layer was dried over anhydr. $MgSO_4$, filtered, and conc. *in vacuo* to dryness. Purification by silica gel column chromatography using a EtOAc:hexanes gradient afforded the title compound. ^1H NMR (500 MHz, $CDCl_3$): δ 4.41 (1H, s), 4.38-4.26 (4H, m), 1.52-1.45 (1H, m), 1.33 (6H, t, J = 7.1 Hz), 0.86-0.79 (2H, m), 0.71-0.66 (2H, m).

INTERMEDIATE **42**

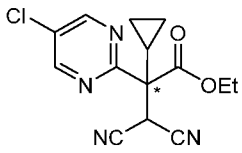
Diethyl 2-(dicyanomethyl)-2-methylmalonate



Using a similar procedure as described in intermediate **41**, the following intermediate was prepared. ^1H NMR (500 MHz, $CDCl_3$): δ 4.55 (1 H, s), 4.28-4.39 (4 H, m), 1.82 (3 H, s), 1.34 (6 H, t, J = 7.12 Hz).

INTERMEDIATE **43**, **43A** and **43B** and the S and R isomers thereof

Ethyl 2-(5-chloropyrimidin-2-yl)-3,3-dicyano-2-cyclopropylpropanoate



Step A- Ethyl 2-cyano-2-cyclopropylacetate: To a flask, under an inert atmosphere of nitrogen, was added diethyl carbonate (29.1 g, 247 mmol), sodium hydride (15.3 g, 382 mmol), and toluene (80 mL). To this was added 2-cyclopropylacetonitrile (10 g, 123 mmol) in toluene (40 mL) dropwise with stirring at reflux, over a period of 30 min. The resulting mixture was stirred for 2 h at reflux, then cooled to 0°C. To this was added acetic acid (40 mL) dropwise at 0 °C, followed by water (100 mL). The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* and distillation at reduced pressure (86~90°C at ~10 mmHg) to

afford the title compound.

Step B- Ethyl 2-cyclopropyl-3-imino-3-methoxypropanoate hydrochloride: In a flask containing ethyl 2-cyano-2-cyclopropylacetate (10.6 g, 69.2 mmol) and EtOH (100 mL) at 0°C was introduced gaseous hydrogen chloride for 4 h. The reaction mixture was conc. *in vacuo* at RT to afford the title compound.

Step C- Ethyl 3-amino-2-cyclopropyl-3-iminopropanoate: In a flask containing ethyl 2-cyclopropyl-3-ethoxy-3-iminopropanoate hydrochloride (15.6 g, 66.2 mmol) and EtOH (50 mL) at 0°C was added ammonia (70 mL, 206 mmol, 3 N). The resulting mixture was stirred for 3 h at 0°C, then stirred for 16 h at RT. The reaction mixture was conc. *in vacuo* at RT to afford the title compound.

Step D- Ethyl 2-(5-chloropyrimidin-2-yl)-2-cyclopropylacetate: To a flask, under an inert atmosphere of nitrogen, was added sodium (2.7 g, 117 mmol) and EtOH (200 mL), the resulting mixture was stirred for 1 h at RT. To this was added ethyl 3-amino-2-cyclopropyl-3-iminopropanoate (15.2 g, 62.5 mmol). The resulting mixture was stirred for 10 min at RT then cooled to 5°C. *N*-(2-chloro-3-(dimethylamino)allylidene)-*N*-methylmethanaminium hexafluorophosphate(V) (8.7 g, 28.4 mmol) (prepared according to Davis et. al. Org. Synth. **2003**, *80*, 200) was then added in portions over 45 min. The resulting mixture was stirred 2 h at RT. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo*. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-10%) to afford the title compound.

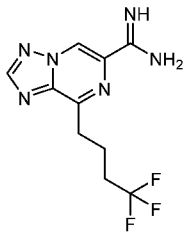
Step E- Ethyl 2-bromo-2-(5-chloropyrimidin-2-yl)-2-cyclopropylacetate: A flask, under an inert atmosphere of nitrogen, was charged with ethyl 2-(5-chloropyrimidin-2-yl)-2-cyclopropylacetate (300 mg, 1.25 mmol) and THF (20 mL) and cooled to 0°C. To this was added lithium bis(trimethylsilyl)amide (1.50 mL, 1.50 mmol, 1M in THF) dropwise with stirring at 0 °C. The resulting mixture was stirred for 1 h at 0°C then NBS (333 mg, 1.87 mmol) was added and the mixture was allowed to stir for 2 h at RT. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-10%) to afford the title compound.

Step F- Ethyl 2-(5-chloropyrimidin-2-yl)-3,3-dicyano-2-cyclopropylpropanoate: To a flask containing ethyl 2-bromo-2-(5-chloropyrimidin-2-yl)-2-cyclopropylacetate (250 mg, 0.78 mmol), malononitrile (258 mg, 3.91 mmol), and DMSO (10 mL) was added potassium

carbonate (216 mg, 1.57 mmol) in portions at RT. The resulting mixture was stirred for 16 h at RT. The reaction mixture was quenched by the addition of sat. aq. NH_4Cl. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (5-20%) to afford the racemic title compound **I-43**. The racemic material was resolved using Chiral-Prep-HPLC (CHIRALCEL OJ-H) to afford isomers **I-43A** (faster eluting) and **I-43B** (slower eluting). ^1H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 2H), 4.78 (s, 1H), 4.36 (q, *J*=7.2 Hz, 2H), 1.81-1.75 (m, 1H), 1.31 (t, *J*=7.2 Hz, 3H), 0.72-0.75 (m, 2H), 0.57-0.44 (m, 2H); *m/z* =305 $[M+1]^+$

INTERMEDIATE **A1**

8-(4,4,4-Trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carboximidamide



Step A- (4,4,4-Trifluorobutyl)zinc(II) bromide: Into a flask, under an inert atmosphere of nitrogen, was placed 1,1,1-trifluoro-4-iodobutane (6.7 g, 28 mmol), zinc metal (3.7 g, 56 mmol) and DMA (10 mL). This was followed by the dropwise addition of a solution of iodine (0.33 g, 1.3 mmol) in DMA (0.5 mL). The resulting mixture was stirred for 3 h at 80°C. The reaction was cooled and directly used in the next step.

Step B- 6-Bromo-8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine: Into a flask, under an inert atmosphere of nitrogen, was placed 6,8-dibromo-[1,2,4]triazolo[1,5-*a*]pyrazine (6.0 g, 22 mmol), $Pd(PPh_3)_2Cl_2$ (0.91 g, 1.3 mmol) and THF (80 mL). The resulting mixture was allowed to stir for 1 h at RT. The intermediate from Step A (11 mL, 28 mmol) was added and the resulting solution was stirred for 16 h at RT. The reaction was quenched by the addition of sat. aq. NH_4Cl. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue purified by silica gel chromatography with EtOAc:petroleum ether (0-20%) to afford the title compound.

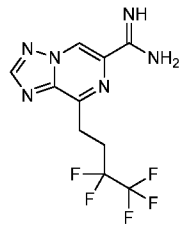
Step C- 8-(4,4,4-Trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carbonitrile: Into a flask, under an inert atmosphere of nitrogen, was placed the intermediate from Step B (2.3 g, 7.4 mmol), zinc cyanide (1.14 g, 9.67 mmol), dppf (0.83 g, 1.5 mmol), $Pd_2(dba)_3$ (0.77 g, 0.74 mmol), zinc metal (0.243 g, 3.72 mmol) and DMF (25 mL). The resulting mixture was

warmed at 120°C for 1 h. The reaction was cooled to RT and quenched by the addition of water and EtOAc. The precipitate was filtered through CELITE and the filtrate was extracted with EtOAc (3X). The organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (5-25%) to afford the title compound.

Step D- 8-(4,4,4-Trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carboximidamide: Into a flask, under an inert atmosphere of nitrogen, was placed NH_4Cl (3.60 g, 67.3 mmol) and toluene (60 mL). This was followed by the dropwise addition of trimethyl aluminum (25.4 mL, 50.8 mmol, 2.0 M in toluene) with stirring at 0°C. The reaction was slowly warmed to RT over 1.5 h. To this was added a solution of the intermediate from Step C (1.62 g, 6.35 mmol) in toluene (10 mL). The resulting mixture was stirring for an additional 2 h at 100°C. The reaction mixture was cooled to 0°C, then quenched by the addition of MeOH:CH_2Cl_2 (1:1). The solid was filtered through CELITE and washed with MeOH:DCM (1:1). The combined filtrate was conc. *in vacuo* to dryness. The pH value was adjusted to 10 with NaOH (1 N). The resulting solution was extracted with EtOAc (3X), and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness to afford the title compound. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.41 (1H, s), 8.50 (1H, s), 5.82 (3H, brs), 3.41 (2H, t, *J*=6.9 Hz), 2.34-2.21 (4H, m). *m/z*=309.0 (M+H).

INTERMEDIATE A**2**

8-(3,3,4,4,4-Pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carboximidamide



Step A- (3,3,4,4,4-Pentafluorobutyl)zinc(II) bromide: Into a flask, under an inert atmosphere of nitrogen, was placed 1,1,1,2,2-pentafluoro-4-iodobutane (21.7 g, 79 mmol), zinc metal (8.4 g, 128 mmol) and DMA (60 mL). This was followed by the dropwise addition of a solution of iodine (0.77 g, 3.05 mmol) in DMA (4 mL). The resulting mixture was stirred for 3 h at 80°C. The reaction was cooled and directly used in the next step.

Step B- 5-Chloro-3-(3,3,4,4,4-pentafluorobutyl)pyrazin-2-amine*:* In a flask, under an inert atmosphere of argon, was added 3,5-dichloropyrazin-2-amine (10.0 g, 61.0 mmol) and $Pd(PPh_3)_2Cl_2$ (4.3 g, 6.1 mmol). The resulting mixture was allowed to stir for 1 h at RT. The intermediate from Step A (65 mL, 79 mmol) was added and the resulting solution was

warmed at 45°C for 3 h. The reaction was then quenched by the addition of sat. aq. NH_4Cl. The resulting solution was extracted with EtOAc (3X), and the organic layers combined, washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified RP-HPLC with acetonitrile:water (0.2% TFA) to afford the title compound.

Step C- *N*'-(5-Chloro-3-(3,3,4,4,4-pentafluorobutyl)pyrazin-2-yl)-*N*,*N*-dimethylformimidamide: In a flask was placed the intermediate from Step B (3.0 g, 11 mmol), DMF-DMA (1.75 mL, 13.1 mmol) and EtOH (30 mL). The resulting mixture was warmed at 90°C for 2 h. The resulting solution was conc. *in vacuo* to afford the title compound, which was used without further purification.

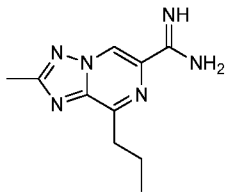
Step D- *N*-(5-Chloro-3-(3,3,4,4,4-pentafluorobutyl)pyrazin-2-yl)-*N*'-hydroxyformimidamide: In a flask was placed the intermediate from Step C (3.5 g, 11 mmol), hydroxylamine hydrochloride (1.1 g, 15 mmol) and MeOH (20 mL). The resulting mixture was stirred at RT for 18 h. The precipitate was filtered, and the filtrate was conc. *in vacuo*. The residue was purified by silica gel chromatography with MeOH:DCM (10%) to afford the title compound.

Step E- 6-Chloro-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine: In a flask, under an inert atmosphere of nitrogen, was placed the intermediate from Step D (2.5 g, 7.9 mmol), 2,2,2-trifluoroacetic anhydride (8.1 mL, 57 mmol) and toluene (12.5 mL). The resulting mixture was warmed at 90°C for 2 h. The reaction was conc. *in vacuo*. Then sat. aq. $NaHCO_3$ was added to adjust the pH to 8. The resulting mixture was extracted with EtOAc (3X). The organic layers were combined, washed with brine, dried over anhydr. Na_2SO_4, filtered, and conc. *in vacuo*. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (0-30%) to afford the title compound.

Step F- 8-(3,3,4,4,4-Pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carbonitrile: Into a flask, under an inert atmosphere of nitrogen, was placed the intermediate from Step E (1.0 g, 3.3 mmol), $Pd_2(dba)_3$ (0.34 g, 0.33 mmol), dppf (0.37 g, 0.67 mmol), zinc cyanide (0.51 g, 4.32 mmol), zinc metal (0.11 g, 1.7 mmol) and DMF (15 mL). The resulting mixture was warmed at 120°C for 5 h. The reaction was cooled to RT, quenched by the addition of brine and EtOAc and the precipitate was filtered. The filtrate was extracted with EtOAc (3X). The organic layers were combined, washed with brine, dried over anhydr. Na_2SO_4, filtered, and conc. *in vacuo*. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (0-20%) to afford the title compound.

Step G- 8-(3,3,4,4,4-Pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carboximidamide: In a flask, under an inert atmosphere of nitrogen, was placed NH_4Cl (1.46 g, 27.3 mmol) and toluene (20 mL). This was followed by the dropwise addition of trimethyl aluminum (14 mL, 2.0 M in toluene) at 0°C. The resulting mixture was stirred for 1 h at RT. To this was added the intermediate from Step F (750 mg, 2.58 mmol). The resulting mixture was warmed at 100°C for 4 h. The reaction mixture was cooled to 0°C, and quenched by the addition of MeOH:DCM (1:1). The solid was filtered through CELITE. The eluent was conc. *in vacuo*. The residue was dissolved in EtOAc. The pH value of the solution was adjusted to pH 10 with NaOH (1 N). The resulting solution was extracted with EtOAc (3X), and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness to afford the title compound. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.44 (1H, s), 8.80 (1H, s), 6.94 (2H, brs), 3.51 (2H, t, *J*=7.8 Hz), 3.08-2.90 (m, 2H). *m/z*=309.0 (M+H).

INTERMEDIATE A3



Step A-Propylzinc(II) iodide: Into a flask, under an inert atmosphere of nitrogen, was placed 1-iodopropane (10.9 g, 64.0 mmol), zinc metal (8.4 g, 128 mmol) and *N*,*N*-dimethylpropionamide (28 mL). This was followed by the dropwise addition of a solution of iodine (0.1 g, 0.43 mmol) in *N*,*N*-dimethylpropionamide (2 mL) at 0°C. The resulting mixture was stirred for 3 h at 80°C. The reaction was cooled and directly used in the next step.

Step B- 5-chloro-3-propylpyrazin-2-amine: In a flask, under an inert atmosphere of argon, was added 3,5-dichloropyrazin-2-amine (7.0 g, 42.7 mmol), bis(triphenylphosphine)palladium(II) dichloride (3.0 g, 4.27 mmol) and THF (240 mL). The resulting mixture was allowed to stir for 1 h at RT. The intermediate from Step A (30 mL, 64 mmol) was added and the resulting solution was warmed at 35°C for 2 days. The reaction was then quenched by the addition of brine. The resulting solution was extracted with EtOAc (3X) and the organic layers combined, washed with brine, dried over anhydr. Na_2SO_4, and filtered. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (5-20%) to afford the title compound.

Step C- *N*′-(5-chloro-3-propylpyrazin-2-yl)-*N*,*N*-dimethylacetimidamide: In a flask was placed 5-chloro-3-propylpyrazin-2-amine (6.0 g, 35.0 mmol), 1,1-dimethoxy-*N*,*N*-dimethylethanamine (5.6 g, 42.0 mmol) and ethanol (60 mL). The resulting mixture was

stirred for 3 h at 90°C. The ethanol was removed *in vacuo*. The residue was diluted with EtOAc, washed with brine, dried over anhydr. Na_2SO_4, filtered, and conc. *in vacuo*. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (5-20%) to afford the title compound.

Step D- *N*-(5-chloro-3-propylpyrazin-2-yl)-*N'*-hydroxyacetimidamide: Into a flask was placed *N'*-(5-chloro-3-propylpyrazin-2-yl)-*N*,*N*-dimethylacetimidamide (6.4 g, 26.6 mmol), MeOH (60 mL) and hydroxylamine hydrochloride (2.7 g, 38.3 mmol). The resulting mixture was stirred for 16 h at RT, then conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (5-30%) to afford the title compound.

Step E- 6-chloro-2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazine: Into a flask was placed *N'*-(5-chloro-3-propylpyrazin-2-yl)-*N*-hydroxyacetimidamide (6.0 g, 26.2 mmol), toluene (60 mL) and 2,2,2-trifluoroacetic anhydride (40.2 g, 192 mmol). The resulting mixture was stirred for 2 days at 90°C. The reaction was conc. *in vacuo*. Then sat. aq. Na_2HCO_3 was added to adjust the pH to 8. The resulting mixture was extracted with EtOAc (3X), and the organic layers combined, washed with brine, dried over anhydr. Na_2SO_4, and filtered. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (5-30%) to afford the title compound.

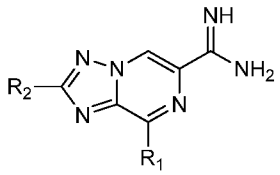
Step F- Synthesis of 2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carbonitrile: In a flask, under an inert atmosphere of argon, was added 6-chloro-2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazine (4.6 g, 21.8 mmol), tris(dibenzylideneacetone)dipalladium-chloroform adduct (2.3 g, 2.18 mmol), 1,1'-bis(diphenylphosphino)ferrocene (2.4 g, 4.37 mmol), zinc metal (0.7 g, 10.92 mmol), zinc cyanide (3.3 g, 28.40 mmol) and DMA (50 mL). The resulting mixture was stirred for 6 h at 120°C then cooled to RT and diluted with EtOAc (50 mL), MeOH (50 mL) and DCM (50 mL). The solid was filtered through CELITE. The combined filtrate was conc. *in vacuo* to dryness. The residue was dissolved in EtOAc, washed with brine, dried over anhydr. Na_2SO_4, and filtered. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (15-60%) to afford the title compound.

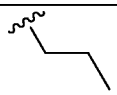
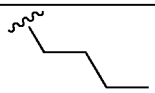
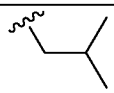
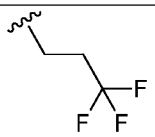
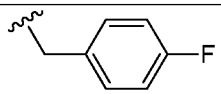
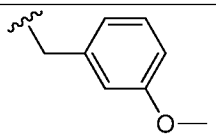
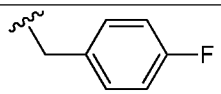
Steap G- 2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carboximidamide: In a flask, under an inert atmosphere of argon, was added NH_4Cl (11.0 g, 205 mmol) and toluene (200 mL), the resulting mixture was cooled to 0°C and trimethyl aluminum (78 mL, 155 mmol) was added dropwise. The resulting mixture was stirred for 1 h at RT before 2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carbonitrile (3.9 g, 19.38 mmol) was added. The resulting mixture was stirred for additional 3 h at 100°C then cooled to 0°C and quenched by

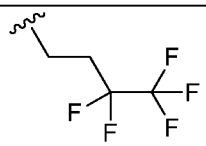
the addition of DCM:MeOH in a ratio of 1:1 (200 mL). The precipitate was removed by filtration through CELITE. The resulting filtrate was conc. *in vacuo*. The residue was dissolved in EtOAc. The pH value of the solution was adjusted to pH 10 with NaOH (1 N). The resulting solution was extracted with a mixture DCM:MeOH (10:1, 6X), and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and conc. *in vacuo* to dryness affording the title compound. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.27 (s, 1H), 6.90-6.72 (br, 3H), 3.15 (t, *J*=7.2 Hz, 2H), 2.57 (s, 3H), 1.94-1.84 (m, 2H), 0.98 (t, *J*=7.2 Hz, 3H); *m/z* =219.2 $[M+1]^+$.

Using a similar procedure to that described in Intermediate **A1, A2** and **A3**, the following compounds in Table **5** were prepared using either commercial starting reagents or from compounds known in the literature.

Table 5

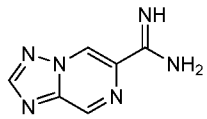


Int.	R_1	R_2	m/z (M+H)
I-A4		H	205
I-A5		H	219.2
I-A6		H	219.2
I-A7		H	259.0
I-A8		H	271.1
I-A9		H	283.1
I-A10		Me	285.1

Int.	R_1	R_2	m/z (M+H)
I-A11		Me	323.0

INTERMEDIATE **A12**

[1,2,4]Triazolo[1,5-*a*]pyrazine-6-carboximidamide

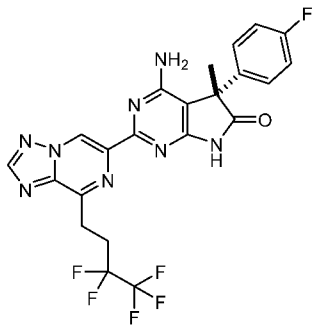


Step A-[1,2,4]triazolo[1,5-*a*]pyrazine-6-carbonitrile: Into a flask, under an inert atmosphere of nitrogen, was placed 6-bromo-[1,2,4]triazolo[1,5-*a*]pyrazine (1.0 g, 5.02 mmol), $Pd_2(dba)_3$ (460 mg, 0.50 mmol), dppf (557 mg, 1.00 mmol), zinc cyanide (649 mg, 5.53 mmol), zinc metal (164 mg, 2.51 mmol) and DMA (20 mL). The resulting mixture was warmed at 100°C for 4 h. The reaction was cooled to RT, quenched by the addition of brine and EtOAc and the precipitate was filtered. The filtrate was extracted with EtOAc (3X). The organic layers were combined, washed with brine, dried over anhydr. Na_2SO_4, filtered, and conc. *in vacuo*. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (0-50%) to afford the title compound.

Step-B-[1,2,4]Triazolo[1,5-*a*]pyrazine-6-carboximidamide: In a flask, under an inert atmosphere of nitrogen, was placed [1,2,4]triazolo[1,5-*a*]pyrazine-6-carbonitrile (440 mg, 3.03 mmol) and MeOH (10 mL). This was followed by the addition of NaOMe (30% in MeOH) (0.626 mL, 3.34 mmol) at RT. The resulting mixture was stirred for 2 h at RT. To this was added NH_4Cl (178 mg, 3.34 mmol) and AcOH (1.73 mL, 30.3 mmol). The resulting mixture was warmed at 70°C for 4 h. The reaction mixture was cooled to RT and was conc. *in vacuo* to dryness. The resulting solid was azeotroped with EtOAc and toluene to afford the title compound.

EXAMPLE **1A**

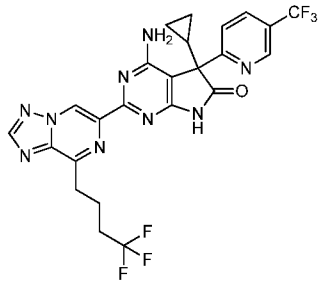
(S)-4-Amino-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one



Into a vial was placed **I-A2** (50 mg, 0.16 mmol), **I-1A** (44 mg, 0.17 mmol), potassium bicarbonate (33 mg, 0.32 mmol) and *t*-BuOH (2 mL). The resulting mixture was warmed at 70°C for 16 h. The reaction was cooled to RT and quenched by the addition of brine. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title product. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.26 (1H, brs), 9.44 (1H, s), 8.23 (1H, s), 7.30 (2H, dd, *J*=5.7, 9.0 Hz), 7.19 (2H, dd, *J*=9.0, 9.0 Hz), 6.66 (2H, brs), 3.55 (2H, t, *J*=7.8 Hz), 3.03-2.88 (2H, m), 1.80 (3H, s); *m/z*=523.4 (M+H).

EXAMPLE **2A**

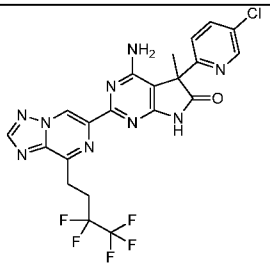
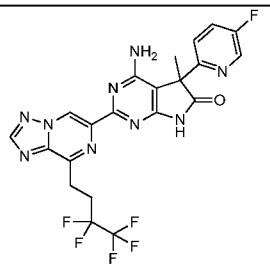
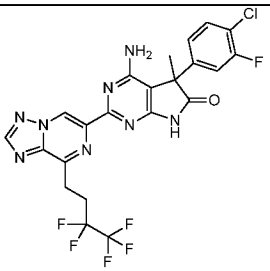
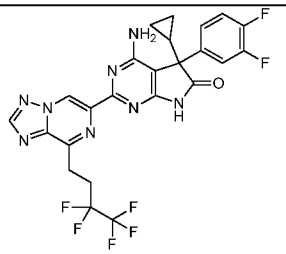
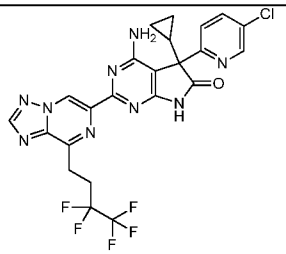
4-Amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one

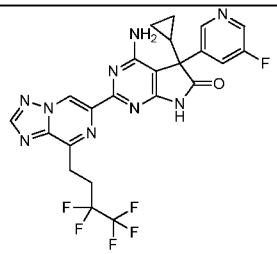
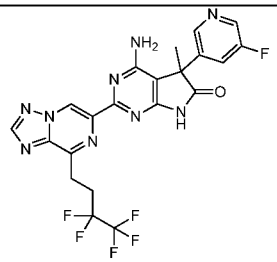
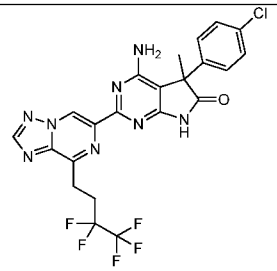
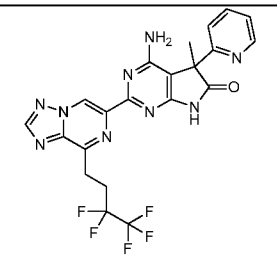
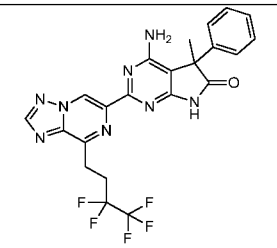
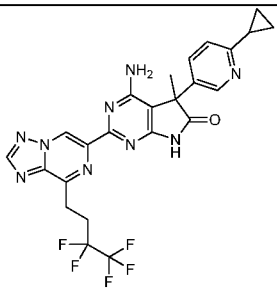


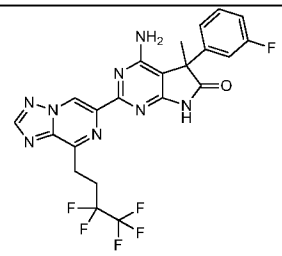
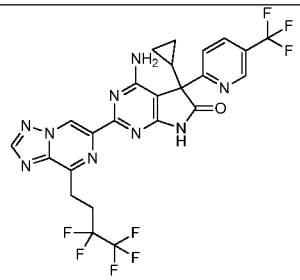
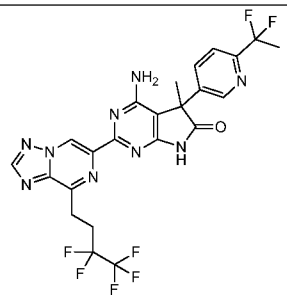
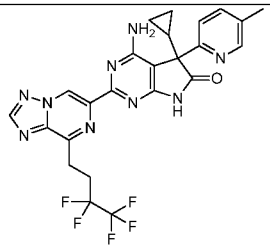
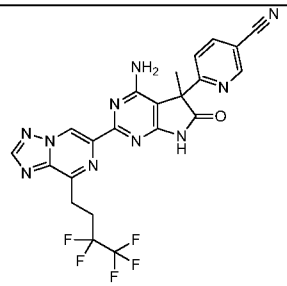
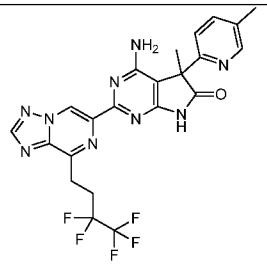
Into a vial was placed **I-A1** (50 mg, 0.18 mmol), **I-28A** (59 mg, 0.18 mmol), potassium bicarbonate (37 mg, 0.37 mmol), and *t*-BuOH (3 mL). The resulting mixture was warmed at 80°C for 16 h. The reaction was cooled to RT and conc. to remove any volatiles. The residue was purified by silica gel chromatography using MeOH:DCM (1-3%) to afford the title product. ^{1}H NMR (300 MHz, CD_3OD): δ 9.62 (1H, s), 8.92 (1H, s), 8.64 (1H, s), 8.22 (1H, dd, *J*=2.4, 8.4 Hz), 8.06 (1H, d, *J*=8.4 Hz), 3.42 (2H, t, *J*=7.8 Hz), 2.43-2.22 (4H, m), 2.03-1.98 (1H, m), 0.75-0.59 (4H, m); *m/z*=564.3 (M+H).

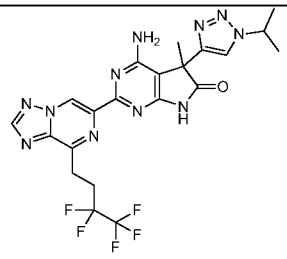
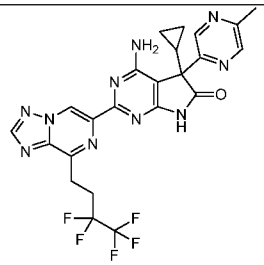
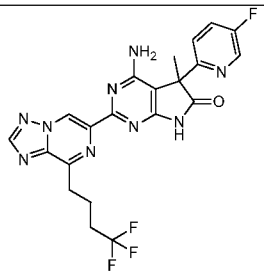
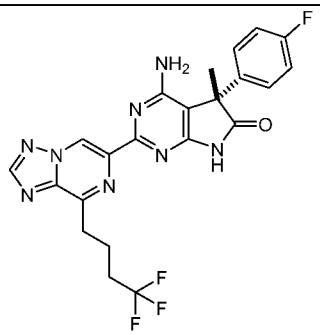
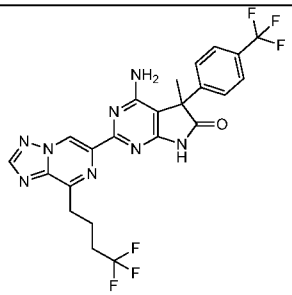
Using essentially the same procedures described in Examples **1** & **2**, the following compounds in **Table 6** were prepared.

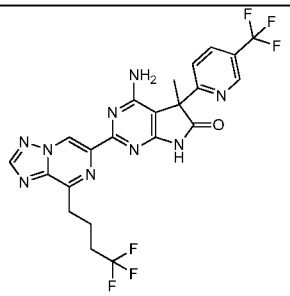
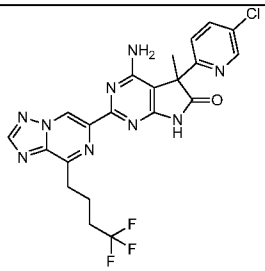
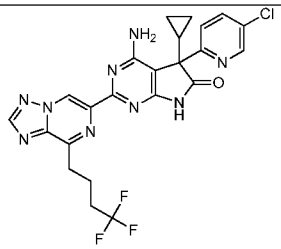
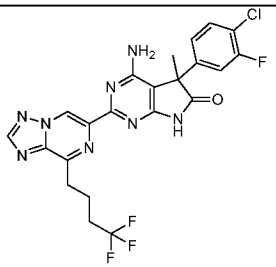
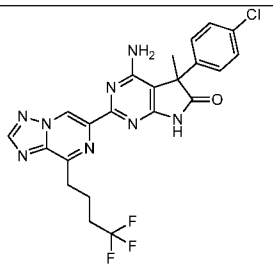
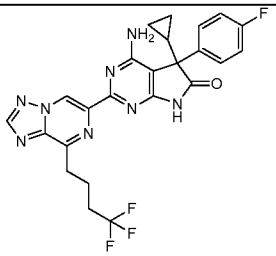
Table 6

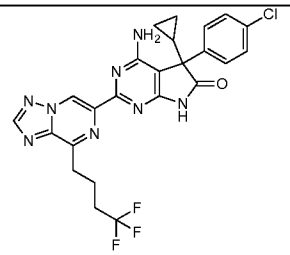
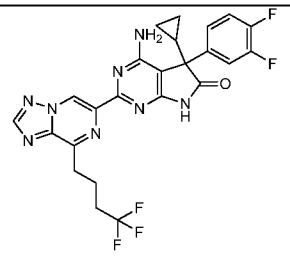
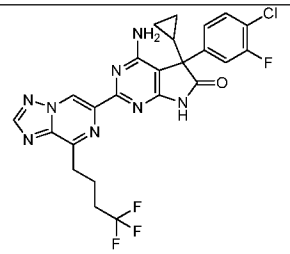
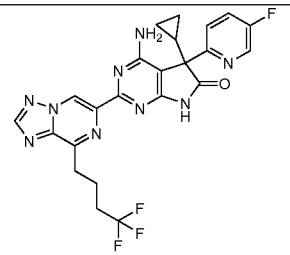
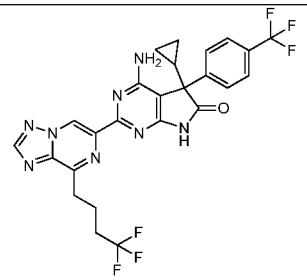
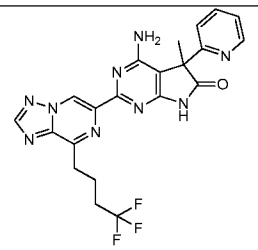
Ex	Structure	Name	MS (M+1)	Chiral starting material
3A		4-amino-5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	540.4	**I-9A**
4B		4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	524.2	**I-8B**
5B		4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	557.3	**I-4B**
6A		4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	567.1	**I-32A**
7A		4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	566.3	**I-35A**

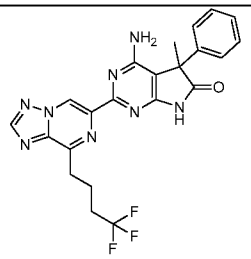
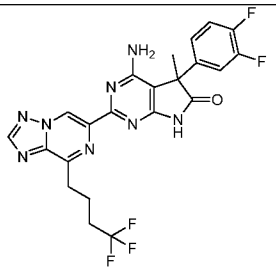
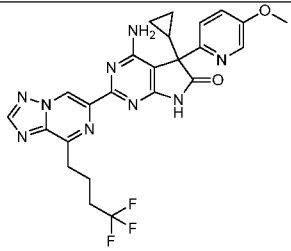
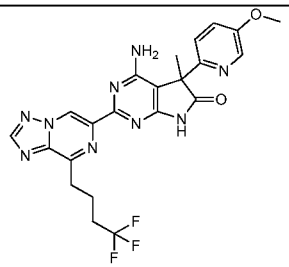
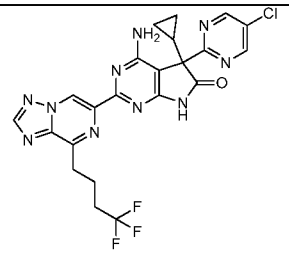
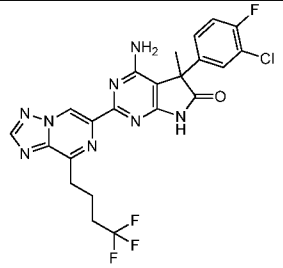
8B		4-amino-5-cyclopropyl-5-(5-fluoropyridin-3-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	550.1	**I-39B**
9A		4-amino-5-(5-fluoropyridin-3-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	524.1	**I-24A**
10A		4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	539.1	**I-2A**
11B		4-amino-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	506.3	**I-22B**
12B		4-amino-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-phenyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	505.0	**I-11B**
13B		4-amino-5-(6-cyclopropylpyridin-3-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	546.3	**I-21B**

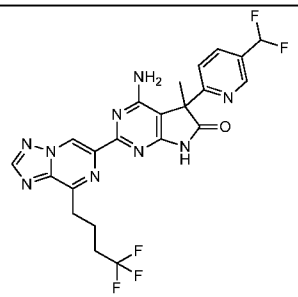
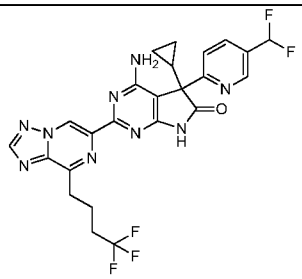
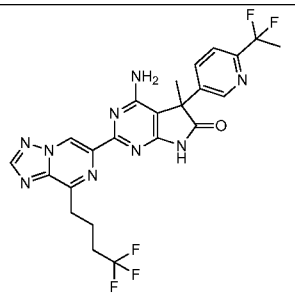
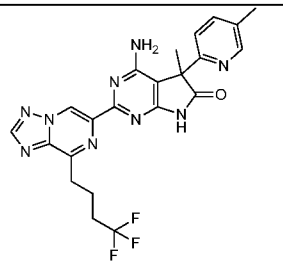
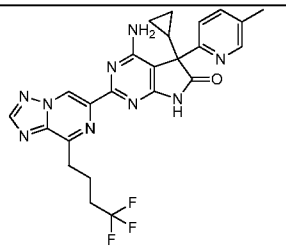
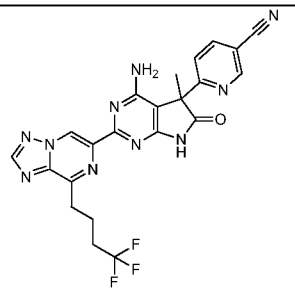
14B		4-amino-5-(3-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	523.2	**I-7B**
15A		4-amino-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	600.3	**I-28A**
16B		4-amino-5-(6-(1,1-difluoroethyl)pyridin-3-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	570.3	CHIRAL PAK IB (Rac-**I-23)**
17B		4-amino-5-cyclopropyl-5-(5-methylpyridin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	546.2	CHIRAL PAK IC (Rac-**I-37**)
18A		6-(4-amino-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)nicotinonitrile	531.3	**I-15A**
19B		4-amino-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	520.2	**I-14B**

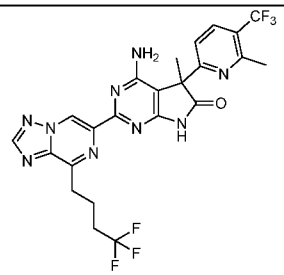
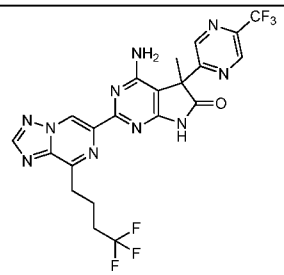
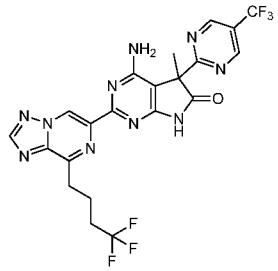
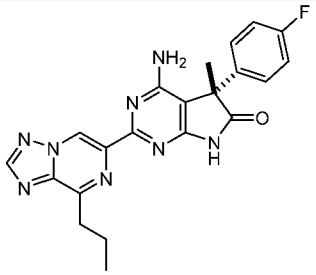
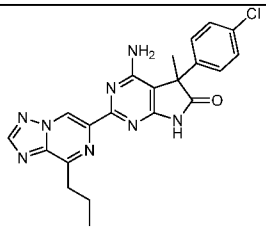
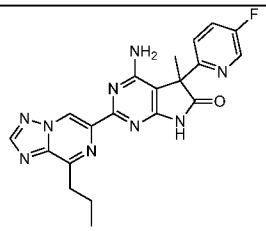
20A		4-amino-5-(1-isopropyl-1*H*-1,2,3-triazol-4-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	538.1	**I-26A**
21B		4-amino-5-cyclopropyl-5-(5-methylpyrazin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-d]pyrimidin-6(7*H*)-one (slow eluting)	547.3	CHIRAL PAK IB (rac **I-40)**
22B		4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	488.3	**I-8B**
23A		(S)-4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	487.1	**I-1A**
24B		4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	537.1	**I-3B**

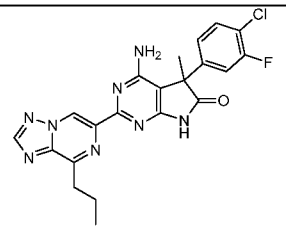
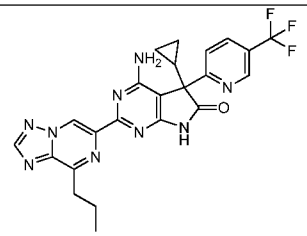
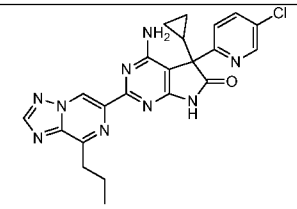
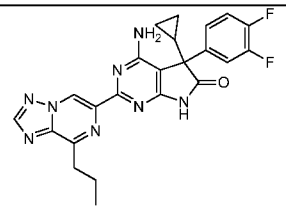
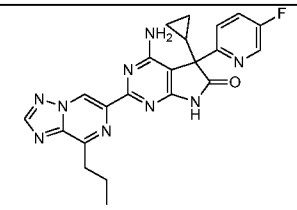
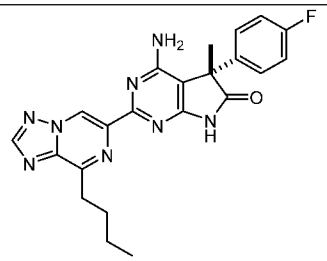
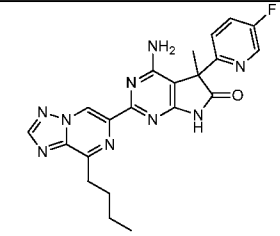
25B		4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	538.4	**I-13B**
26A		4-amino-5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	504.1	**I-9A**
27A		4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	530.3	**I-35A**
28B		4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	521.3	**I-4B**
29A		4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	503.2	**I-2A**
30B		4-amino-5-cyclopropyl-5-(4-fluorophenyl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	513.4	**I-29B**

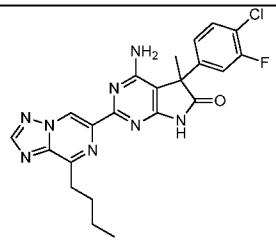
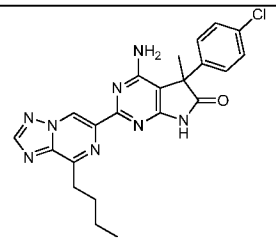
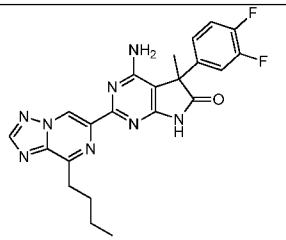
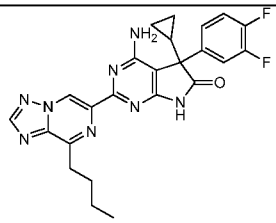
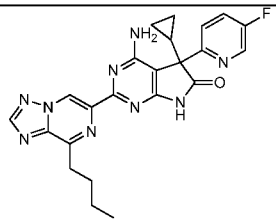
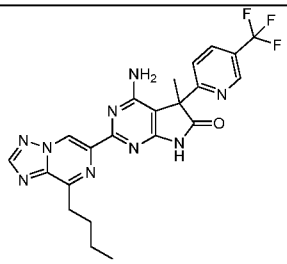
31B		4-amino-5-(4-chlorophenyl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	529.4	**I-30B**
32A		4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	531.3	**I-32A**
33A		4-amino-5-(4-chloro-3-fluorophenyl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	547.3	**I-31A**
34A		4-amino-5-cyclopropyl-5-(5-fluoropyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	514.1	**I-34A**
35A		4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	563.0	**I-33A**
36B		4-amino-5-methyl-5-(pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	470.2	**I-22B**

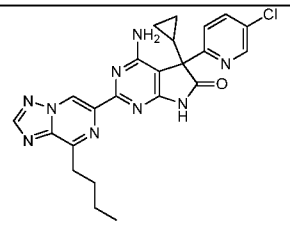
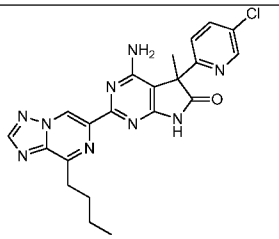
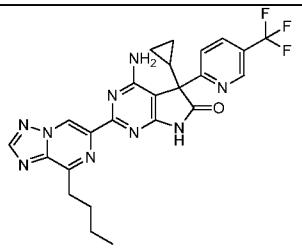
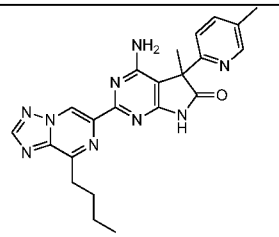
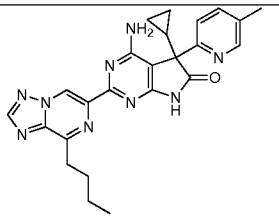
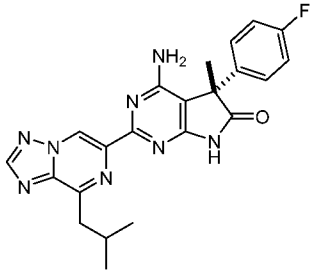
37B		4-amino-5-methyl-5-phenyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	469.3	**I-11B**
38B		4-amino-5-(3,4-difluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	505.1	**I-5B**
39A		4-amino-5-cyclopropyl-5-(5-methoxypyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	526.2	**I-36A**
40A		4-amino-5-(5-methoxypyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	500.3	**I-10A**
41A		4-amino-5-(5-chloropyrimidin-2-yl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	531.4	**I-43A**
42B		4-amino-5-(3-chloro-4-fluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	521.2	**I-6B**

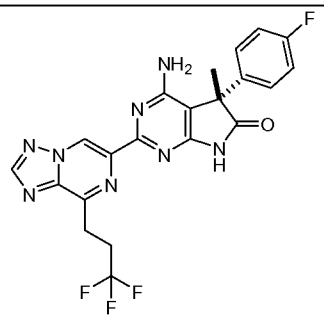
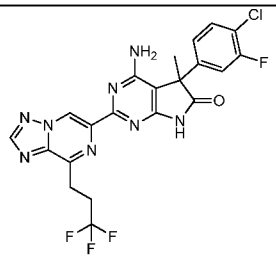
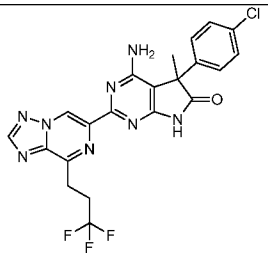
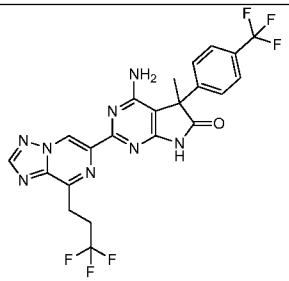
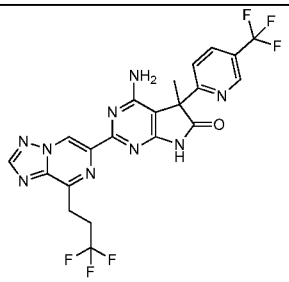
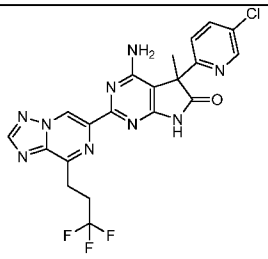
43B		4-amino-5-(5-(difluoromethyl)pyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	520.4	**I-20B**
44B		4-amino-5-cyclopropyl-5-(5-(difluoromethyl)pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	546.1	CHIRAL PAK IC (Rac-**I-38)**
45B		4-amino-5-(6-(1,1-difluoroethyl)pyridin-3-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	534.2	CHIRAL PAK IB (Rac- **I-23**)
46B		4-amino-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	484.1	**I-14B**
47B		4-amino-5-cyclopropyl-5-(5-methylpyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	510.4	CHIRAL PAK IC (Rac-**I-37**)
48A		6-(4-amino-5-methyl-6-oxo-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile	495.3	**I-15A**

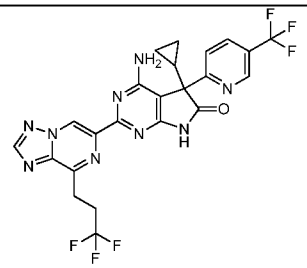
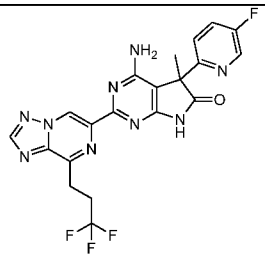
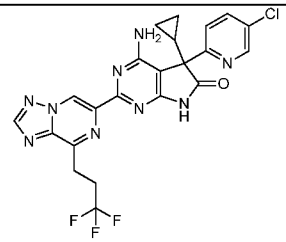
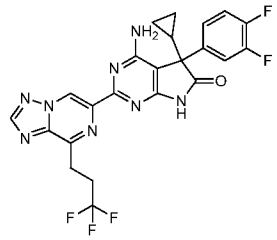
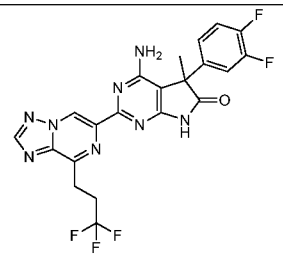
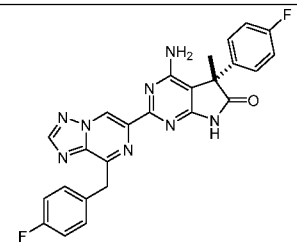
49B		4-amino-5-methyl-5-(6-methyl-5-(trifluoromethyl)pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7H)-one (slow eluting)	552.3	CHIRAL PAK-IA (Rac **I-25**)
50B		4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyrazin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	539.2	**I-17B**
51B		4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	539.2	LUX CELLULOSE-4 (**Rac I-18)**
52A		(S)-4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	419.3	**I-1A**
53A		4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	435.2	**I-2A**
54B		4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	420.2	**I-8B**

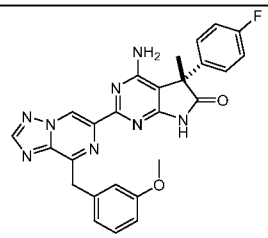
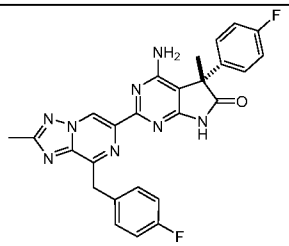
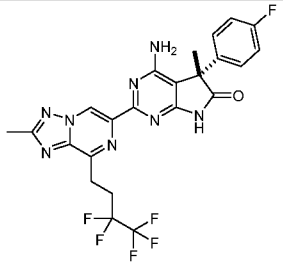
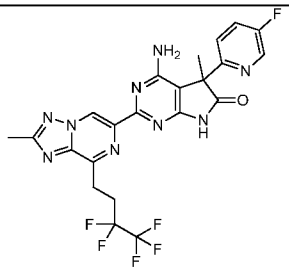
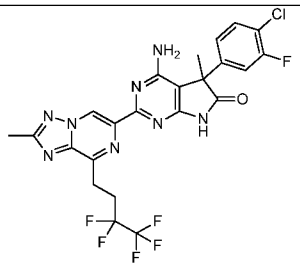
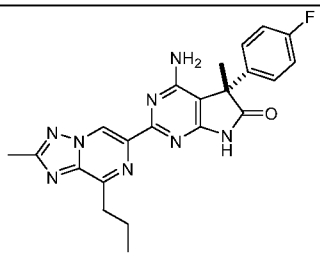
55B		5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	453.3	**I-4B**
56A		4-amino-5-cyclopropyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	496.3	**I-28A**
57A		4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	462.3	**I-35A**
58A		4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	463.2	**I-32A**
59A		4-amino-5-cyclopropyl-5-(5-fluoropyridin-2-yl)-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	446.1	**I-34A**
60A		(S)-4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	433.3	**I-1A**
61B		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-fluoropyridin-2-yl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	434.2	**I-8B**

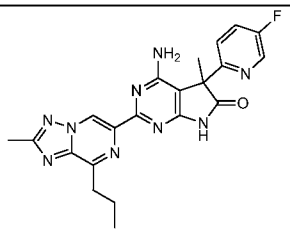
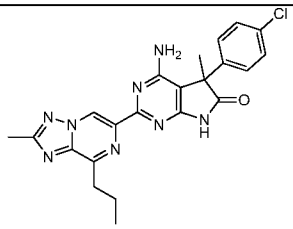
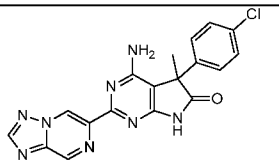
62B		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-chloro-3-fluorophenyl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	467.2	**I-4B**
63A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-chlorophenyl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	449.1	**I-2A**
64B		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(3,4-difluorophenyl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	451.1	**I-5B**
65A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-cyclopropyl-5-(3,4-difluorophenyl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	477.4	**I-32A**
66A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-cyclopropyl-5-(5-fluoropyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	460.3	**I-34A**
67B		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	484.4	**I-13B**

68A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-chloropyridin-2-yl)-5-cyclopropyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	476.3	**I-35A**
69A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-chloropyridin-2-yl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	450.2	**I-9A**
70A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-cyclopropyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	510.4	**I-28A**
71B		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-methyl-5-(5-methylpyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	430.3	**I-14B**
72B		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-cyclopropyl-5-(5-methylpyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	456.4	CHIRAL PAK IC (Rac-**I-37**)
73A		(S)-4-amino-5-(4-fluorophenyl)-2-(8-isobutyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	433.3	**I-1A**

74A		(S)-4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	473.3	**I-1A**
75B		4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	507.2	**I-4B**
76A		4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	489.1	**I-2A**
77B		4-amino-5-methyl-5-(4-(trifluoromethyl)phenyl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	523.2	**I-3B**
78B		4-amino-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	524.1	**I-13B**
79A		4-amino-5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	490.3	**I-9A**

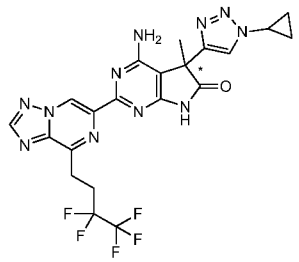
80A		4-amino-5-cyclopropyl-5-(5-(trifluoromethyl)pyridin-2-yl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	550.3	**I-28A**
81B		4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	474.3	**I-8B**
82A		4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	516.3	**I-35A**
83A		4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	517.0	**I-32A**
84B		4-amino-5-(3,4-difluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	491.0	**I-5B**
85B		(S)-4-amino-2-(8-(4-fluorobenzyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-fluorophenyl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	485.0	**I-16B**

86B		(S)-4-amino-5-(4-fluorophenyl)-2-(8-(3-methoxybenzyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	497.1	**I-16B**
87B		(S)-4-amino-2-(8-(4-fluorobenzyl)-2-methyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-fluorophenyl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	499.1	**I-16B**
88B		(S)-4-amino-5-(4-fluorophenyl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	537.1	**I-16B**
89B		4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	538.1	**I-8B**
90B		4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	571.3	**I-4B**
91A		(S)-4-amino-5-(4-fluorophenyl)-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	433.3	**I-1A**

92B		4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	434.3	**I-8B**
93A		4-amino-5-(4-chlorophenyl)-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	449.2	**I-2A**
94A		2-([1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-4-amino-5-(4-chlorophenyl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	393.0	**I-2A**

EXAMPLE **95B**

4-Amino-5-(1-cyclopropyl-1*H*-1,2,3-triazol-4-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5H-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one



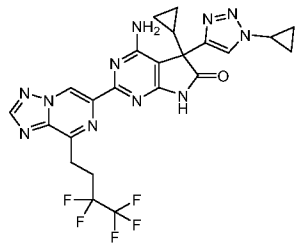
Step A-4-Amino-5-ethynyl-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one: Into a vial was placed **I-A2** (100 mg, 0.324 mmol), **I-19B** (67.9 mg, 0.357 mmol), potassium bicarbonate (39.0 mg, 0.389 mmol) and *t*-BuOH (5 mL). The resulting mixture was warmed at 70°C for 16 h. The reaction was cooled to RT and quenched by the addition of brine. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title product.

Step B- 4-amino-5-(1-cyclopropyl-1*H*-1,2,3-triazol-4-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5H-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one: To a flask containing potassium carbonate (306 mg, 2.21 mmol), copper(II) sulfate (21

mg, 0.13 mmol), cyclopropanamine (63 mg, 1.11 mmol) and MeOH (7.4 mL) at RT was added 1*H*-imidazole-1-sulfonyl azide hydrochloride (278 mg, 1.33 mmol) in water (3.7 mL). The resulting mixture was stirred for 16 h at 70°C. This was followed by the addition of sodium (*R*)-2-((*S*)-1,2-dihydroxyethyl)-4-hydroxy-5-oxo-2,5-dihydrofuran-3-olate (70 mg, 0.35 mmol) and the intermediate from Step A (100 mg, 0.22 mmol). The resulting mixture was stirred for 16 h at 70 °C. The reaction was then cooled to RT and quenched by the addition of ammonia (100 mL). The resulting solution was extracted with EtOAc (3X) and the organic layers combined, washed with ammonia then brine, dried over anhydr. Na_2SO_4, and filtered. The residue was purified by silica gel chromatography with EtOAc:petroleum ether (5-20%). The crude product was purified by Prep-HPLC, water:acetonitrile (with 0.05% ammonia) to afford the title compound. ^{1}H NMR (CD_3OD, 300 MHz): δ 9.61 (s, 1H), 8.61 (s, 1H), 7.95 (s, 1H), 3.92-3.85 (m, 1H), 3.65-3.59 (m, 2H), 3.04-2.86 (m, 2H), 1.81 (s, 3H), 1.25-1.19 (m, 4H); *m/z*=536.3 $[M+1]^+$.

EXAMPLE **96B**

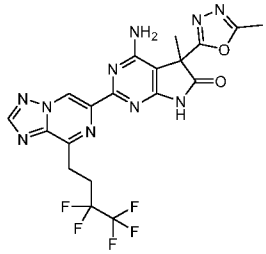
4-amino-5-cyclopropyl-5-(1-cyclopropyl-1*H*-1,2,3-triazol-4-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one



Using essentially the same procedures described in Example **95**, Example **96** was prepared, using intermediate **I-A2** and **I-27B** as starting material. *m/z*=562.2 $[M+1]^+$.

EXAMPLE **97A** and **97B**

4-Amino-5-methyl-5-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one



Step A- Ethyl 4-amino-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-d]pyrimidine-5-

carboxylate: Into a vial was placed **I-42** (312 mg, 1.31 mmol), **I-A2** (336 mg, 1.09 mmol), potassium bicarbonate (218 mg, 2.18 mmol) and *t*-BuOH (5 mL). The resulting mixture was warmed at 70°C for 16 h. The reaction was cooled to RT and quenched by the addition of brine. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title compound.

Step B-4-Amino-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbohydrazide: Into a flask was placed the intermediate from Step A (456 mg, 0.91 mmol), MeOH (8 mL) and hydrazine hydrate (228 mg, 4.56 mmol). The resulting mixture was warmed at 65°C for 4 h. The reaction was cooled to RT and conc. to remove any volatiles. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title compound.

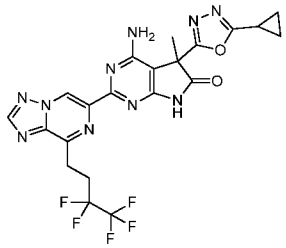
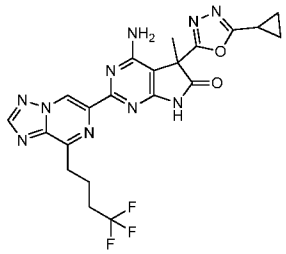
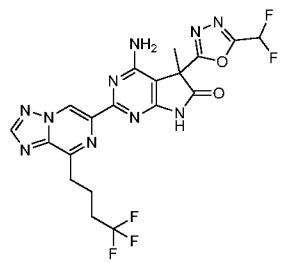
Step C-*N'*-Acetyl-4-amino-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo [1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidine-5-carbohydrazide: Into a vial was placed AcOH (18 µL, 0.32 mmol), DMF (6 mL), HATU (123 mg, 0.32 mmol) and Et_3N (0.086 mL, 0.62 mmol). After 20 min, the intermediate from Step B (150 mg, 0.31 mmol) was added. The resulting mixture was stirred at RT for 16 h. The reaction was quenched by the addition of brine, and the resulting solution was extracted with EtOAc (3X). The organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title compound.

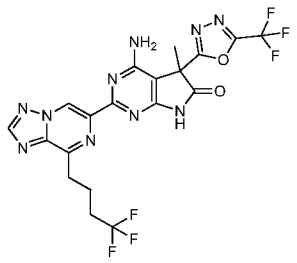
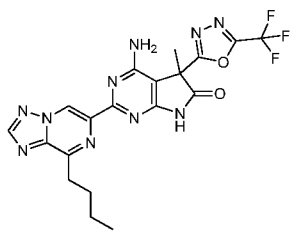
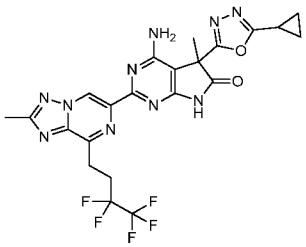
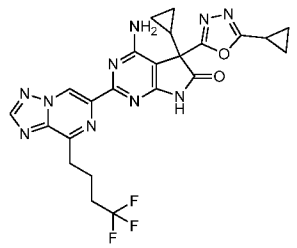
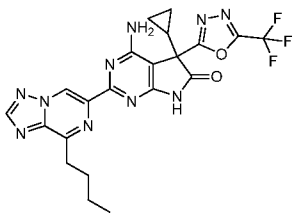
Step D-4-Amino-5-methyl-5-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one: Into a flask was placed the intermediate from Step C (150 mg, 0.28 mmol) and polyphosphoric acid (2 mL). The resulting mixture was warmed at 80°C for 16 h. The reaction was quenched by the addition of ice water. The pH of the resulting mixture was adjusted to pH 8 with sat. aq. $NaHCO_3$. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title compound as a racemate. The racemic material was resolved using chiral SFC (IA column) to afford isomers **Ex-97A** (faster eluting) and **Ex-97B** (slower eluting) of the title compound. ^1H NMR (400 MHz, CD_3OD): δ 9.68 (1H, s),

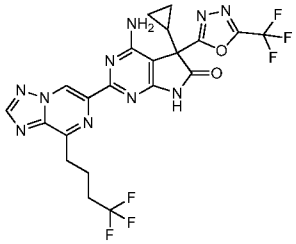
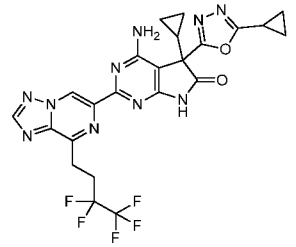
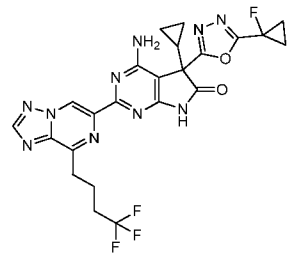
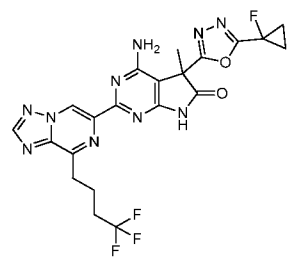
8.67 (1H, s), 3.70-3.65 (2H, m), 3.07-2.93 (2H, m), 2.57 (3H, s), 1.98 (3H, s); *m/z* = 511.1 (M+H).

Using essentially the same procedures described in Example **97**, the following compounds in **Table 7** were prepared.

Table 7

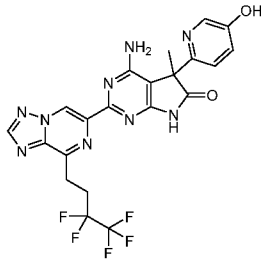
Ex.	Structure	Name	MS (M+1)	Chiral separation conditions
98B		4-amino-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (slow eluting)	537.5	CHIRALPAK IB
99A		4-amino-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	501.1	CHIRALPAK IB
100A		4-amino-5-(5-(difluoromethyl)-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	511.3	CHIRALPAK IA

101A		4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	529.3	CHIRALPAK IA
102A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-methyl-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	475.2	CHIRALPAK IA
103A		4-amino-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	551.0	CHIRALPAK IA
104A		4-amino-5-cyclopropyl-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	527.4	CHIRALPAK IA
105A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-cyclopropyl-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5*H*-	501.2	CHIRALPAK IA

		pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)		
106A		4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	555.1	CHIRALPAK IA
107A		4-amino-5-cyclopropyl-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (fast eluting)	563.3	CHIRALPAK IA
108A		4-amino-5-cyclopropyl-5-(5-(1-fluorocyclopropyl)-1,3,4-oxadiazol-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-d]pyrimidin-6(7H)-one (fast eluting)	545.2	CHIRALPAK IB
109A		4-amino-5-(5-(1-fluorocyclopropyl)-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-d]pyrimidin-6(7*H*)-one (fast eluting)	519.2	CHIRALPAK IB

EXAMPLE **110A**

4-Amino-5-(5-hydroxypyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one



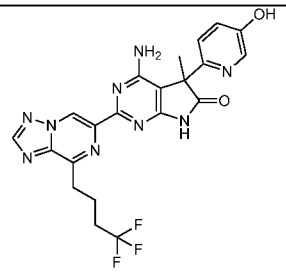
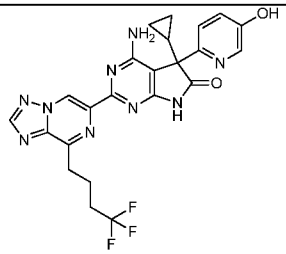
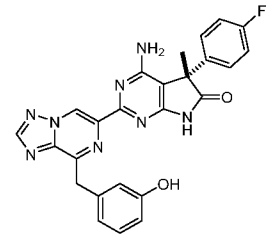
Step A-4-Amino-5-(5-methoxypyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one: Into a vial was placed **I-A2** (100 mg, 0.324 mmol), **I-10A** (98 mg, 0.357 mmol), potassium bicarbonate (39.0 mg, 0.389 mmol) and *t*-BuOH (8 mL). The resulting mixture was warmed at 70°C for 16 h. The reaction was cooled to RT and quenched by the addition of brine. The resulting solution was extracted with EtOAc (3X) and the organic layers were combined, dried over anhydr. Na_2SO_4, filtered and the filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel chromatography using MeOH:DCM (10%) to afford the title product.

Step B-4-Amino-5-(5-hydroxypyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: Into a vial, under an inert atmosphere of nitrogen, was placed intermediate from step A (90 mg, 0.16 mmol) and DCM (9 mL) and the reaction mixture was cooled to 0°C. To the mixture was added tribromoborane (0.9 mL, 9.52 mmol) dropwise at 0°C. The reaction was then stirred 16 h at rt. The reaction mixture was cooled to 0°C, then quenched by the addition of sat. aq. $NaHCO_3$. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with MeOH:DCM (1-6%) to afford the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 9.63 (s, 1H), 8.63 (s, 1H), 8.15 (d, *J*=2.4 Hz, 1H), 7.32 (d, *J*=8.7 Hz, 1H), 7.20 (dd, *J*=2.4, 8.7 Hz, 1H), 3.68-3.62 (m, 2H), 3.07-2.89 (m, 2H), 1.86 (s, 3H); *m/z* =522.1 $[M+1]^+$.

Using essentially the same procedures described in Example **110A**, the following compounds in **Table 8** were prepared.

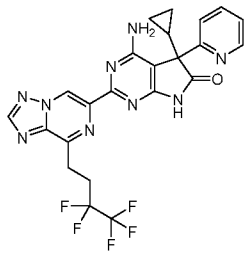
Table 8

Ex.	Structure	Name	MS (M+1)	Chiral starting material

111A		4-amino-5-(5-hydroxypyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	486.4	**Ex-40A**
112A		4-amino-5-cyclopropyl-5-(5-hydroxypyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	512.2	**Ex-39A**
113B		(S)-4-amino-5-(4-fluorophenyl)-2-(8-(3-hydroxybenzyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	483.1	**Ex-86B**

EXAMPLE **114A**

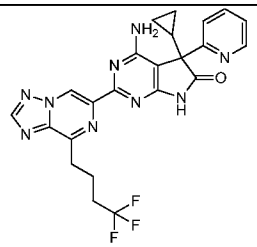
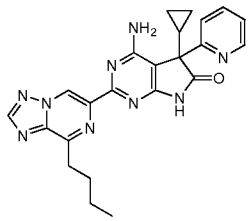
4-amino-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(pyridin-2-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one



Into a 40-mL vial were placed 4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (130 mg, 0.23 mmol), Pd/C (130 mg, 10%), ammonium formate (56 mg, 0.88 mmol) and MeOH (13 mL). The resulting solution was stirred 1 h at 60°C then cooled to RT and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with MeOH:DCM (10%) to afford the title compound. ^{1}H NMR (400 MHz, CD_3OD) δ 9.65 (s, 1H), 8.65 (s, 1H), 8.62-8.56 (m, 1H), 7.93-7.82 (m, 2H), 7.40-7.37 (m, 1H), 3.66 (t, *J*=8.0 Hz, 2H), 3.05-2.92 (m, 2H), 2.01-1.94 (m, 1H), 0.73-052 (m, 4H); *m/z* =532.1 $[M+1]^+$.

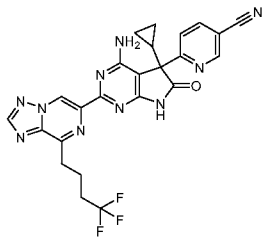
Using essentially the same procedures described in Example **114A**, the following compounds in **Table 9** were prepared.

Table 9

Ex.	Structure	Name	MS (M+1)	Chiral starting material
115A		4-amino-5-cyclopropyl-5-(pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	496.0	**Ex-27A**
116A		4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-cyclopropyl-5-(pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	442.3	**EX-68A**

EXAMPLE **117A**

6-(4-Amino-5-cyclopropyl-6-oxo-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile

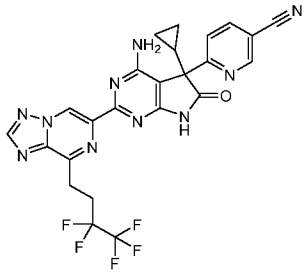


Into a microwave vial, under an inert atmosphere of nitrogen, was placed 4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (120 mg, 0.23 mmol), water (50 µL), zinc cyanide (85 mg, 0.72 mmol), tris(dibenzylideneacetone)dipalladium(0)-chloroform (85 mg, 0.093 mmol), dicyclohexyl(2',6'-dimethoxybiphenyl-2-yl)phosphine (85 mg, 0.21 mmol) and DMF (5 mL). The reaction mixture was then heated to 150°C for 40 min in a microwave reactor. The reaction mixture was cooled to RT, quenched by the addition of brine. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (30-100%). The

reaction mixture was filtered and purified by reverse phase HPLC acetonitrile:water (with 0.05% ammonium bicarbonate modifier) to afford the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 9.58 (s, 1H), 8.88 (dd, *J*=0.9, 2.1 Hz, 1H), 8.60 (s, 1H), 8.22 (dd, *J*=2.1, 8.4 Hz, 1H), 7.98 (dd, *J*=0.9, 8.4 Hz, 1H), 3.38 (t, *J*=7.5 Hz, 2H), 2.37-2.16 (m, 4H), 1.98-1.89 (m, 1H), 0.71-0.51 (m, 4H); *m/z* =521.2 $[M+1]^+$.

EXAMPLE **118A**

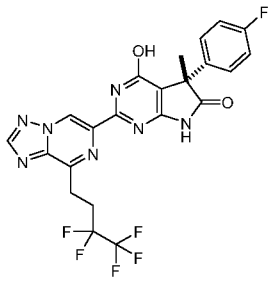
6-(4-Amino-5-cyclopropyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)nicotinonitrile



Using essentially the same procedures described in Example **117A**, Example **118A** was prepared, using 4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one as starting material. *m/z* =557.4 $[M+1]^+$.

EXAMPLE **119A**

(S)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one

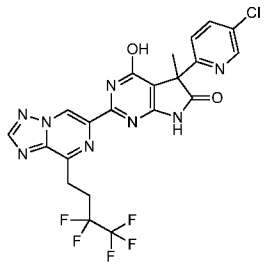
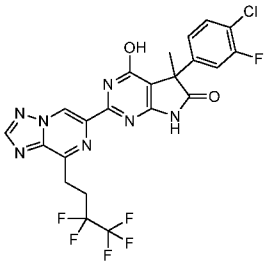
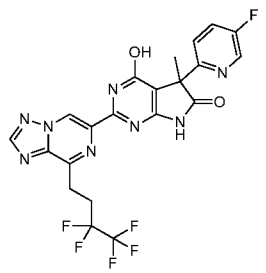
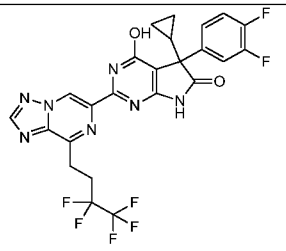


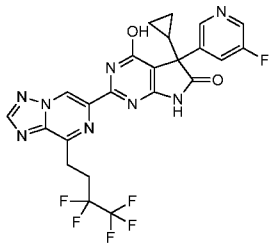
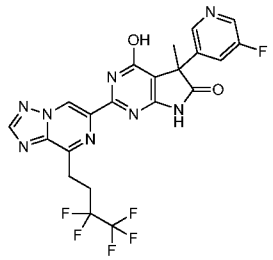
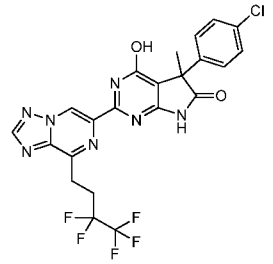
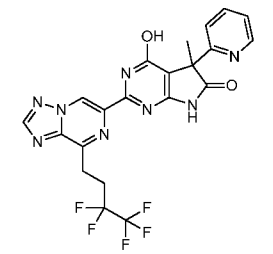
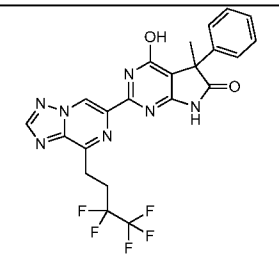
Into a vial, under an inert atmosphere of nitrogen, was placed Example **1A** (100 mg, 0.19 mmol), *tert*-butyl nitrite (138 mg, 1.34 mmol), DMF (10 mL) and water (50 µL). The resulting mixture was stirred for 30 min at 80°C, then cooled to RT and quenched by the addition of water. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with DCM:MeOH (10%) to afford the title compound. ^{1}H NMR (500, DMSO-d_6): δ 12.73 (s, 1H). 11.37 (s, 1H),

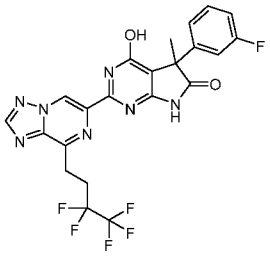
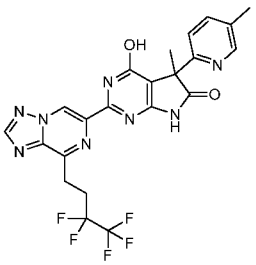
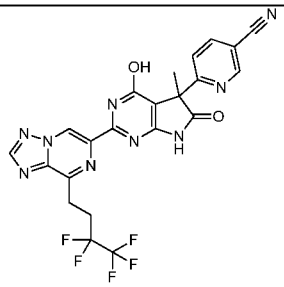
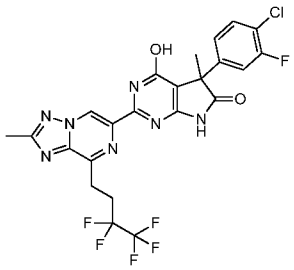
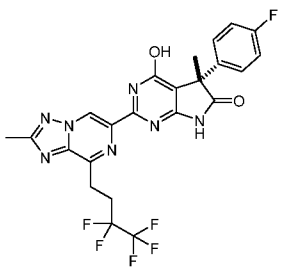
9.51 (s, 1H), 8.93 (s, 1H), 7.46-7.43 (m, 2H), 7.20-7.16 (m, 2H), 3.57 (t, *J*=8.0 Hz, 2H), 3.25-3.05 (m, 2H,), 1.75 (s, 3 H), *m/z* =524.0 $[M+1]^+$.

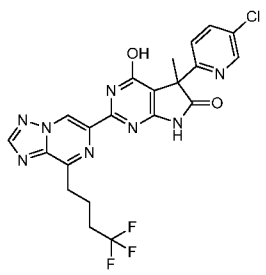
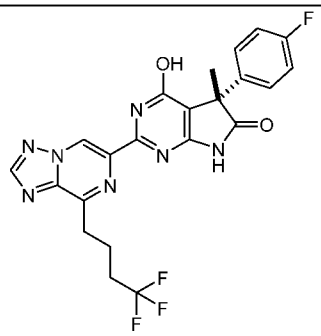
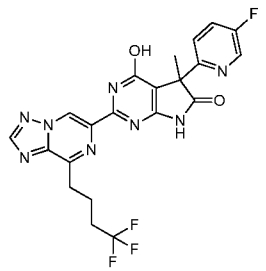
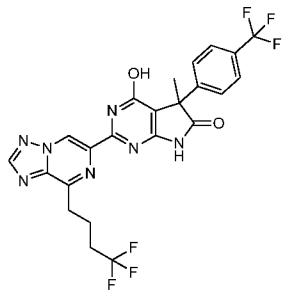
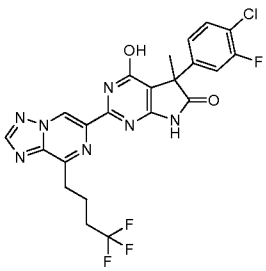
Using essentially the same procedures described in Example **119A**, the following compounds in **Table 10** were prepared. The conditions employed may utilize slight variations of reagents such as *tert*-butyl nitrite, isopentyl nitrite, or a combination of sodium nitrite and an acid such as sulfuric acid in 1,2-DCE, DMA, DMF, MeCN, THF, or combinations of solvents thereof at elevated temperatures of 40–80°C.

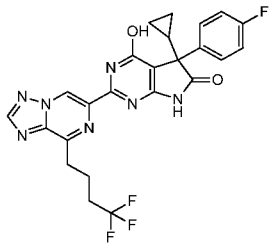
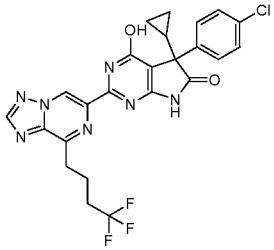
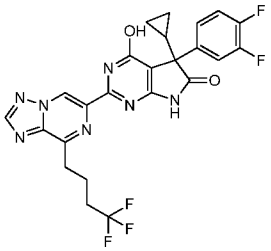
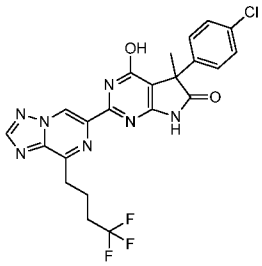
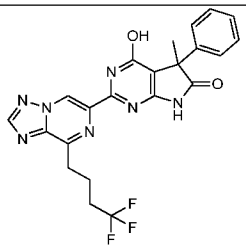
Table 10

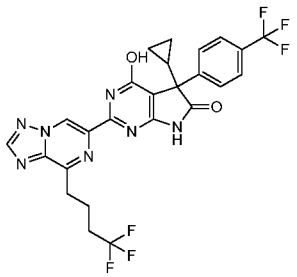
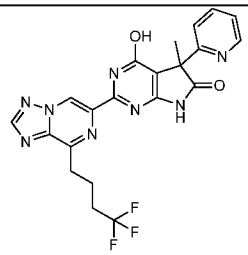
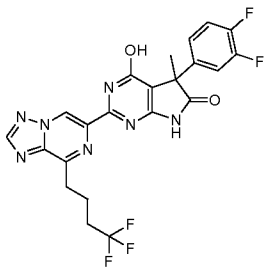
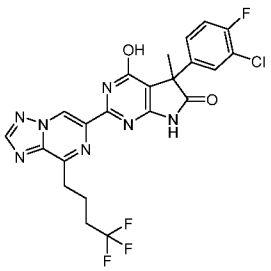
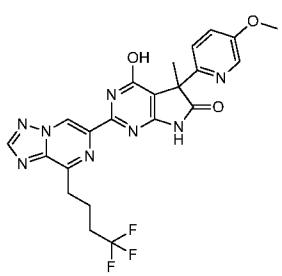
Ex.	Structure	Name	MS (M+1)	Chiral starting material
120A		5-(5-chloropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	541.1	**Ex-3A**
121B		5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	558.3	**Ex-5B**
122B		5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	525.1	**Ex-4B**
123A		5-cyclopropyl-5-(3,4-difluorophenyl)-4-hydroxy-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-	568.1	**Ex-6A**

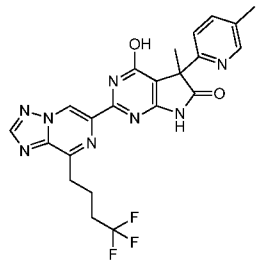
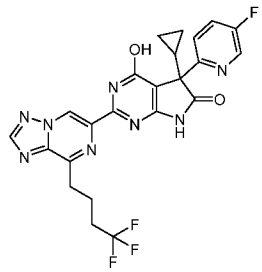
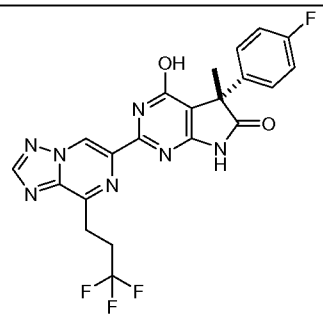
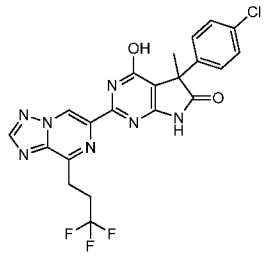
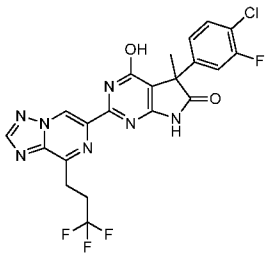
		6(7*H*)-one		
124B		5-cyclopropyl-5-(5-fluoropyridin-3-yl)-4-hydroxy-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	551.2	**Ex-8B**
125A		5-(5-fluoropyridin-3-yl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	525.1	**Ex-9A**
126A		5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	540.0	**Ex-10A**
127B		4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	507.3	**Ex-11B**
128B		4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-phenyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	506.0	**Ex-12B**

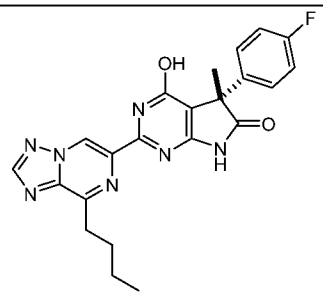
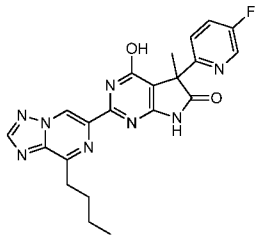
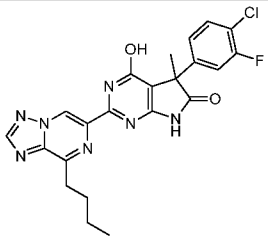
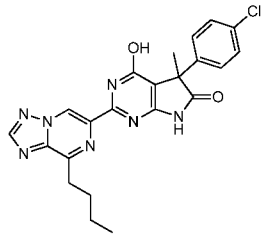
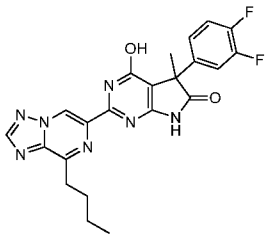
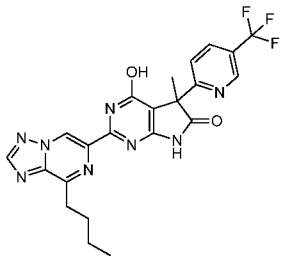
129B		5-(3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one	524.3	**Ex-14B**
130B		4-hydroxy-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	521.1	**Ex-19B**
131A		6-(4-hydroxy-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidin-5-yl)nicotinonitrile	532.3	**Ex-18A**
132B		5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	572.0	**Ex-90B**
133B		(S)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	538.0	**Ex-88B**

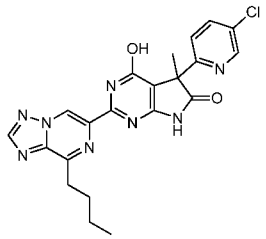
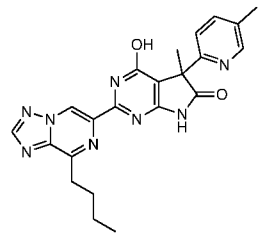
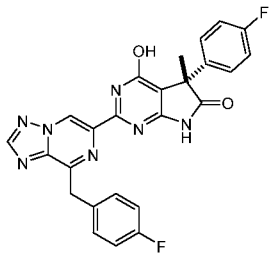
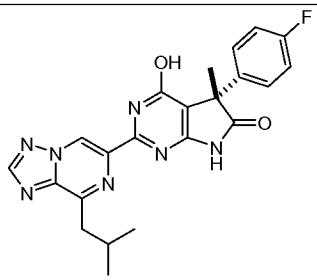
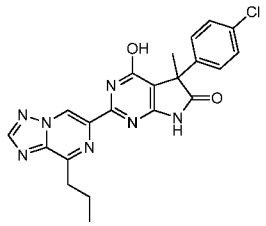
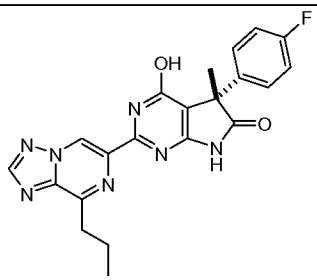
134A		5-(5-chloropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	505.3	**Ex-26A**
135A		5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one	488.3	**Ex-23A**
136B		5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	489.1	**Ex-22B**
137B		4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	538.3	**Ex-24B**
138B		5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	522.2	**Ex-28B**

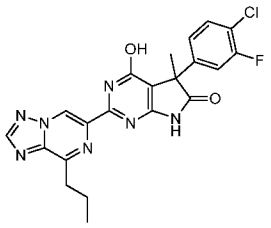
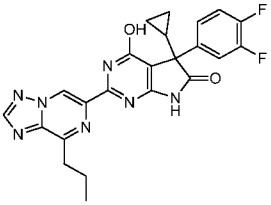
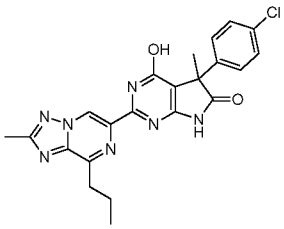
139B		5-cyclopropyl-5-(4-fluorophenyl)-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	514.1	**Ex-30B**
140B		5-(4-chlorophenyl)-5-cyclopropyl-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	530.5	**Ex-31B**
141A		5-cyclopropyl-5-(3,4-difluorophenyl)-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	532.0	**Ex-32A**
142A		5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	504.0	**Ex-29A**
143B		4-hydroxy-5-methyl-5-phenyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	470.3	**Ex-37B**

144A		5-cyclopropyl-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	564.0	**Ex-35A**
145B		4-hydroxy-5-methyl-5-(pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	471.1	**Ex-36B**
146B		5-(3,4-difluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	506.1	**Ex-38B**
147B		5-(3-chloro-4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one	522.3	**Ex-42B**
148A		4-hydroxy-5-(5-methoxypyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	501.3	**Ex-40A**

149B		4-hydroxy-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	485.1	**Ex-46B**
150A		5-cyclopropyl-5-(5-fluoropyridin-2-yl)-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one	515.1	**Ex-34A**
151A		(S)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	474.1	**Ex-74A**
152A		5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	490.2	**Ex-76A**
153B		5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	508.0	**Ex-75B**

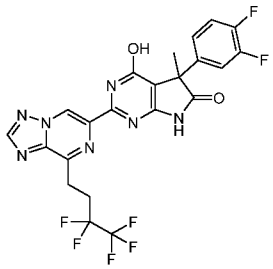
154A		(S)-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	434.2	**Ex-60A**
155B		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	435.1	**Ex-61B**
156B		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	468.2	**Ex-62B**
157A		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-chlorophenyl)-4-hydroxy-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	450.2	**Ex-63A**
158B		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(3,4-difluorophenyl)-4-hydroxy-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	452.1	**Ex-64B**
159B		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-4-hydroxy-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	485.1	**Ex-67B**

160A		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-chloropyridin-2-yl)-4-hydroxy-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	451.2	**Ex-69A**
161B		2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-4-hydroxy-5-methyl-5-(5-methylpyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	431.2	**Ex-71B**
162B		(S)-2-(8-(4-fluorobenzyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	486.1	**Ex-85B**
163A		(S)-5-(4-fluorophenyl)-4-hydroxy-2-(8-isobutyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	434.2	**Ex-73A**
164A		5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	436.1	**Ex-53A**
165A		(S)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	420.1	**Ex-52A**

166B		5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	454.1	**Ex-55B**
167A		5-cyclopropyl-5-(3,4-difluorophenyl)-4-hydroxy-2-(8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	464.1	**Ex-58A**
168A		5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	450.2	**Ex-93A**

EXAMPLE **169B**

5-(3,4-Difluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one

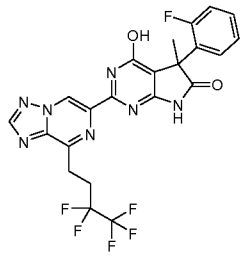


Step A-4-Amino-5-(3,4-difluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: The title compound was prepared using essentially the same procedures described in Example **1A**, using intermediate **I-A2** and **I-5B** as starting material. *m/z* =541 $[M+1]^+$.

Step B-5-(3,4-difluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: The title compound was prepared using essentially the same procedures described in Example **119A**, using intermediate from step A as starting material. *m/z* =542.0 $[M+1]^+$.

EXAMPLE **170A**

5-(2-Fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one

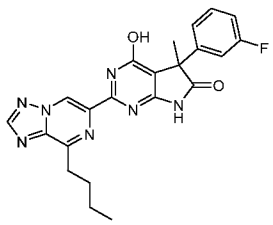


Step A-4-Amino-5-(2-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: The title compound was prepared using essentially the same procedures described in Example **1A**, using intermediate **I-A2** and **I-12B** as starting material. *m/z* =523.1 $[M+1]^+$.

Step B-5-(2-Fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: The title compound was prepared using essentially the same procedures described in Example **119A**, using intermediate from step A as starting material. *m/z*=524.2 $[M+1]^+$.

EXAMPLE **171A**

2-(8-Butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(3-fluorophenyl)-4-hydroxy-5-methyl-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one

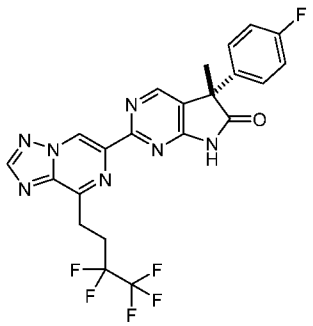


Step A-4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(3-fluorophenyl)-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-*d*]pyrimidin-6-one: The title compound was prepared using essentially the same procedures described in Example **1A**, using intermediate **I-A5** and **I-7B** as starting material. *m/z*=433.3 $[M+1]^+$.

Step B-2-(8-butyl-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(3-fluorophenyl)-4-hydroxy-5-methyl-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: The title compound was prepared using essentially the same procedures described in Example **119A**, using intermediate from step A as starting material. *m/z* =434.1 $[M+1]^+$.

EXAMPLE **172A**

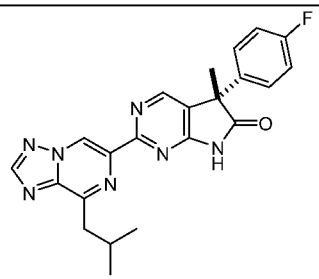
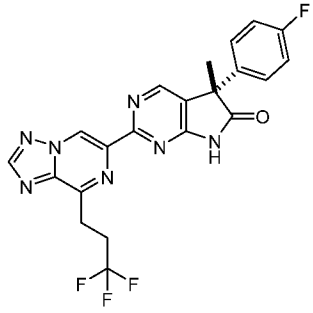
(S)-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one

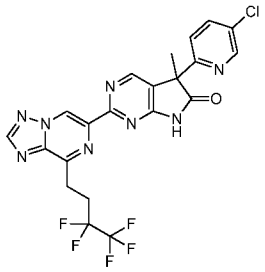
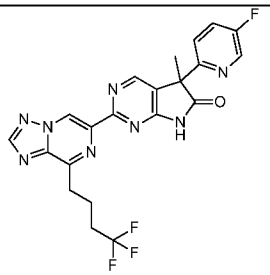


Into a vial, under an inert atmosphere of nitrogen, was placed Example **1A** (100 mg, 0.191 mmol), *tert*-butyl nitrite (138 mg, 1.340 mmol) and anhydr. DMF (10 mL) The resulting mixture was stirred for 30 min at 80°C, then cooled to RT and quenched by the addition of water. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. in vacuo to dryness. The residue was purified by silica gel column chromatography with DCM:MeOH (10%) to afford Example **119A** and the title compound. ^{1}H NMR (300, MeOD): δ 9.75 (s, 1H), 8.68 (s, 1H), 8.57 (s, 1H), 7.49-7.44 (m, 2H), 7.16-7.10 (m, 2H), 3.70-3.65 (m, 2H), 3.11-3.93 (m, 2H,), 1.91 (s, 3 H), *m/z* =508.2 $[M+1]^+$.

Using essentially the same procedures described in Example **172A**, the following compounds in **Table 11** were prepared.

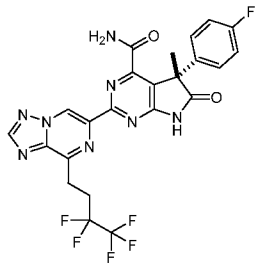
Table 11

Ex.	Structure	Name	MS (M+1)	Chiral starting material
173A		(S)-5-(4-fluorophenyl)-2-(8-isobutyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	418.2	**Ex-73A**
174A		(S)-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one	458.1	**Ex-74A**

175A		5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	525.1	**Ex-3A**
176B		5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one	473.1	**Ex-22B**

EXAMPLE **177A**

5-(4-Fluorophenyl)-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine-4-carboxamide



Step A-4-Bromo-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one: Into a vial, under an inert atmosphere of N_2, was placed 4-Amino-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one (410 mg, 0.79 mmol), *tert*-butyl nitrite (324 mg, 3.14 mmol), copper(II) bromide (1227 mg, 5.49 mmol) and DCE (8 mL). The resulting mixture was stirred at 65°C for 1 h then cooled to RT, diluted with EtOAc. The organic layer was washed with a 9:1 mixture of sat. NH_4Cl:NH_4OH, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-60%) to afford the title compound.

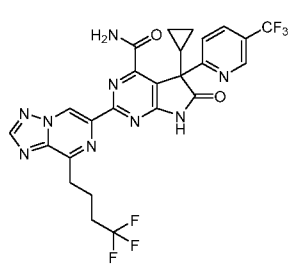
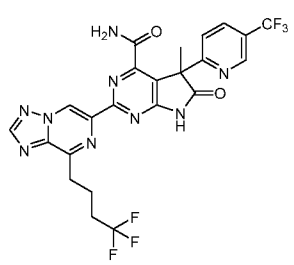
Step B- 5-(4-Fluorophenyl)-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5*H*-pyrrolo[2,3-*d*]pyrimidine-4-carbonitrile: Into a vial, under an inert atmosphere of N_2, was placed intermediate from step A (160 mg, 0.27 mmol), copper(I) cyanide (86 mg, 0.96 mmol) and DMF (4 mL). The

resulting mixture was stirred for 3 h at 150°C. then cooled to RT, diluted with EtOAc. The organic layer was washed with a 9:1 mixture of sat. NH_4Cl:NH_4OH, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-0%) to afford the title compound.

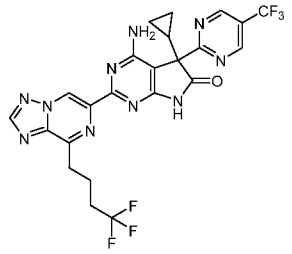
Step C-5-(4-Fluorophenyl)-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-*d*]pyrimidine-4-carboxamide: Into a vial was placed intermediate from step B (35 mg, 0.066 mmol) and HCl (4 mL, 12 N). The resulting mixture was stirred for 1 h at 40°C then cooled to 0°C and quenched by the addition of water and EtOAc. The pH value was adjusted to pH 8 with sat. $NaHCO_3$. The mixture was extracted with EtOAc (3X). The organic layer was washed with brine, dried over anhydr. Na_2SO_4, and filtered. The filtrate was conc. *in vacuo* to dryness. The residue was purified by silica gel column chromatography with EtOAc:petroleum ether (0-80%) to afford the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 9.99 (s, 1H), 8.67 (s, 1H), 7.23-7.18 (m, 2H), 6.98 (dd, *J*=8.7, 8.7 Hz, 2H), 3.69-3.64 (m, 2H), 3.05-2.87 (m, 2H), 2.04 (s, 3H); *m/z* =551.0 $[M+1]^+$.

Using essentially the same procedures described in Example **177A**, the following compounds in **Table 12** were prepared.

Table 12

Ex.	Structure	Name	MS (M+1)	Chiral starting material
178A		5-cyclopropyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine-4-carboxamide	**592.1**	**Ex-2A**
179B		5-methyl-6-oxo-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine-4-carboxamide	**566.1**	**Ex-25B**

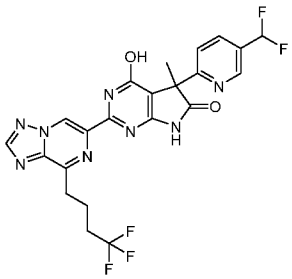
EXAMPLE **180A**



4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)-5,7-dihydro-6*H*-pyrrolo[2,3-*d*]pyrimidin-6-one

The title compound was prepared using essentially the same procedures described in Example **1A**, using intermediate **I-A1** and **I-44** as starting material. The racemic material was resolved using chiral SFC (IB column) to afford isomers **Ex-180A** (faster eluting) and **Ex-180B** (slower eluting) of the title compound *m/z* =531.4[M+1]$^+$

EXAMPLE **181A**

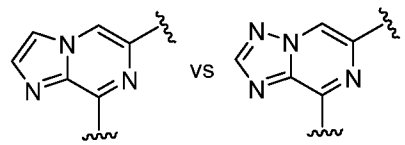


4-hydroxy-5-(5-(difluoromethyl)pyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one

The title compound was prepared using essentially the same procedures described in Example **119A**, using **Ex-43B** as starting material. *m/z* =521.2 [M+1]$^+$.

Pharmacokinetic Profile in Rats

The triazolo-pyrazinyl compounds of Formula **I** have longer PK $T_{1/2}$ (hr) in rats than the corresponding imidazo-pyrazinyl analogs .



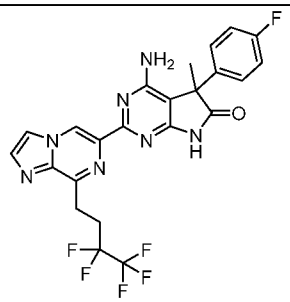
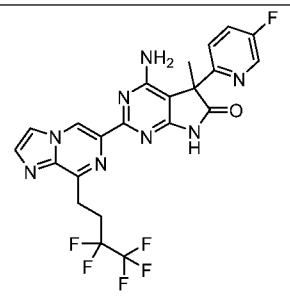
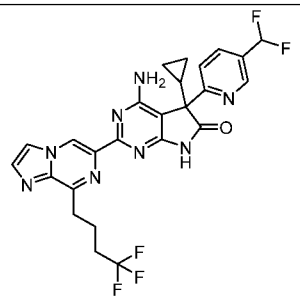
Certain imidazo-pyrazinyl analogs are disclosed in International Application No. PCT/US2015/33084, filed May 29, 2015.

Table 13 provides the pharmacokinetic profiles for rats for a representative set of compounds. The results were obtained using the following the procedure:

IV Cassette PK Assay:

Adult male Wistar-Han rats were fasted overnight and administered a cassette IV dose of mixture of several compounds via a previously implanted catheter in the femoral vein. Animals were allowed access to food 4h post dose. Blood samples were collected into EDTA-containing tubes at the following time points: 0.03, 0.13, 0.25, 0.5, 1, 2, 4, 8h post-dose. Blood samples were stored on ice until plasma was harvested by centrifugation. Plasma was transferred to a 96-well plate and stored at -20°C until analysis. Concentrations of each compound in rat plasma were determined by LC-MS/MS following protein precipitation.

Table 13

Compounds of Formula I		**Imidazo-Pyrazinyl Analogs**	
Ex.	**Cassette PK $T_{1/2}$ (hr)**	**Imidazo-Pyrazinyl Analog**	**Cassette PK $T_{1/2}$ (hr)**
1A	3.35		1.04
4B	2.97		1.41
44B	3.94		2.12

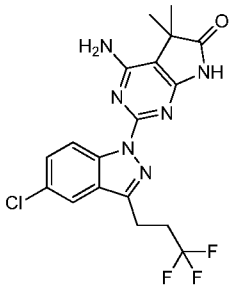
Cell-based sGC Functional Assay (CASA Assay)

Rationale

sGC is a heme-containing enzyme that converts GTP to secondary messenger cGMP. Increases in cGMP levels affect several physiological processes including vasorelaxation through multiple downstream pathways. The rate by which sGC catalyzes cGMP formation is greatly increased by NO and by recently discovered NO-independent activators and stimulators. Heme-dependent activators (HDAs) preferentially activate sGC containing a ferrous heme group. To determine the effect of sGC activators on enzyme activity, the CASA assay was developed to monitor the generation of cGMP in a cell line that stably expresses the heterodimeric sGC protein.

Methods

A CHO-K1 cell line stably expressing the sGC α1/β1 heterodimer was generated using a standard transfection protocol. CHO-K1 cells were transfected with plasmids pIREShyghsGCα1 and pIRESneo-hsGCβ1 simultaneously using FUGENE reagent. Clones that stably express both subunits were selected with hygromycin and neomycin for ~2 weeks. Clone #7 was chosen for the assay and was designated CHO-K1/sGC. CHO-K1/sGC cells were maintained in F-K12 medium containing 10% heat-inactivated Fetal Bovine Serum (FBS), 100 μg/mL penicillin/streptomycin, 0.5 mg/mL hygromycin and 0.25 mg/mL G418. The cells were then cryopreserved in LN2. On the day of the assay, cells thawed and resuspended in EBSS Assay Buffer (Sigma, E3024) supplemented with 5mM $MgCl_2$, 10mM HEPES (4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid) and 0.05% BSA (bovine serum albumin) (EAB) and cell density was then adjusted to 4X105/mL with EAB. IBMX (3-isobutyl-1-methylxanthin, 0.5mM) was added to inhibit degradation of cGMP. Compounds were diluted from DMSO stock solutions and added to the assay at a final DMSO concentration of 2.5%. Cells were incubated with compounds in the presence and absence of 1 μM of Diethylenetriamine/nitric oxide adduct (DETA-NO; Sigma, 17018) for 1hr at 37 °C. At the end of the incubation period, the reaction was terminated and the cells were lysed with the detection reagents from Cisbio Kits. The level of intracellular cGMP was determined using an HTRF-based assay kit (CisBio, 62GM2PEC), which detects the displacement of a fluorescence labeled cGMP from its specific antibody. The cGMP produced by test compounds was directly compared to the maximum cGMP production (this value was set to equal 100% activation.) of the published sGC-HDA Compound A:



Compound A

(Example 1 in WO 2010/065275, published June 10, 2010). The test compounds' activities were then expressed as a percentage of Compound A, the standard in every experiment. This percent activation was calculated either in the presence or absence of DETA-NO which was then plotted. IP and maximum fold induction was derived using ADA analysis software for 4P fit.

The compounds in the Examples of the instant invention had inflection points (IP) less than or equal to 10 μM and more particularly less than or equal to about 1 μM. Most preferred compounds had an IP of less than or equal to about 500 nM.Data for the compounds of the Examples is provided in Table **14**.

Table 14

Ex.	IP (nM)	% Act.
1A	186.5	196
2A	127.8	111
3A	40.4	161
4B	117.5	157
5B	20.9	147
6A	27.0	140
7A	41.4	185
8B	294.5	177
9A	63.0	119
10A	15.8	137
11B	25.2	208
12B	11.1	122
13B	80.6	109
14B	5.5	90
15A	315.7	139
16B	13.1	77
17B	36.1	119
18A	38.6	75
19B	14.7	71
20A	176.1	131
21B	43.1	99
22B	38.3	130
23A	29.6	163
24B	27.1	133
25B	27.0	131
26A	27.8	162
27A	277.6	178
28B	20.0	171
29A	11.4	101
30B	36.7	117

Ex.	IP (nM)	% Act.
31B	13.0	104
32A	77.4	144
33A	5.6	107
34A	427.9	235
35A	416.3	164
36B	56.5	82
37B	11.5	112
38A	11.0	120
39A	20.1	96
40A	98.9	130
41A	27.8	151
42B	8.7	82
43B	45.6	69
44B	110.9	120
45B	44.2	156
46B	10.1	67
47B	143.7	114
48A	77.9	85
49B	595.1	127
50B	150.2	191
51B	15.1	144
52A	63.2	96
53A	26.9	122
54B	318.2	210
55B	45.6	99
56A	384.0	81
57A	576.8	119
58A	242.0	169
59A	263.0	119
60A	22.6	121

Ex.	IP (nM)	% Act.
61B	9.7	177
62B	51.0	267
63A	21.9	187
64B	5.1	90
65A	2.6	104
66A	34.2	162
67B	25.5	119
68A	18.7	113
69A	13.7	158
70A	41.8	133
71B	5.5	118
72B	28.5	82
73A	44.1	101
74A	55.6	110
75B	20.0	136
76A	153.6	120
77B	332.8	112
78B	550.4	83
79A	324.6	152
80A	2488.0	115
81B	698.4	115
82A	555.4	125
83A	269.7	100
84B	55.7	101
85B	10.6	106
86B	26.4	126
87B	80.2	138
88B	65.0	137
89B	260.2	109
90B	36.6	135

Ex.	IP (nM)	% Act.
91A	668.1	105
92B	4828.0	167
93A	439.0	159
94A	79.4	138
95B	256.7	74
96B	134.3	108
97B	219.5	106
98B	86.1	164
99A	47.5	113
100A	127.4	184
101A	120.6	154
102A	29.1	132
103A	218.6	104
104A	257.9	117
105A	26.7	176
106A	15.5	95
107A	74.7	76
108A	14.7	107
109A	7.3	92
110A	138.9	70
111A	369.5	75
112A	212.5	91
113B	762.9	171
114A	143.6	122
115A	232.7	118
116A	19.7	85
117A	49.2	140
118A	84.1	72
119A	133.7	124
120A	155.3	107

Ex.	IP (nM)	% Act.
121B	130.4	222
122B	140.6	100
123A	203.6	78
124B	1051.0	88
125A	575.1	87
126A	131.9	102
127B	1255.0	129
128B	127.9	106
129B	51.7	66
130B	503.1	109
131A	1471.0	99
132B	441.9	119
133B	856.2	87
134A	856.8	134
135A	182.9	108
136B	513.9	69
137B	596.7	102
138B	343.9	164
139B	672.8	169
140B	277.3	150
141A	183.5	133
142A	207.2	137
143A	301.0	114
144A	1296.0	87
145B	1218.0	64
146B	45.5	154
147B	213.5	94
148A	1092.0	96
149B	990.3	63
150A	1222.0	74

Ex.	IP (nM)	% Act.
151A	1489.0	120
152A	132.6	70
153B	310.1	104
154A	27.2	100
155B	163.0	159
156B	23.3	102
157A	72.7	161
158B	102.0	232
159B	208.6	73
160A	50.2	96
161B	303.0	95
162B	96.7	100
163A	1635.0	109
164A	780.0	253
165A	1518.0	114
166B	711.4	117
167A	1088.0	70
168A	1454.0	77
169B	110.9	116
170A	9.5	125
171A	136.9	90
172A	212.5	122
173A	574.0	176
174A	1346.0	133
175A	384.1	115
176B	526.0	166
177A	127.7	168
178A	199.0	108
179B	90.2	101
180B	487.5	97

181B	749.0	55

Acute Efficacy in spontaneously hypertensive rats (SHR)

Spontaneously hypertensive rats (SHR, male, Charles River) were implanted with DSI TA11PA-C40 telemetry device (Data Sciences, Inc., St. Paul, MN) under isoflurane or ketamine/metomidine anesthesia. The telemetry unit catheter was inserted into the descending aorta via the femoral artery and the telemetry device was implanted subcutaneously in the left flank area. Animals were allowed to recover from surgery for 14 days before the start of any studies. Blood pressure, heart rate, and activity signals from conscious, freely moving rats were recorded continuously for 30 seconds every 10 minutes. On the day prior to administration of compound, a single oral dose of vehicle (10% transcutol/20% Cremophor/70% water) was administered to all animals to establish baseline control data. The blood pressure lowering efficacy of compound (PO) or vehicle was evaluated following a single oral gavage. Data were collected as hourly averages, and changes in blood pressure were calculated by subtracting control baseline data on an hourly basis. Animals were maintained on normal diet with a 12 hour light-dark cycle.

Maximum peak decreases of systolic blood pressure (SBP) in SHR at a particular P.O. dose (mpk milligrams per kilogram) for the following representative compounds are provided. Category A=SBP in SHRs <20 mmHg; Category B=SBP in SHRs 20-40 mmHg; Category C=SBP in SHRs >40 mmHg.

Table 15

Ex.	Dose, P.O. mpk	Cat.
1A	0.3	C
2A	0.3	A
3A	0.3	B
4B	0.3	C
7A	0.3	B
8B	3	B
9A	1	B
11B	0.3	B
12B	0.1	B

Ex.	Dose, P.O. mpk	Cat.
13B	1	B
17B	0.3	A
18A	0.3	C
20A	1	C
25B	0.3	B
33A	0.3	C
34A	0.3	C
36B	1	B
39A	0.3	B

Ex.	Dose, P.O. mpk	Cat.
41A	0.3	B
44B	1	B
56A	3	B
60A	0.3	C
61B	0.3	C
65A	0.3	C
67B	0.3	B
73A	1	B
74A	1	B

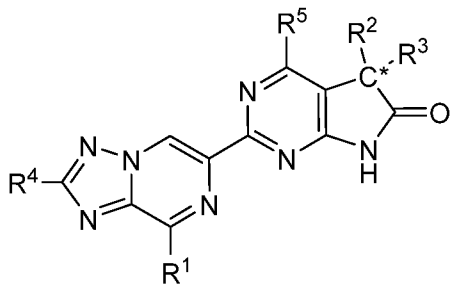
Ex.	Dose, P.O. mpk	Cat.
76A	0.3	A
77B	1	A
78B	3	B
79A	1	B
85B	0.3	C
88B	1	C
94A	1	C
95B	0.3	C
98B	1	B
103A	2	A
104A	3	C
105A	0.3	B
106A	0.3	C
107A	3	C
110A	3	B
112A	3	A

Ex.	Dose, P.O. mpk	Cat.
114A	1	B
115A	1	B
119A	1	B
120A	1	B
121B	1	B
122B	1	B
125A	3	A
132B	1	A
134A	1	B
135A	1	B
136B	3	B
138B	1	C
140B	1	A
141A	1	B
142A	0.3	B
143A	1	B

Ex.	Dose, P.O. mpk	Cat.
146B	0.3	B
151A	3	B
152A	3	B
154A	0.3	B
155B	1	B
156B	0.3	C
158B	0.3	C
160A	0.3	B
164A	2	B
165A	3	B
166B	3	B
173A	1	A
177A	1	C
178A	1	B
179B	0.3	B

WHAT IS CLAIMED IS:

1. A compound having structural Formula **I**:



I

or a pharmaceutically acceptable salt thereof wherein

C* indicates a potential chiral carbon atom;

R^1 is

(1) hydrogen

(2) (C_{1-6})alkyl,

(3) halo(C_{1-6})alkyl,

(4) (C_{1-6})alkyl-O-,

(5) halo(C_{1-6})alkyl-O-,

(6) (C_{1-6})alkyl-NH-,

(7) halo(C_{1-6})alkyl-NH-,

(8) -(C_{1-3})alkyl-(C_{3-7})cycloalkyl,

(9) -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7,

(10) aryl unsubstituted or substituted by one, two, or three R^7,

(11) (C_{3-7})cycloalkyl, or

(12) -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, and wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7;

R^2 is

(1) (C_{1-3})alkyl, or

(2) (C_{3-7})cycloalkyl;

R^3 is

(1) aryl unsubstituted or substituted by one, two, or three R^6,

(2) five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6,

(3) (C_{1-3})alkyl, or

(4) (C_{3-7})cycloalkyl;

R^4 is

(1) hydrogen,

(2) (C_{1-3})alkyl,

(3) halo(C_{1-3})alkyl, or

(4) (C_{3-7})cycloalkyl;

R^5 is

(1) hydrogen,

(2) hydroxy,

(3) $-N(R^{8a})(R^{8b})$,

(4) -COOH,

(5) $-C(O)NH_2$,

(6) (C_{1-3})alkyl,

(7) (C_{3-7})cycloalkyl, or

(8) four- to six-membered monocyclic heterocyclyl containing 1 N heteroatom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9;

each R^6 is independently

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl,

(3) (C_{1-3})alkoxy,

(4) halo(C_{1-3})alkoxy,

(5) (C_{3-7})cycloalkyl, unsubstituted or substituted by halo,

(6) halo,

(7) cyano,

(8) hydroxy,

(9) $-NH_2$,

(10) $-(C_{1-3})$alkyl-COOH, or

(11) $-(C_{1-3})$alkyl-COO(C_{1-4})alkyl;

each R^7 is independently

(1) (C_{1-3})alkoxy,

(2) halo,

(3) hydroxy, or

(4) (C_{1-3})alkyl;

R^{8a} and R^{8b} are independently

(1) hydrogen,

(2) (C_{1-3})alkyl, or

(3) (C_{3-7})cycloalkyl; and

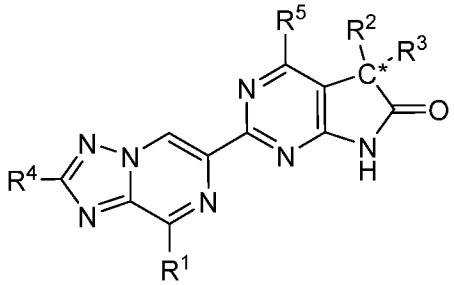
R^9 is

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl, or

(3) hydroxy.

2. A compound having structural Formula **I**:



I

or a pharmaceutically acceptable salt thereof wherein

C* indicates a potential chiral carbon atom;

R^1 is

(1) hydrogen

(2) (C_{1-6})alkyl,

(3) halo(C_{1-6})alkyl,

(4) (C_{1-6})alkyl-O-,

(5) halo(C_{1-6})alkyl-O-,

(6) (C_{1-6})alkyl-NH-,

(7) halo(C_{1-6})alkyl-NH-,

(8) -(C_{1-3})alkyl-(C_{3-7})cycloalkyl,

(9) -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7,

(10) aryl unsubstituted or substituted by one, two, or three R^7,

(11) (C_{3-7})cycloalkyl, or

(12) -(C_{1-3})alkyl-heteroaryl wherein the heteroaryl is a 5- or 6-membered ring containing one, two, or three heteroatoms independently selected from the group consisting of N, O, and S, and wherein heteroaryl is unsubstituted or substituted by one, two, or three R^7;

R^2 is

(1) (C_{1-3})alkyl, or

(2) (C_{3-7})cycloalkyl;

R^3 is

(1) aryl unsubstituted or substituted by one, two, or three R^6, or

(2) five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6;

R^4 is

(1) hydrogen,

(2) (C_{1-3})alkyl,

(3) halo(C_{1-3})alkyl, or

(4) (C_{3-7})cycloalkyl;

R^5 is

(1) hydrogen,

(2) hydroxy,

(3) -$N(R^{8a})(R^{8b})$,

(4) -COOH,

(5) -$C(O)NH_2$,

(6) (C_{1-3})alkyl,

(7) (C_{3-7})cycloalkyl, or

(8) four- to six-membered monocyclic heterocyclyl containing 1 N heteroatom, wherein the heterocyclyl is unsubstituted or substituted by one to two R^9;

each R^6 is independently

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl,

(3) (C_{1-3})alkoxy,

(4) halo(C_{1-3})alkoxy,

(5) (C_{3-7})cycloalkyl, unsubstituted or substituted by halo,

(6) halo,

(7) cyano,

(8) hydroxy,

(9) -NH_2,

(10) –(C_{1-3})alkyl-COOH, or

(11) –(C_{1-3})alkyl-COO(C_{1-4})alkyl;

each R^7 is independently

(1) (C_{1-3})alkoxy,

(2) halo,

(3) hydroxy, or

(4) (C_{1-3})alkyl;

R^{8a} and R^{8b} are independently

(1) hydrogen,

(2) (C_{1-3})alkyl, or

(3) (C_{3-7})cycloalkyl; and

R^9 is

(1) (C_{1-3})alkyl,

(2) halo(C_{1-3})alkyl, or

(3) hydroxy.

3. The compound of claim 1 or a pharmaceutically acceptable salt thereof wherein: R^3 is aryl unsubstituted or substituted by one, two, or three R^6.

4. The compound of any of claims 1 or 3 or a pharmaceutically acceptable salt thereof wherein: R^5 is -N(R^{8a})(R^{8b}).

5. The compound of any of claims 1 to 4 or a pharmaceutically acceptable salt thereof wherein: R^1 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7.

6. The compound of any of claims 1 or 3 or a pharmaceutically acceptable salt thereof wherein R^5 is hydroxy.

7. The compound of claim 6 or a pharmaceutically acceptable salt thereof wherein: R^1 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, or -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7.

8. The compound of claim 1 or a pharmaceutically acceptable salt thereof wherein R^3 is five- or six-membered heteroaryl containing one, two, or three heteroatoms independently selected from the group consisting of N, O and S, wherein heteroaryl is unsubstituted or substituted by one, two, or three R^6.

9. The compound of claim 8 or a pharmaceutically acceptable salt thereof wherein: R^5 is -N(R^{8a})(R^{8b}).

10. The compound of claim 9 or a pharmaceutically acceptable salt thereof wherein: R^1 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, or -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7.

11. The compound of claim 8 or a pharmaceutically acceptable salt thereof wherein R^5 is hydroxy.

12. The compound of claim 11 or a pharmaceutically acceptable salt thereof wherein: R^1 is (C_{1-6})alkyl, halo(C_{1-6})alkyl, or -(C_{1-3})alkyl-aryl, wherein aryl is unsubstituted or substituted by one, two, or three R^7.

13. The compound of claim 1, which is:

4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-cyclopropyl-5-(5-fluoropyridin-3-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-fluoropyridin-3-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

(12) 4-amino-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-phenyl-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(6-cyclopropylpyridin-3-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(3-fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-(6-(1,1-difluoroethyl)pyridin-3-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,

4-amino-5-cyclopropyl-5-(5-methylpyridin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

6-(4-amino-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile,

4-amino-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(1-isopropyl-1H-1,2,3-triazol-4-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-methylpyrazin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(4-fluorophenyl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chlorophenyl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chloro-3-fluorophenyl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-fluoropyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-5-(pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-5-phenyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(3,4-difluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-methoxypyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-methoxypyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-chloropyrimidin-2-yl)-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(3-chloro-4-fluorophenyl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-(difluoromethyl)pyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-(difluoromethyl)pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(6-(1,1-difluoroethyl)pyridin-3-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-methylpyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

6-(4-amino-5-methyl-6-oxo-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile,

4-amino-5-methyl-5-(6-methyl-5-(trifluoromethyl)pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyrazin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-fluoropyridin-2-yl)-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-fluoropyridin-2-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-chloro-3-fluorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-chlorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(3,4-difluorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-cyclopropyl-5-(3,4-difluorophenyl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-cyclopropyl-5-(5-fluoropyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-chloropyridin-2-yl)-5-cyclopropyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-chloropyridin-2-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-cyclopropyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5-(5-methylpyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-cyclopropyl-5-(5-methylpyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-2-(8-isobutyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chlorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-5-(4-(trifluoromethyl)phenyl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-(trifluoromethyl)pyridin-2-yl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-chloropyridin-2-yl)-5-cyclopropyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(3,4-difluorophenyl)-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(3,4-difluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-(4-fluorobenzyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-2-(8-(3-methoxybenzyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-(4-fluorobenzyl)-2-methyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chloro-3-fluorophenyl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-fluoropyridin-2-yl)-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-chlorophenyl)-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-([1,2,4]triazolo[1,5-a]pyrazin-6-yl)-4-amino-5-(4-chlorophenyl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(1-cyclopropyl-1H-1,2,3-triazol-4-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(1-cyclopropyl-1H-1,2,3-triazol-4-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-Amino-5-methyl-5-(5-methyl-1,3,4-oxadiazol-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-(difluoromethyl)-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-cyclopropyl-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-(1-fluorocyclopropyl)-1,3,4-oxadiazol-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-(1-fluorocyclopropyl)-1,3,4-oxadiazol-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(5-hydroxypyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

4-amino-5-(5-hydroxypyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-5-(5-hydroxypyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-(4-fluorophenyl)-2-(8-(3-hydroxybenzyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-5-cyclopropyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(pyridin-2-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

4-amino-5-cyclopropyl-5-(pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-amino-2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-cyclopropyl-5-(pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

6-(4-amino-5-cyclopropyl-6-oxo-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile,

6-(4-amino-5-cyclopropyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile,

5-(4-Fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo [1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-chloropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-5-(3,4-difluorophenyl)-4-hydroxy-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-5-(5-fluoropyridin-3-yl)-4-hydroxy-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-fluoropyridin-3-yl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-phenyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

4-hydroxy-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

6-(4-hydroxy-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-5-yl)nicotinonitrile,

5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(2-methyl-8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-chloropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-5-(4-fluorophenyl)-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chlorophenyl)-5-cyclopropyl-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-5-(3,4-difluorophenyl)-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-hydroxy-5-methyl-5-phenyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-(trifluoromethyl)phenyl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-hydroxy-5-methyl-5-(pyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(3,4-difluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(3-chloro-4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one

4-hydroxy-5-(5-methoxypyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

4-hydroxy-5-methyl-5-(5-methylpyridin-2-yl)-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-5-(5-fluoropyridin-2-yl)-4-hydroxy-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-fluoropyridin-2-yl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-chlorophenyl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(3,4-difluorophenyl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-4-hydroxy-5-methyl-5-(5-(trifluoromethyl)pyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-chloropyridin-2-yl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-4-hydroxy-5-methyl-5-(5-methylpyridin-2-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

2-(8-(4-fluorobenzyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(4-fluorophenyl)-4-hydroxy-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-4-hydroxy-2-(8-isobutyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chloro-3-fluorophenyl)-4-hydroxy-5-methyl-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-cyclopropyl-5-(3,4-difluorophenyl)-4-hydroxy-2-(8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-chlorophenyl)-4-hydroxy-5-methyl-2-(2-methyl-8-propyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(3,4-difluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

5-(2-fluorophenyl)-4-hydroxy-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

2-(8-butyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(3-fluorophenyl)-4-hydroxy-5-methyl-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one,

5-(4-Fluorophenyl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-2-(8-isobutyl-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-methyl-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-5-methyl-2-(8-(3,3,3-trifluoropropyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-chloropyridin-2-yl)-5-methyl-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(5-fluoropyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5H-pyrrolo[2,3-d]pyrimidin-6(7H)-one,

5-(4-fluorophenyl)-5-methyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine-4-carboxamide,

5-cyclopropyl-6-oxo-2-(8-(3,3,4,4,4-pentafluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine-4-carboxamide,

5-methyl-6-oxo-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-a]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyridin-2-yl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidine-4-carboxamide,
4-amino-5-cyclopropyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5-(5-(trifluoromethyl)pyrimidin-2-yl)-5,7-dihydro-6H-pyrrolo[2,3-d]pyrimidin-6-one, or
4-hydroxy-5-(5-(difluoromethyl)pyridin-2-yl)-5-methyl-2-(8-(4,4,4-trifluorobutyl)-[1,2,4]triazolo[1,5-*a*]pyrazin-6-yl)-5*H*-pyrrolo[2,3-*d*]pyrimidin-6(7*H*)-one,
or a pharmaceutically acceptable salt thereof.

14. A method for activating soluble guanylate cyclase comprising the step of administering an amount efficacious therefor of the compound of any of claims 1 to 13 or a pharmaceutically acceptable salt thereof.

15. A method for the treatment of one or more conditions selected from cardiovascular disease, endothelial dysfunction, diastolic dysfunction, atherosclerosis, hypertension, heart failure, pulmonary hypertension, angina pectoris, thrombosis, restenosis, myocardial infarction, stroke, cardiac insufficiency, fibrosis, pulmonary hypertonia, erectile dysfunction, asthma bronchiale, chronic kidney disease, diabetes or cirrhosis of the liver in a patient comprising administering a therapeutically effective amount of the compound of any of claims 1 to 13, or a pharmaceutically acceptable salt thereof, to a patient in need thereof.

16. A method for the treatment of hypertension comprising administering a therapeutically effective amount of the compound of any of claims 1 to 13, or a pharmaceutically acceptable salt thereof, to a patient in need thereof.

17. A method for the treatment of heart failure comprising administering a therapeutically effective amount of the compound of any of claims 1 to 13, or a pharmaceutically acceptable salt thereof, to a patient in need thereof.

18. A pharmaceutical composition comprised of the compound of any of claims 1 to 13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

19. The pharmaceutical composition of claim 18 further comprising one or more additional active agents is selected from an angiotensin converting enzyme inhibitor, an

angiotensin II receptor antagonist, a neutral endopeptidase inhibitor, an aldosterone antagonist, a renin inhibitor, an endothelin receptor antagonist, an aldosterone synthase inhibitor, a phosphodiesterase-5 inhibitor, a vasodilator, a calcium channel blocker, a potassium channel activator, a diuretic, a sympatholitic, a beta-adrenergic blocking drug, an alpha adrenergic blocking drug, a central alpha adrenergic agonist, a peripheral vasodilator, a lipid lowering agent or a metabolic altering agent.

20. The use of the compound of any of claims 1 to 13 or a pharmaceutically acceptable salt thereof, for the preparation of a medicament useful for the treatment of one or more conditions selected from cardiovascular disease, endothelial dysfunction, diastolic dysfunction, atherosclerosis, hypertension, heart failure, pulmonary hypertension, pulmonary arterial hypertension, angina pectoris, thromboses, restenoses, myocardial infarction, stroke, cardiac insufficiency, pulmonary hypertonia, erectile dysfunction, asthma bronchiale, chronic kidney insufficiency, diabetes or cirrhosis of the liver in a patient.

21. The use of claim 20, wherein the medicament comprises a therapeutically effective amount of the compound or stereoisomer thereof.

22. The use of the compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament useful for activating soluble guanylate cyclase.

23. A medicament comprising at least one compound of any of claims 1 to 13 for use in the treatment of one or more conditions selected from cardiovascular disease, endothelial dysfunction, diastolic dysfunction, atherosclerosis, hypertension, heart failure, pulmonary hypertension, pulmonary arterial hypertension, angina pectoris, thromboses, restenoses, myocardial infarction, stroke, cardiac insufficiency, pulmonary hypertonia, erectile dysfunction, asthma bronchiale, chronic kidney insufficiency, diabetes or cirrhosis of the liver.

24. The medicament of claim 23, wherein the medicament comprising one or more additional active agents is selected from an angiotensin converting enzyme inhibitor, an angiotensin II receptor antagonist, a neutral endopeptidase inhibitor, an aldosterone antagonist, a renin inhibitor, an endothelin receptor antagonist, an aldosterone synthase inhibitor, a phosphodiesterase-5 inhibitor, a vasodilator, a calcium channel blocker, a potassium channel

activator, a diuretic, a sympatholitic, a beta-adrenergic blocking drug, an alpha adrenergic blocking drug, a central alpha adrenergic agonist, a peripheral vasodilator, a lipid lowering agent or a metabolic altering agent.