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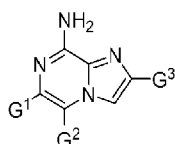
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(54) Title: MODULATORS OF THE ADENOSINE A2A RECEPTOR



(57) Abstract: The present invention relates to the compounds of formula (I) and salts, stereoisomers, tautomers, isotopologues, or N-oxides thereof. The present invention is further concerned with the use of such a compounds (I) or salt, stereoisomer, tautomer, isotopologues, or N-oxide thereof as modulators of the adenosine A2A receptor in the treatment of cancer and a pharmaceutical composition comprising said compounds.

Modulators of the adenosine A2A receptor

Field of the Invention

The present invention relates to substituted imidazo[1,2-*a*]pyrazine compounds and salts, stereoisomers, tautomers, isotopologues, or N-oxides thereof. The present invention is further concerned with the use of substituted imidazo[1,2-*a*]pyrazine compounds or salts, stereoisomers, tautomers, isotopologues, or N-oxides thereof as medicament and a pharmaceutical composition comprising said compounds.

Background of the Invention

Cancer cells produce large quantities of mutated proteins (called neoantigens), which - when presented to the immune system - might lead to natural eradication of the tumor. However, to counteract this process, cancer cells produce also specific immunosuppressive metabolites that change the microenvironment and impair the function of immune cells. One of the key metabolites, which works this way is adenosine. Its immunosuppressive function is mediated by adenosine receptors, which are members of the G protein-coupled receptor (GPCR) family and possess seven transmembrane alpha helices. There are 4 subtypes of adenosine receptors described so far: A1, A2A, A2B, A3. They can be coupled to adenylate cyclase either positively (A2A, A2B) or negatively (A1, A3). Only forms A1 and A2A are heavily distributed in immune cells and mainly responsible for immunosuppression mediated by adenosine.

Stressed or injured tissues (i.e. tumor tissue) release endogenous ATP, which works as a pro-inflammatory agent. Hydrolysis of ATP by endonucleases (such as CD39 and CD73) leads to adenosine formation. Its binding to A2A and A2B receptors leads to cAMP elevation in immune cells and results in the activation of the CREB/ATF pathway (cAMP-responsive element (CRE)-binding protein/activating transcription factor), the cell's main immunosuppressive mechanism [Grenz et al Antioxid Redox Signal 2011;15:2221-34,23. Fredholm et al Prog Neurobiol 2007;83:263-76.,24.Sitkovsky Trends Immunol 2009;30:102-8]. Its activation has been shown to either induce anergy of CD4+ T cells or their conversion into Tregs. This subpopulation of T cells is further activated by adenosine and produces immunosuppressive cytokines such as TGF- β and IL-10. Another group of immunosuppressing cells which respond to higher concentration of adenosine are MDSC, which undergo differentiation upon activation by this metabolite (Morrello et al Oncoimmunology. 2016 Mar; 5(3): e1108515). On the other hand, stimulation of adenosine might also lead to decreased cytotoxic activity, e.g. CD8+ lymphocytes lower their

secretion of IL-2, Th1 cytokines and IFN- γ , while NK cells produce lower levels of GzmB, NKG2d, CD69 and CD27 [Sitkovsky Trends Immunol 2009;30:102-8]. Dendritic cells and macrophages are also affected by increased amounts of adenosine upon which they start to produce immunosuppressing agents such as IL-8, IL10 and TGF β , and stop production of immunostimulatory cytokines such as IL12, TNF α , IFN γ . Adenosine also stimulates in macrophages the conversion of M1 to M2. [Allard et al Curr Opin Pharmacol. 2016 Aug;29:7-16; Allard et al. Immunol Cell Biol 2017 Apr; 95(4) :333-339.]

The above clearly shows that antagonizing adenosine receptors and thus reactivating the anti-tumor immune response may be an effective way of fighting all types of cancer. [Allard et al Curr Opin Pharmacol. 2016 Aug;29:7-16]. It was shown in an allograft model that the use of A2A antagonists not only slows down the tumor growth but also blocks metastasis (in this particular case to lungs). Moreover, a strong synergistic correlation with checkpoint inhibitor antibodies has been demonstrated, likely improving the treatment [Iannone Am J Cancer Res. 2014 Mar 1;4(2):172-81, Cancer Immunol Res. 2015 May;3(5):506-17; Allard et al. Immunol Cell Biol 2017 Apr; 95(4) :333-339.].

Antagonists of the A2A receptor have already been shown as promising therapeutic for other diseases. The A2A receptor is abundant in the brain, where it plays a crucial role in the regulation of dopamine and glutamate release. Not surprisingly, the A2A receptor antagonists have been proposed useful in treatment of neurodegenerative disorders such as Parkinson's, Huntington's and Alzheimer's disease causing motor impairment, which can be improved by employment of A2A antagonists [Tuite P, et al., J. Expert Opin. Investig. Drugs. 2003; 12, 1335-52; Popoli P. et al. J Neurosci. 2002; 22, 1967-75; and Dall'Igna, et al., Experimental Neurology, 2007, 241-245]. Additionally, A2A antagonists may be used for the treatment of psychosis, stroke, extra pyramidal syndrome, e.g., dystonia, akathisia, pseudoparkinsonism and tardive dyskinesia (see Jenner P. J Neurol. 2000; 247 Suppl2: 1 143-50) and attention related disorders such as attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD). Furthermore, A2A antagonists have been shown as useful agents for the treatment of amyotrophic lateral sclerosis (US 2007037033), cirrhosis, fibrosis and fatty liver (WO 01/058241) and the mitigation of addictive behavior (WO 06/009698). Adenosine A2A antagonists may be useful for the treatment and prevention of dermal fibrosis in diseases such as scleroderma (Chan et al. Arthritis & Rheumatism, 2006, 54(8), 2632-2642). Recently antagonists of A2A receptors were shown to possess the therapeutic potential as neuroprotectants (Stone TW. et al., Drug. Dev. Res. 2001, 52, 323-330), in the treatment of migraine (Kurokawa et al., 2009. Program No. 714.4/B101. 2009 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience) and sleep disorders (Dunwiddie TV et al., Ann. Rev. Neurosci. 2001, 24, 31- 55). WO 2017/098421 discloses inhibitors of CD73, wherein CD73 catalyzes the conversion of AMP to adenosine and is thought to be the major contributor to extracellular adenosine, in particular in the tumor microenvironment. CD73 inhibition results in decreased extracellular adenosine such that the activity of the A2A receptor is decreased, resulting in less (or no) immunosuppression – exactly the effect achieved with A2A receptor antagonists. It can thus be assumed that the diseases disclosed in WO 2017/098421 may also be treated by A2A antagonists.

There is growing evidence that also the A2B receptor plays an important role in cancer progression, especially in immune suppression in tumor microenvironment, as well as tumor proliferation, angiogenesis, metastasis (Zhan-Guo Gao et al., Int J Mol Sci. 2019; 20(20): 5139). It was

shown that A2BR expression is significantly upregulated under many pathological conditions such as hypoxia, inflammation and cancer (Borea PA et al., Trends Pharmacol Sci. 2016; 37(6):419-434, Borea PA et al., Physiol Rev. 2018; 98(3):1591-1625, Cekic C and Linden J Nat Rev Immunol. 2016; 16(3):177-92.). Particularly bladder urothelial carcinoma expresses high levels of A2BAR and it is suggested to be associated with a poor patient prognosis (Zhou Y et al.; Oncotarget. 2017; 8(30):48755-48768). Moreover, it was postulated that A2BR controls cellular proliferation via HIF-1 α activation, which may indicate that A2BR may be a key regulator of oral squamous cell carcinoma progression (Kasama H et al. BMC Cancer. 2015; 15:563). Additionally, A2BR antagonists have already been suggested as promising therapeutic approach for other diseases such as idiopathic pulmonary fibrosis (J. Clin. Invest. 116:2173-2182 (2006)), systemic sclerosis (H Karmouty-Quintana; Arthritis & Rheumatology 2018; Vol. 70, No. 10, 1673-1684) and broader - all the fibrotic diseases (Bruce N. Cronstein F1000 Biol Reports 2011, 3:21). Yet another indication where A2BR might play significant role is Irritable Bowel Disease (Teita Asano and Mitsuko Takenaga J Clin Med. 2017 6(11): 104). Moreover, it was shown that analgesic effects might be achieved by antagonization of A2BR (J Pharmacol Exp Ther. 2004; 308(1):358-66.).

In view of the above, there is the need for further compounds, which antagonize the A2A receptor in order to be capable of treating the afore-mentioned diseases. Furthermore, there is also the need for further compounds, which antagonize the A2B receptor.

Objects and Summary of the Invention

It is therefore an object of the present invention to provide compounds, which antagonize the adenosine A2A receptor.

It is another object of the present invention to provide compounds, which are capable of treating diseases, which are linked to the adenosine A2A receptor.

It is another object of the present invention to provide compounds, which antagonize the adenosine A2B receptor.

It is another object of the present invention to provide compounds, which are capable of treating diseases, which are linked to the adenosine A2B receptor.

It is another object of the present invention to provide compounds, which antagonize the adenosine A2A and A2B receptor.

It is another object of the present invention to provide compounds, which are capable of treating diseases, which are linked to the adenosine A2A and A2B receptor.

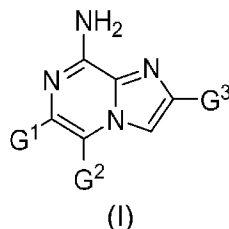
It is still another object of the present invention to provide compounds, which are suitable for the treatment of a disease selected from the group consisting of cancer, Parkinson's disease, Huntington's disease, Alzheimer's disease, psychosis, stroke, extra pyramidal syndrome (in particular dystonia, akathisia, pseudoparkinsonism and tardive dyskinesia), attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), amyotrophic lateral sclerosis, cirrhosis, fibrosis, fatty liver, addictive behavior, dermal fibrosis (in particular dermal fibrosis in scleroderma), sleep disorders, AIDS, autoimmune diseases, infections, atherosclerosis and ischemia-reperfusion injury.

In particular, it is an object of the present invention to provide compounds, which are suitable for the treatment of cancer, wherein this relates to the treatment of the tumor and the block of metastases.

The above objects can be achieved by the compounds of formula (I) as defined herein, and uses thereof.

The inventors of the present invention *inter alia* found that the compounds of formula (I), as defined herein below (see first aspect), antagonize adenosine A2A receptor activity. Furthermore, the inventors of the present invention *inter alia* found that the compounds of formula (I), as defined herein below (see first aspect), antagonize adenosine A2B receptor activity. Furthermore, the inventors of the present invention *inter alia* found that the compounds of formula (I), as defined herein below (see first aspect), antagonize adenosine both A2A and A2B receptor activity. Accordingly, the compounds of formula (I) or a pharmaceutical composition comprising a compound of formula (I), as defined herein below (see second aspect), can be used for the treatment of diseases linked to the adenosine A2A receptor, in particular the diseases given herein and most preferably cancer. Furthermore, the compounds of formula (I) or a pharmaceutical composition comprising a compound of formula (I), as defined herein below (see second aspect), can be used for the treatment of diseases linked to the adenosine A2B receptor, in particular the diseases given herein and most preferably cancer. Furthermore, the compounds of formula (I) or a pharmaceutical composition comprising a compound of formula (I), as defined herein below (see second aspect), can be used for the treatment of diseases linked to the adenosine A2A and A2B receptor, in particular the diseases given herein and most preferably cancer.

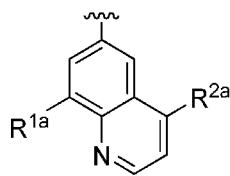
Therefore, in the first aspect A1, the present invention relates to a compound of formula (I)



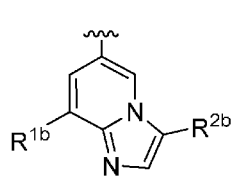
or a salt, stereoisomer, tautomer, isotopologue, or N-oxide thereof, wherein

G¹ is selected from the group consisting of phenyl and a 5- to 6-membered fully unsaturated heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN.

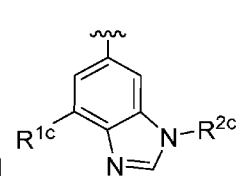
G² is selected from the group consisting of



(Hy-a),



(Hy-b), and



(Hy-c),

G^3 is selected from the group consisting of of

- (i) C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R^3 ;
- (ii) $C(=O)R^5$, $C(=O)OR^6$, $C(=O)SR^6$, $C(=O)N(R^{6a})(R^{6b})$, OR^6 , $S(=O)_nR^6$, $S(=O)_nN(R^{6a})(R^{6b})$, $S(=O)_mOR^6$, $N(R^{6a})(R^{6b})$, $N(R^6)C(=O)R^5$, $N(R^6)C(=O)OR^6$, $N(R^6)C(=O)N(R^{6a})(R^{6b})$, $N(R^6)S(=O)_n(R^6)$, $N(R^6)S(=O)_mN(R^{6a})(R^{6b})$, and $N(R^6)S(=O)_mOR^6$;

R^{1a} is selected from the group consisting of H and Cl;

R^{1b} is selected from the group consisting of H and Cl;

R^{1c} is selected from the group consisting of H and Cl;

R^{2a} is selected from the group consisting of Cl and C_1 - C_3 -alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R^{2b} is selected from the group consisting of Cl and C_1 - C_3 -alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R^{2c} is C_1 - C_3 -alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R^3 is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^4 ;
- (ii) $C(=O)R^7$, $C(=O)OR^8$, $C(=O)SR^8$, $C(=O)N(R^{8a})(R^{8b})$, OR^8 , $S(=O)_nR^8$, $S(=O)_nN(R^{8a})(R^{8b})$, $S(=O)_mOR^8$, $N(R^{8a})(R^{8b})$, $N(R^8)C(=O)R^7$, $N(R^8)C(=O)OR^8$, $N(R^8)C(=O)N(R^{8a})(R^{8b})$, $N(R^8)S(=O)_n(R^8)$, $N(R^8)S(=O)_mN(R^{8a})(R^{8b})$, and $N(R^8)S(=O)_mOR^8$;

R^4 is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁹;
- (ii) C(=O)R¹⁰, C(=O)OR¹¹, C(=O)SR¹¹, C(=O)N(R^{11a})(R^{11b}), OR¹¹, S(=O)_nR¹¹, S(=O)_nN(R^{11a})(R^{11b}), S(=O)_mOR¹¹, N(R^{11a})(R^{11b}), N(R¹¹)C(=O)R¹⁰, N(R¹¹)C(=O)OR¹¹, N(R¹¹)C(=O)N(R^{11a})(R^{11b}), N(R¹¹)S(=O)_n(R¹¹), N(R¹¹)S(=O)_mN(R^{11a})(R^{11b}), and N(R¹¹)S(=O)_mOR¹¹;
- R⁵, R⁶, R^{6a}, R^{6b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;
- R⁷, R⁸, R^{8a}, R^{8b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹³;
- R⁹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C(=O)R¹⁴, C(=O)OR¹⁵, C(=O)SR¹⁵, C(=O)N(R^{15a})(R^{15b}), OR¹⁵, S(=O)_nR¹⁵, S(=O)_nN(R^{15a})(R^{15b}), S(=O)_mOR¹⁵, N(R^{15a})(R^{15b}), N(R¹⁵)C(=O)R¹⁴, N(R¹⁵)C(=O)OR¹⁵, N(R¹⁵)C(=O)N(R^{15a})(R^{15b}), N(R¹⁵)S(=O)_n(R¹⁵), N(R¹⁵)S(=O)_mN(R^{15a})(R^{15b}), and N(R¹⁵)S(=O)_mOR¹⁵;
- R¹⁰, R¹¹, R^{11a}, R^{11b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises

one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁷;

R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;
- (ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)SR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, S(=O)_nR²⁰, S(=O)_nN(R^{20a})(R^{20b}), S(=O)_mOR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b}), N(R²⁰)S(=O)_n(R²⁰), N(R²⁰)S(=O)_mN(R^{20a})(R^{20b}), and N(R²⁰)S(=O)_mOR²⁰;

and/or two R¹² present on one carbon atom together form =O;

R¹³ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;
- (ii) C(=O)R²², C(=O)OR²³, C(=O)SR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, S(=O)_nR²³, S(=O)_nN(R^{23a})(R^{23b}), S(=O)_mOR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b}), N(R²³)S(=O)_n(R²³), N(R²³)S(=O)_mN(R^{23a})(R^{23b}), and N(R²³)S(=O)_mOR²³;

R¹⁴, R¹⁵, R^{15a}, R^{15b} are independently selected from the group consisting of

- (i) H, C₁-C₆-alkyl, C₂-C₆-alkenyl, and C₂-C₆-alkynyl, wherein each substitutable carbon atom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R¹⁶;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable

carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R^{32} ;

R^{16} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, $N(R^{33a})(R^{33b})$, $C(=O)NR^{33a}R^{33b}$, $S(=O)_nNR^{33a}R^{33b}$, OR^{33} and $S(=O)_nR^{33}$;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R^{32} ;

R^{17} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl);

R^{18} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{24} ;
- (ii) $C(=O)R^{25}$, $C(=O)OR^{26}$, $C(=O)SR^{26}$, $C(=O)N(R^{26a})(R^{26b})$, OR^{26} , $S(=O)_nR^{26}$, $S(=O)_nN(R^{26a})(R^{26b})$, $S(=O)_mOR^{26}$, $N(R^{26a})(R^{26b})$, $N(R^{26})C(=O)R^{25}$, $N(R^{26})C(=O)OR^{26}$, $N(R^{26})C(=O)N(R^{26a})(R^{26b})$, $N(R^{26})S(=O)_n(R^{26})$, $N(R^{26})S(=O)_mN(R^{26a})(R^{26b})$, and $N(R^{26})S(=O)_mOR^{26}$;

R^{19} , R^{20} , R^{20a} , R^{20b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{27} ;

R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;

R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

R²⁸ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or

S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{31} ;

R^{29} , R^{30} , R^{31} are independently selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl);

R^{32} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, C_2 - C_4 -haloalkynyl, $C(=O)R^{34}$, $C(=O)OR^{33}$, $C(=O)SR^{33}$, $C(=O)N(R^{33a})(R^{33b})$, OR^{33} , $S(=O)_nR^{33}$, $S(=O)_nN(R^{33a})(R^{33b})$, $S(=O)_mOR^{33}$, $N(R^{33a})(R^{33b})$, $N(R^{33})C(=O)R^{34}$, $N(R^{33})C(=O)OR^{33}$, $N(R^{33})C(=O)N(R^{33a})(R^{33b})$, $N(R^{33})S(=O)_n(R^{33})$, $N(R^{33})S(=O)_mN(R^{33a})(R^{33b})$, and $N(R^{33})S(=O)_mOR^{33}$;

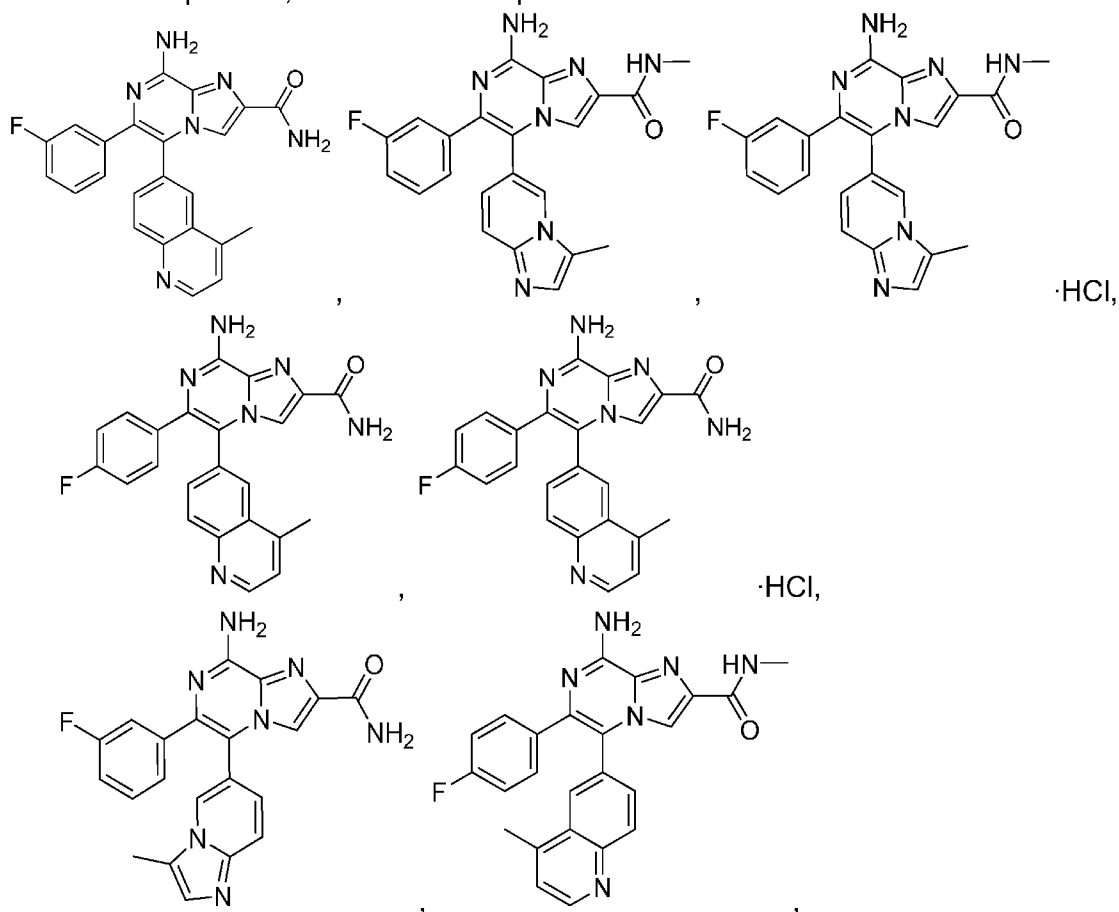
R^{33} , R^{33a} , R^{33b} , R^{34} are independently selected from the group consisting of H, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, and C_2 - C_4 -haloalkynyl;

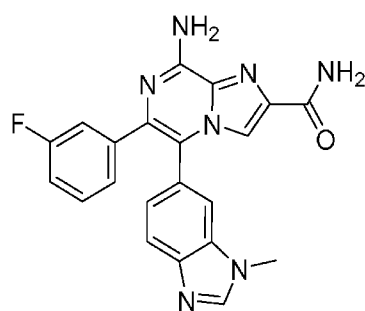
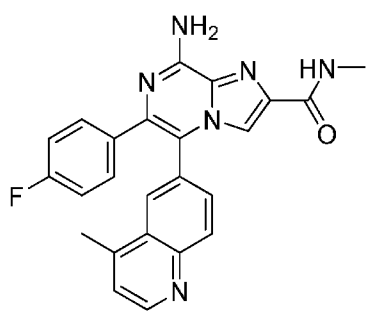
and wherein

n is 0, 1 or 2; and

m is 1 or 2.

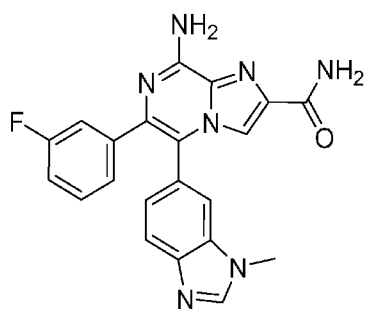
In the first aspect A1a, the present invention relates to a compound of formula (I) as defined above in the first aspect A1, wherein the compound is not:





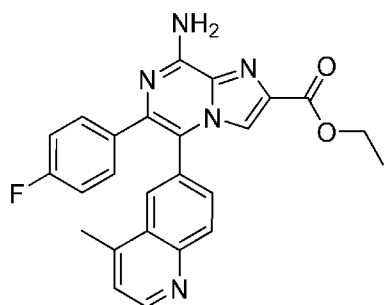
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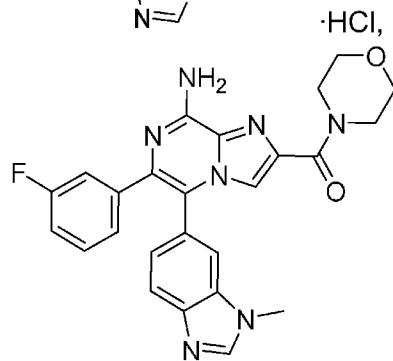
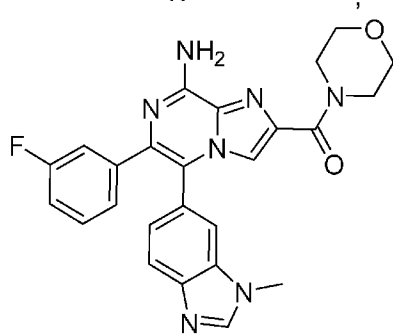
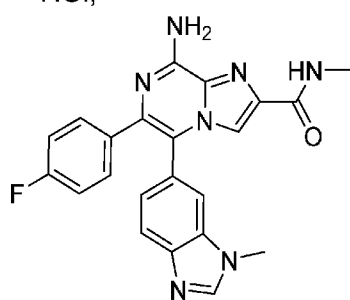
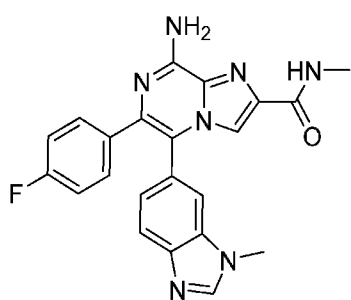
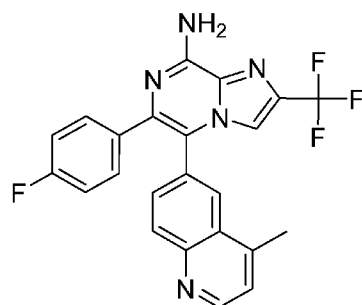
·HCl,

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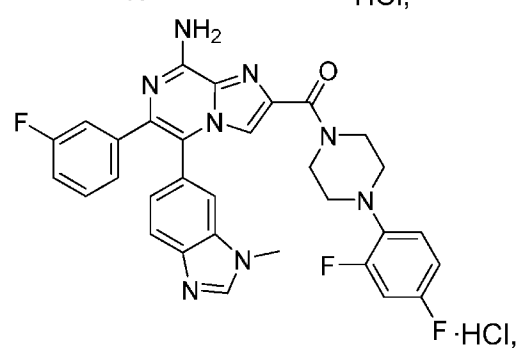
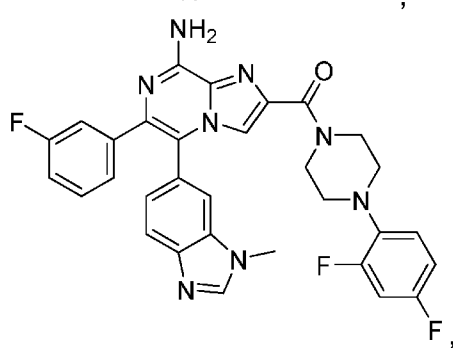
·HCl,

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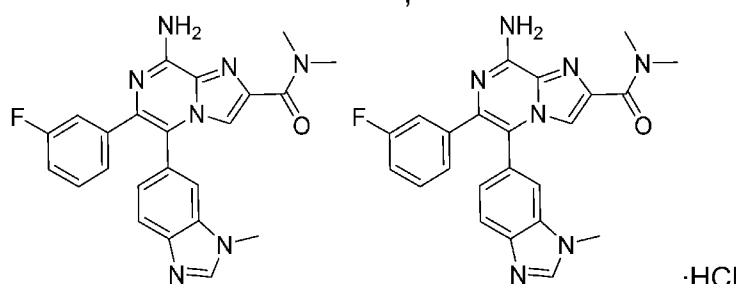
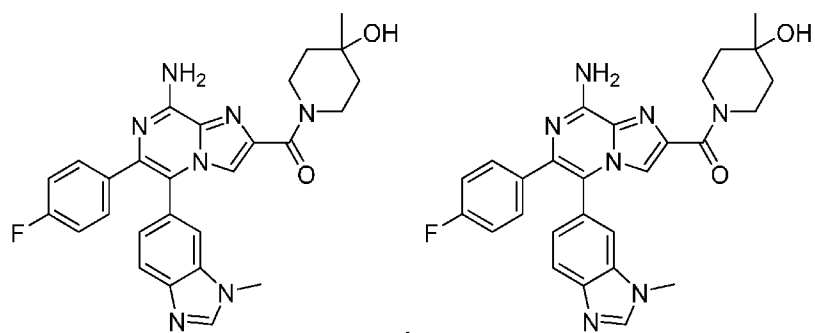
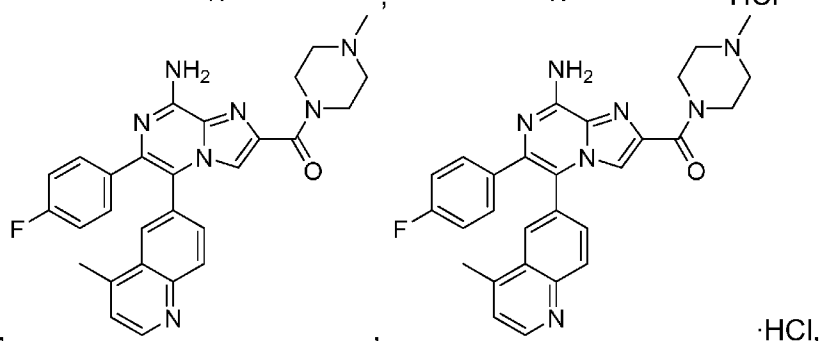
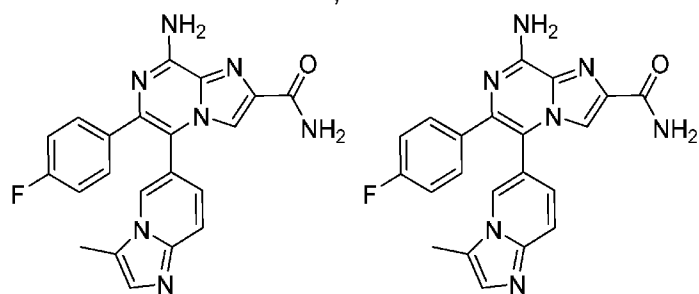
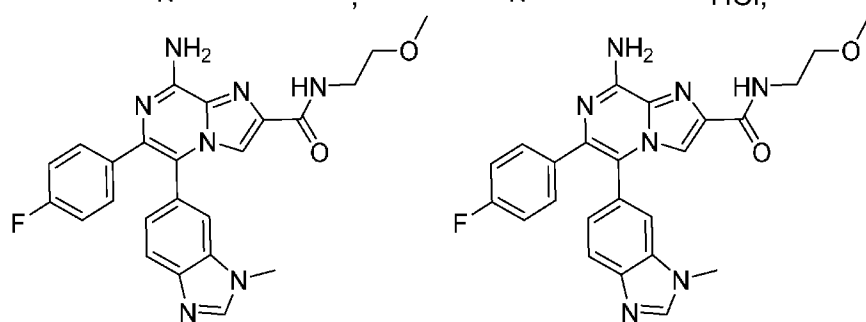
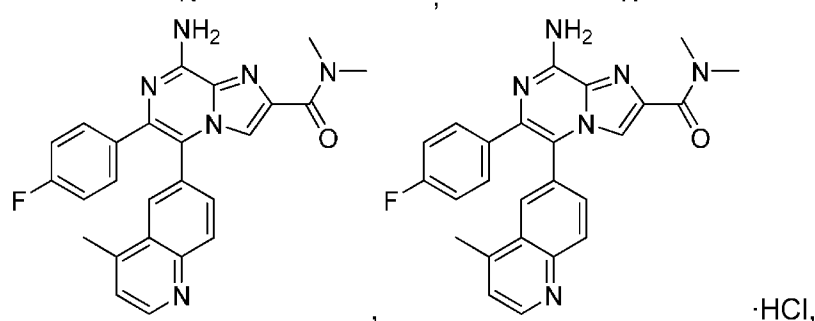


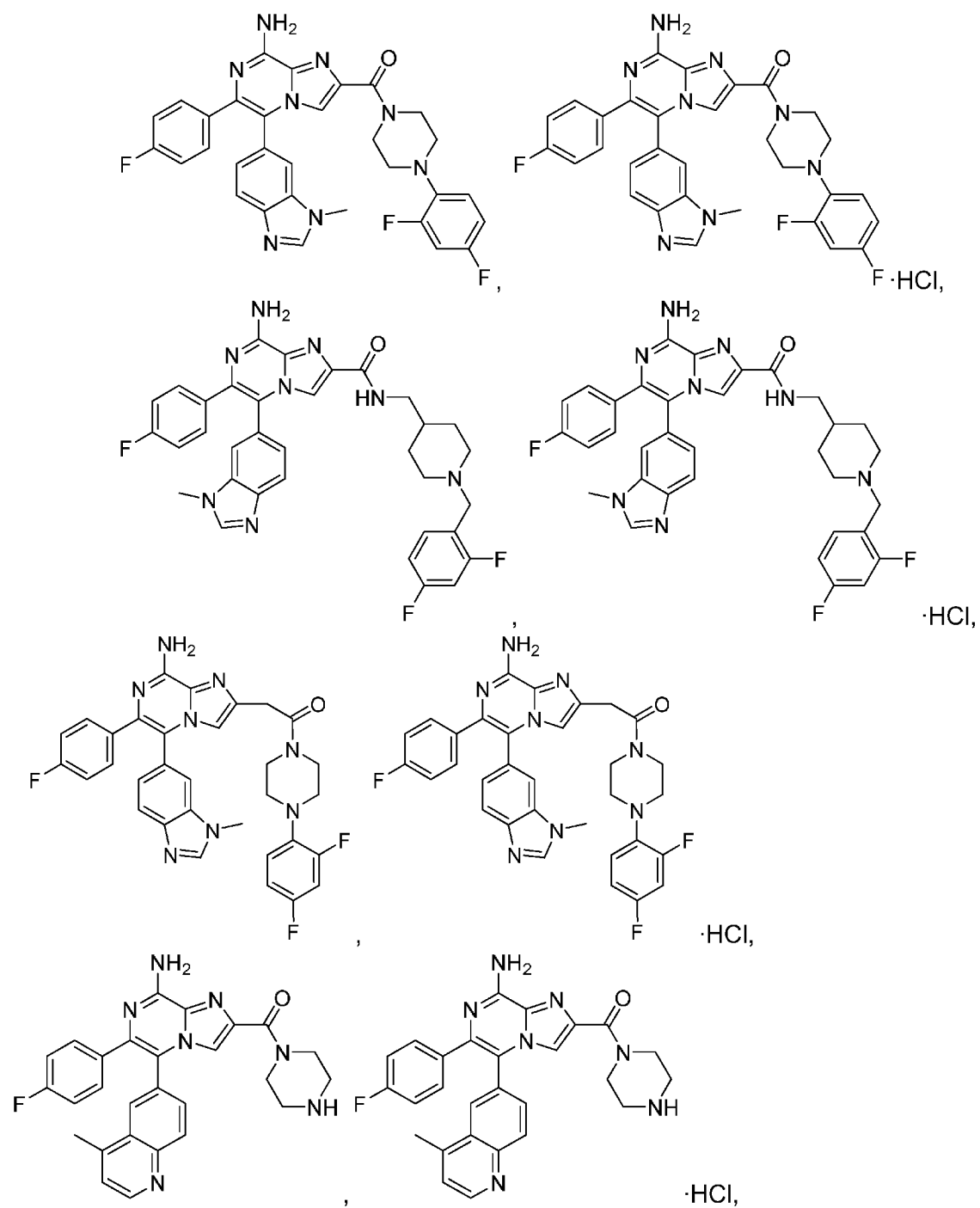
·HCl,

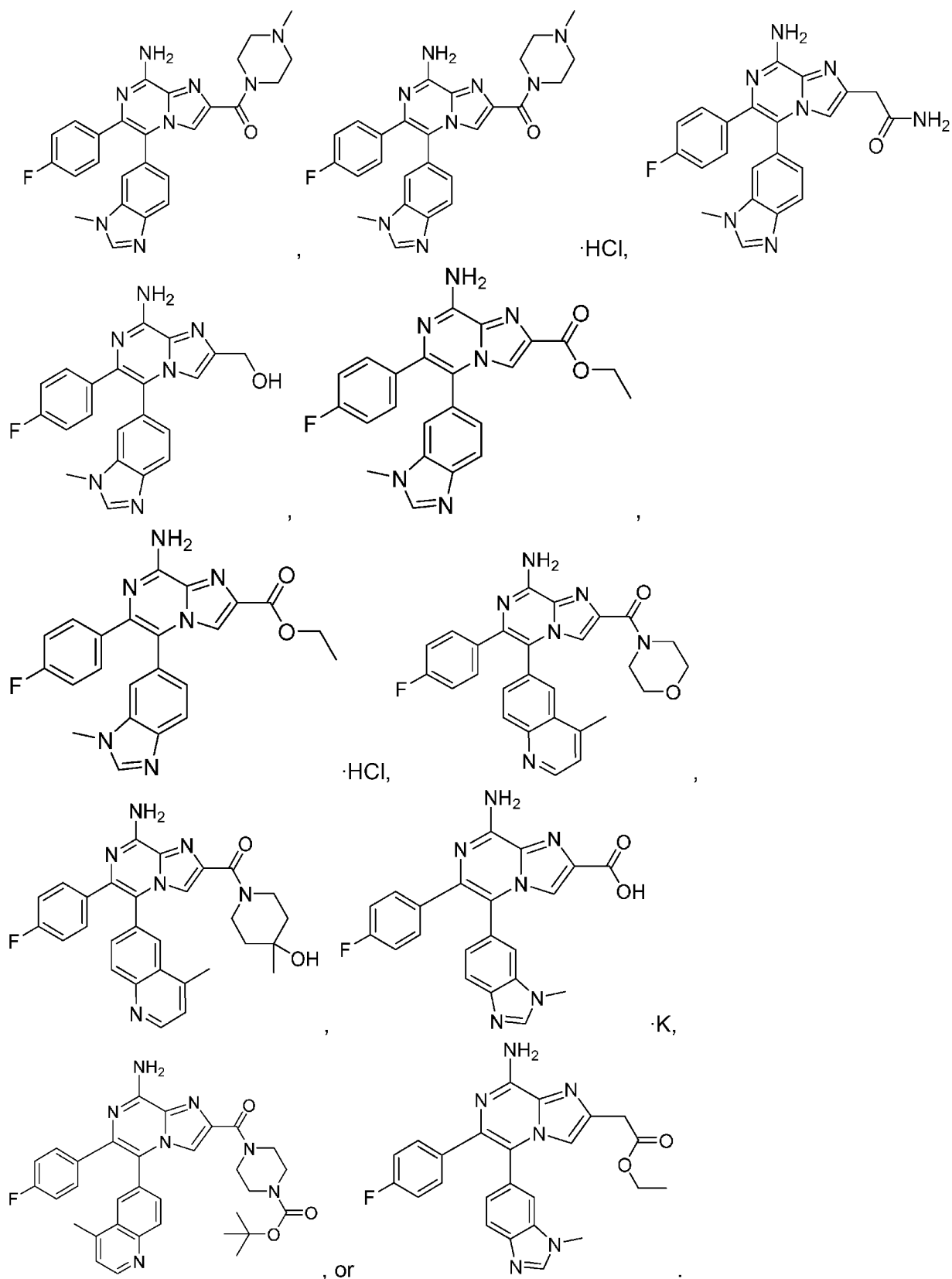
·HCl,



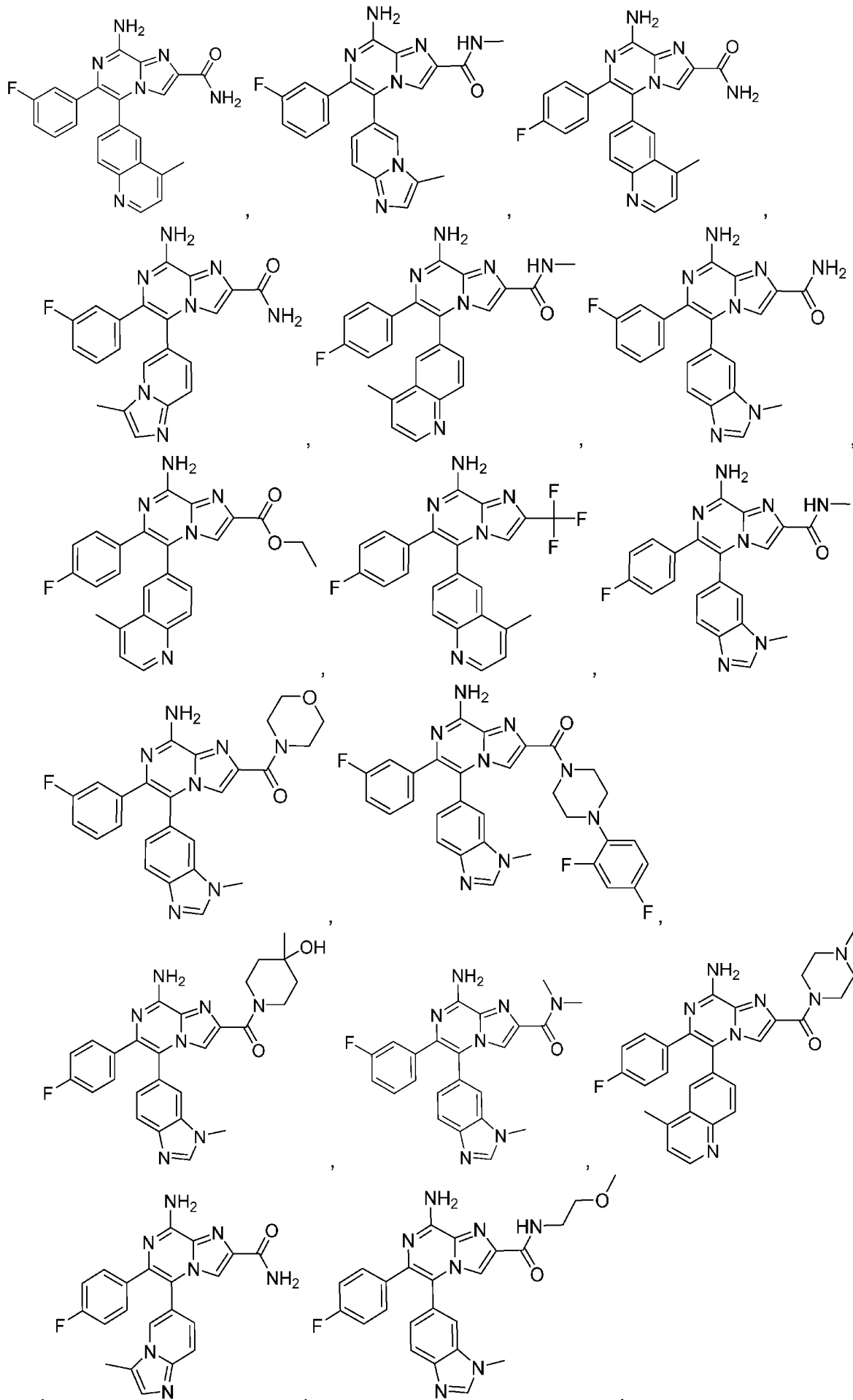
F·HCl,

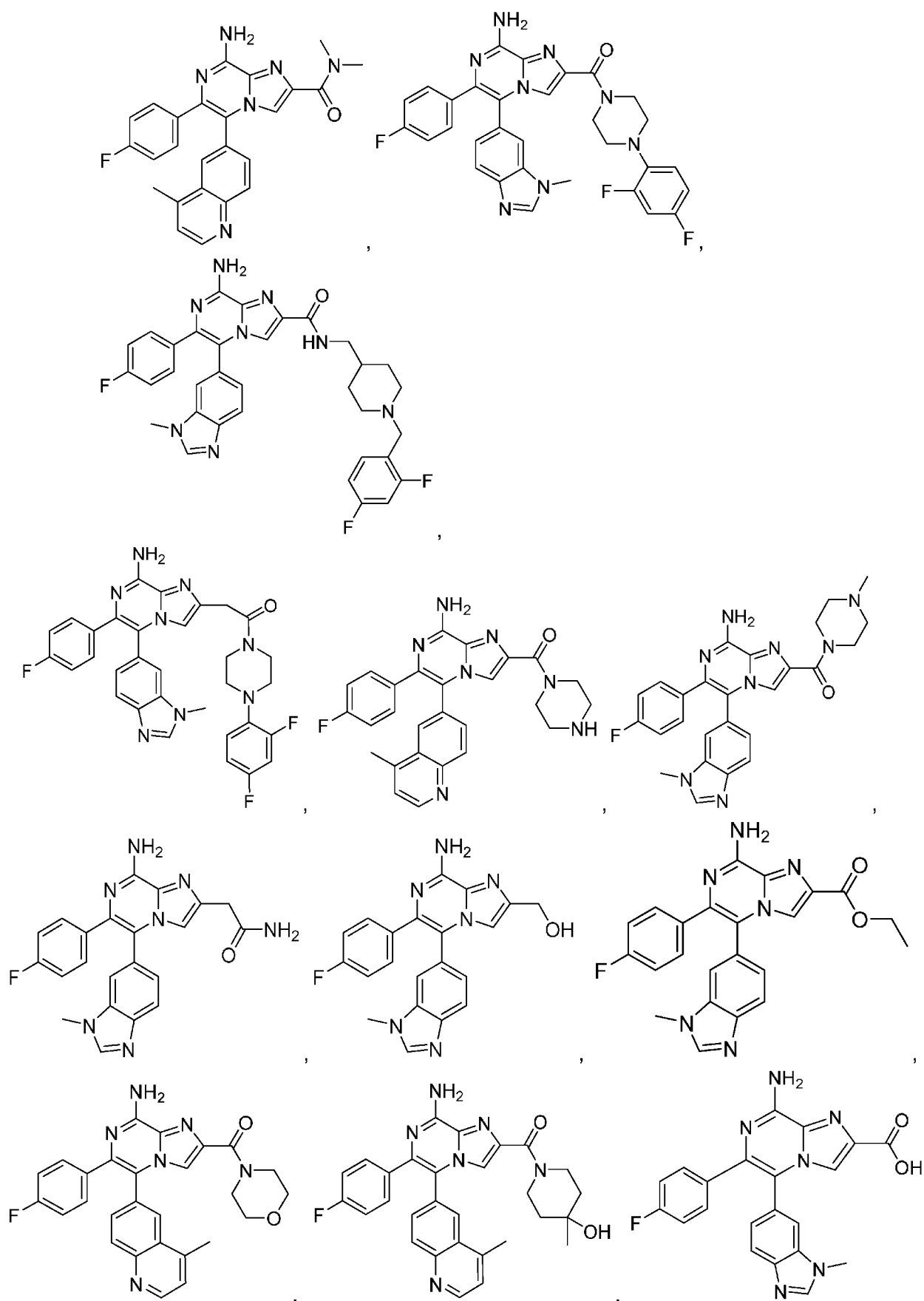
 $\cdot\text{HCl}$, $\cdot\text{HCl}$, $\cdot\text{HCl}$, $\cdot\text{HCl}$, $\cdot\text{HCl}$,

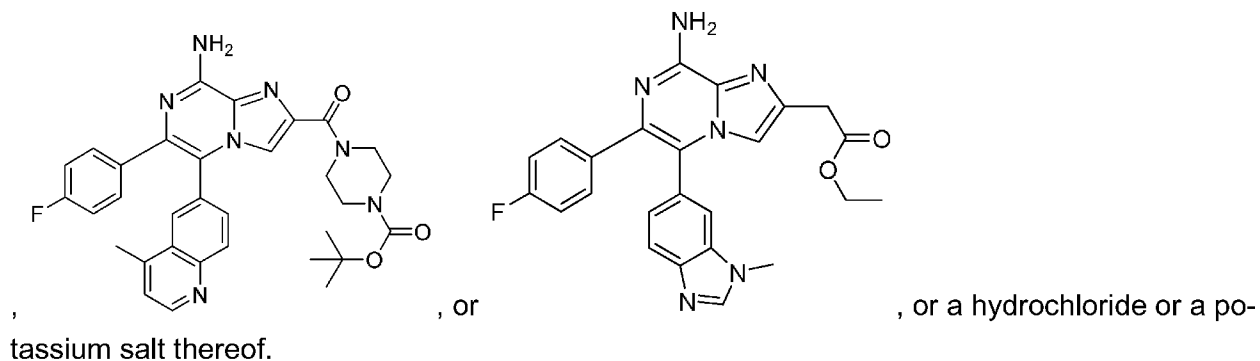




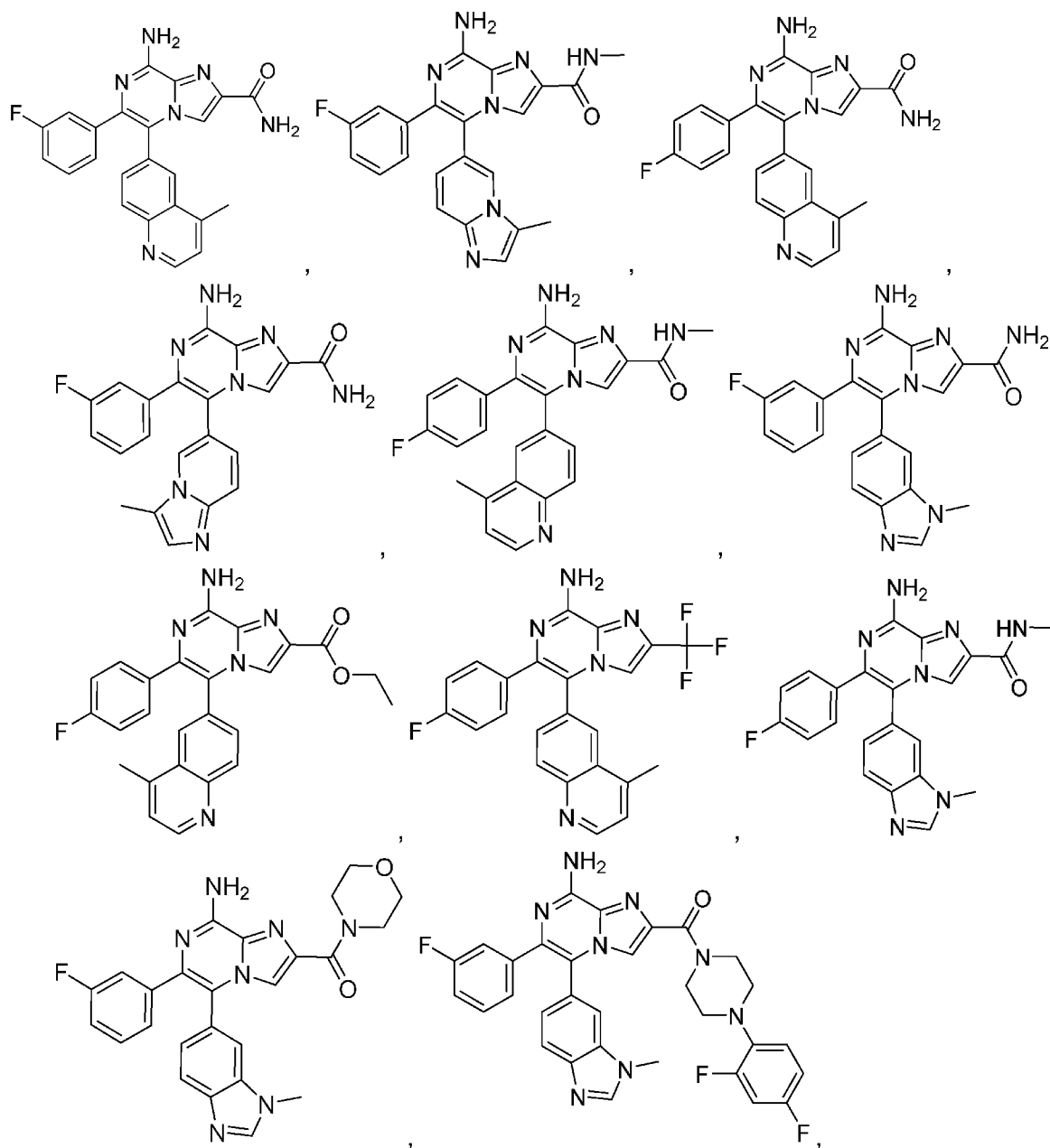
In the first aspect A1b, the present invention relates to a compound of formula (I) as defined above in the first aspect A1, wherein the compound is not:

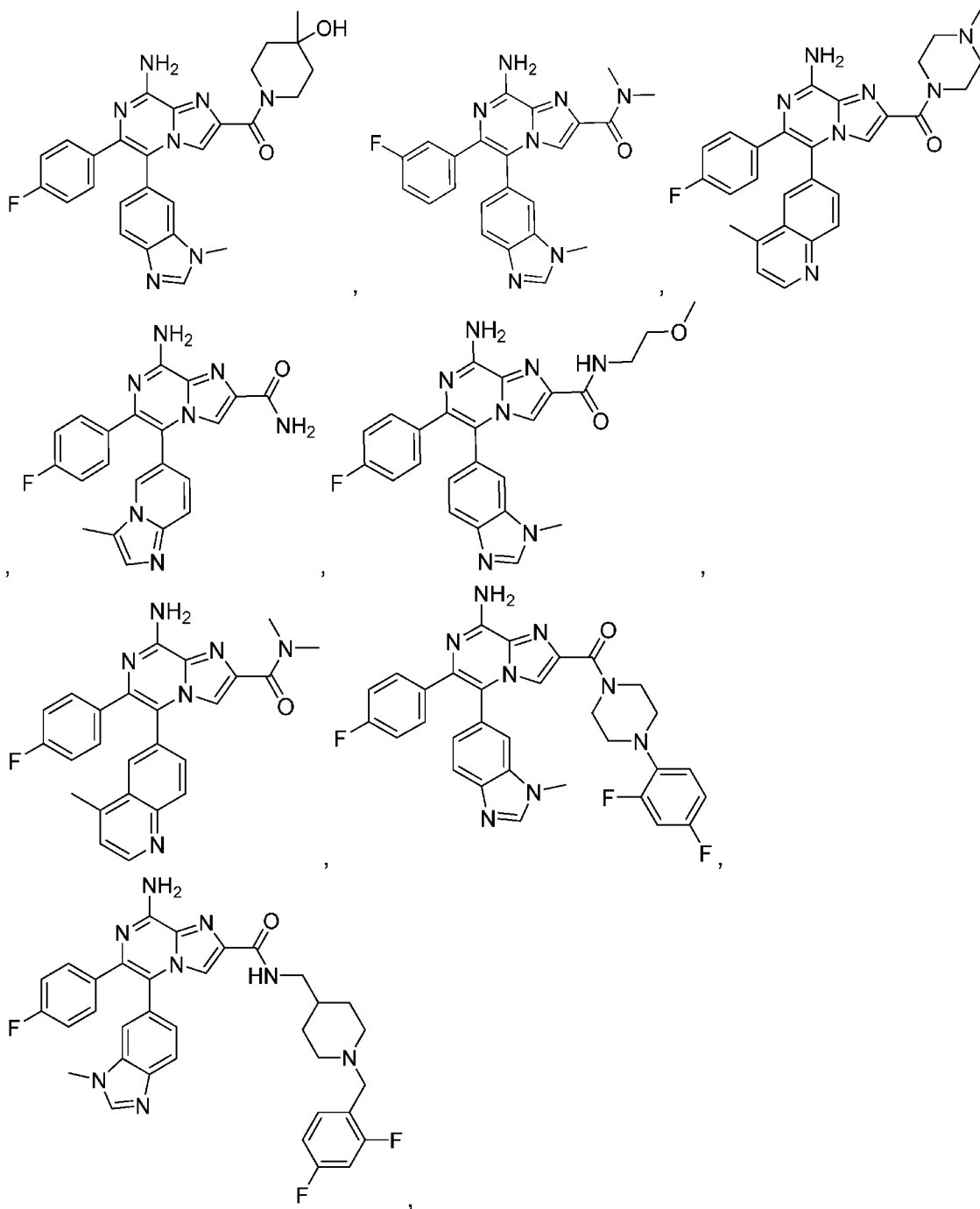


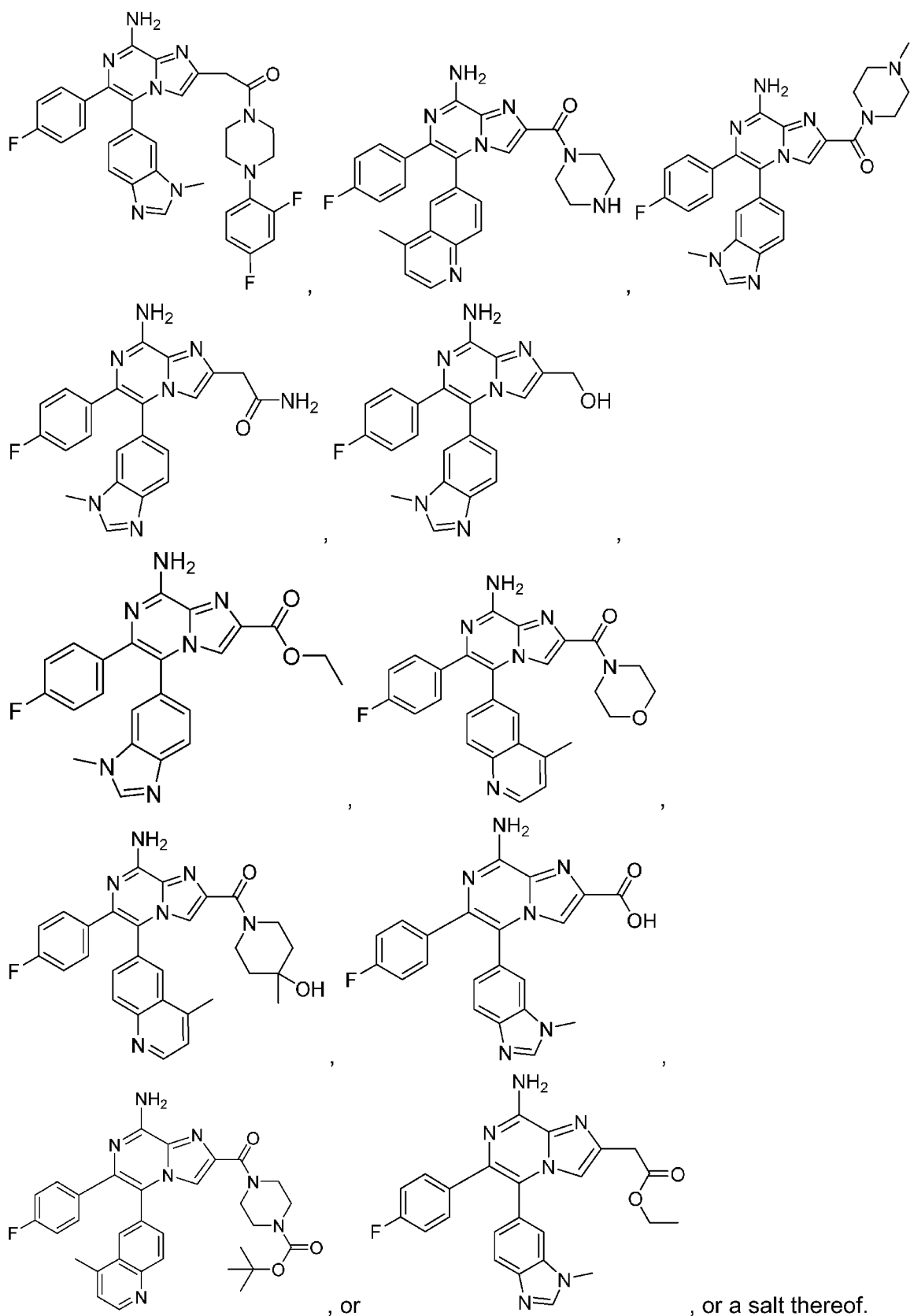




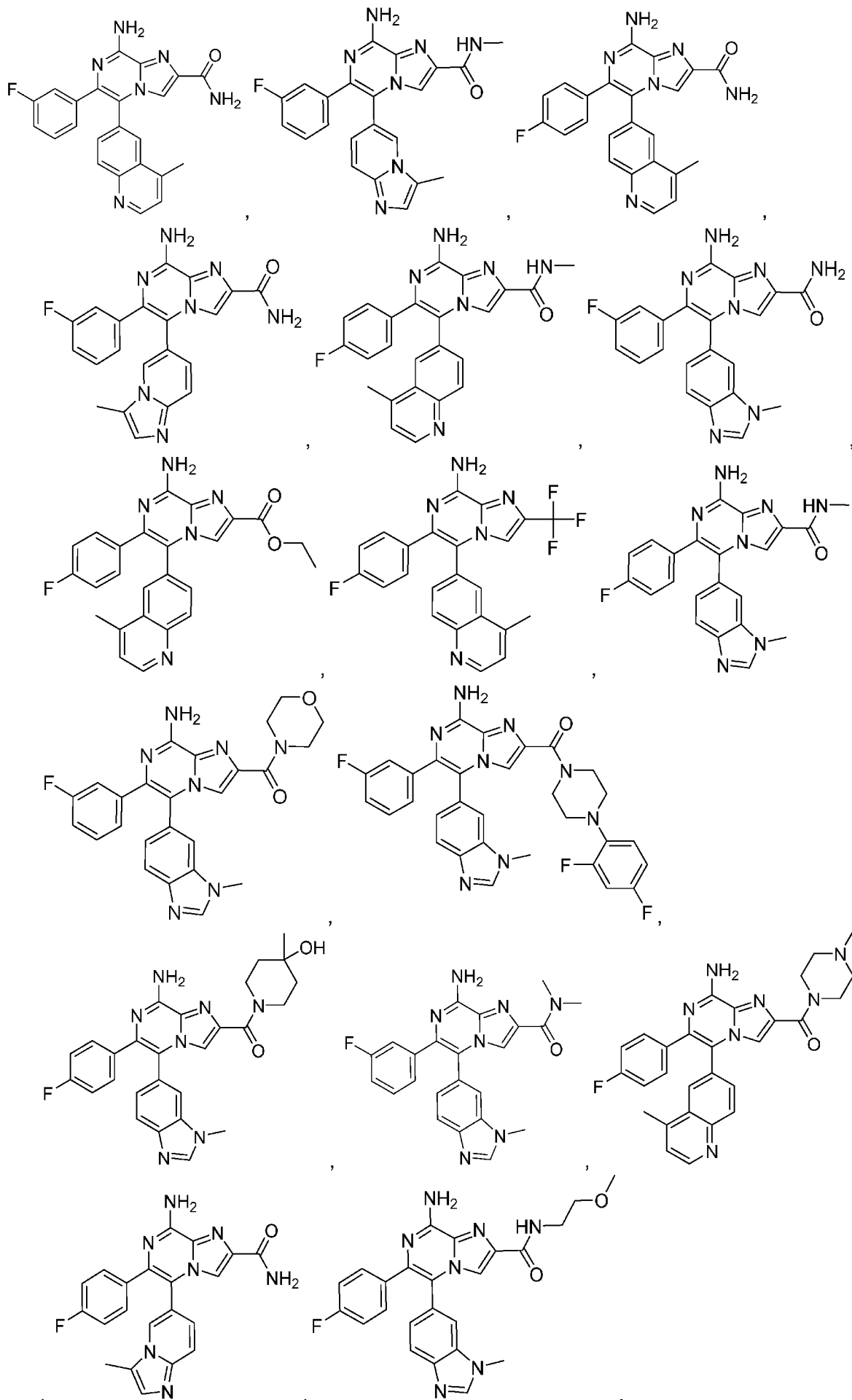
In the first aspect A1c, the present invention relates to a compound of formula (I) as defined
 5 above in the first aspect A1, wherein the compound is not:

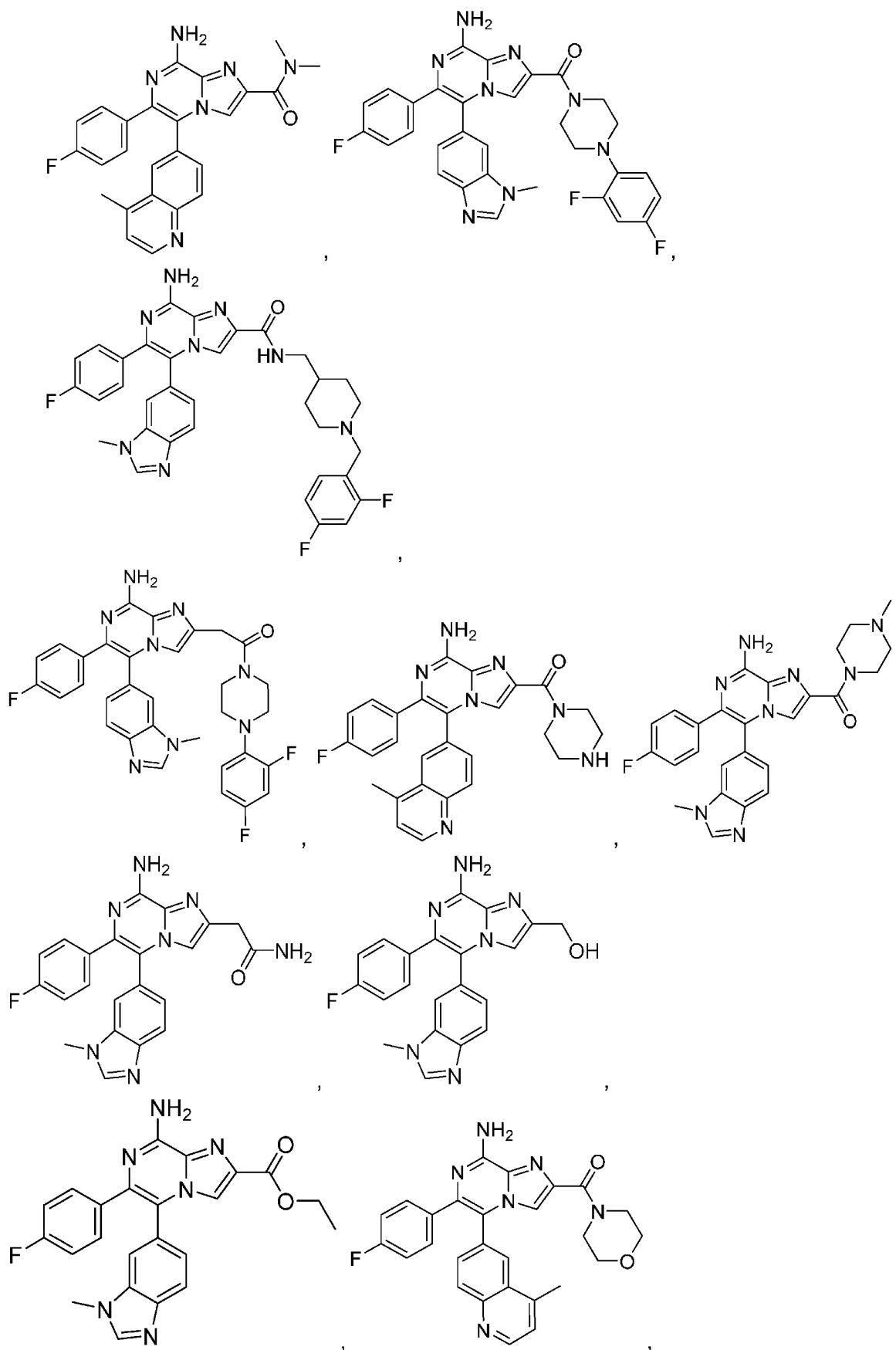


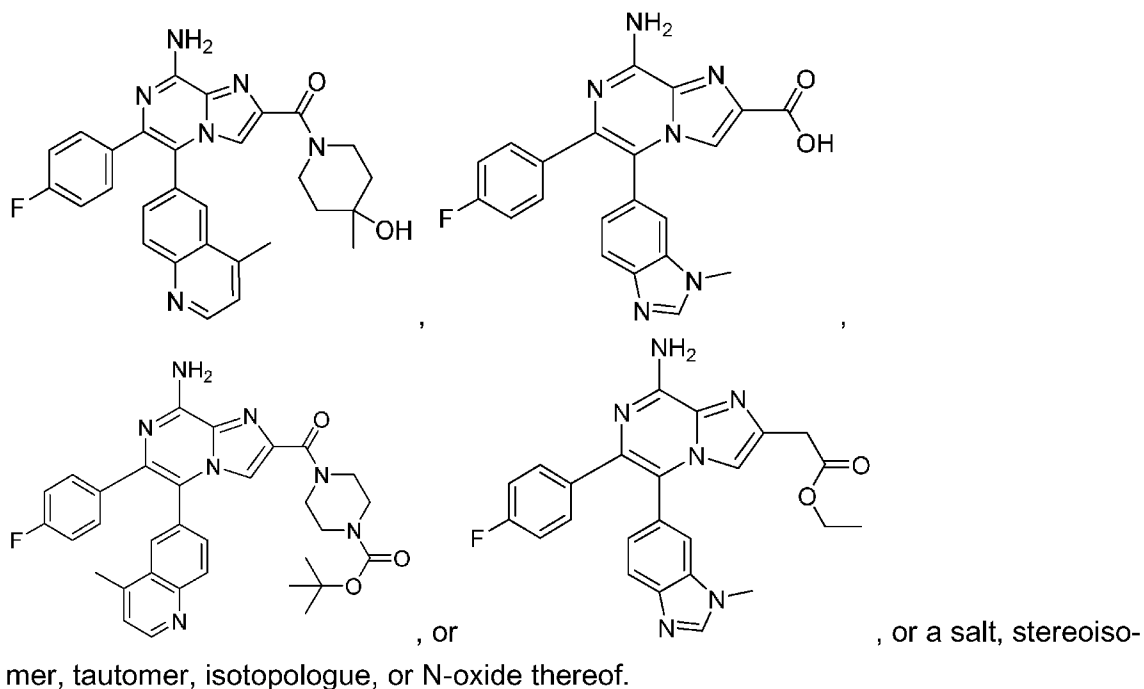




In the first aspect A1d, the present invention relates to a compound of formula (I) as defined above in the first aspect A1, wherein the compound is not:

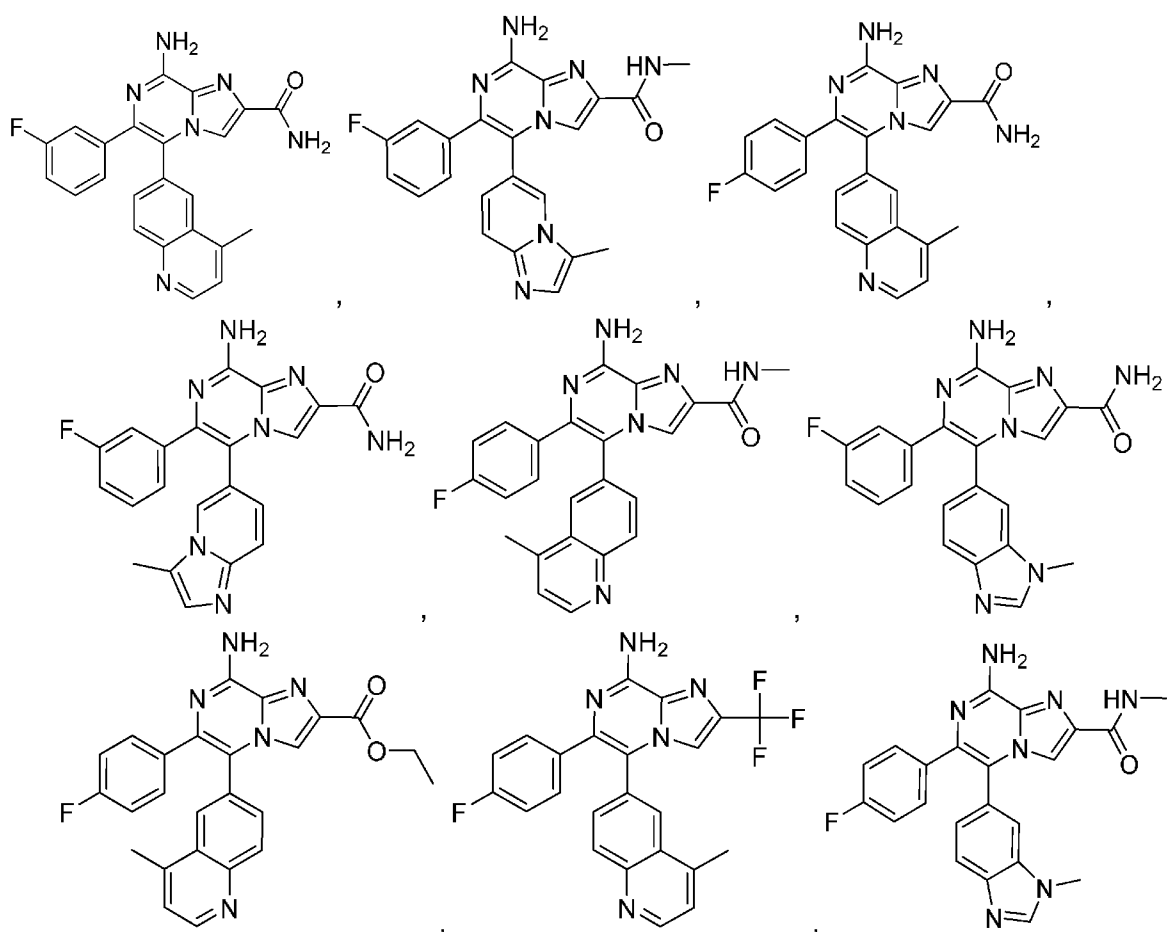


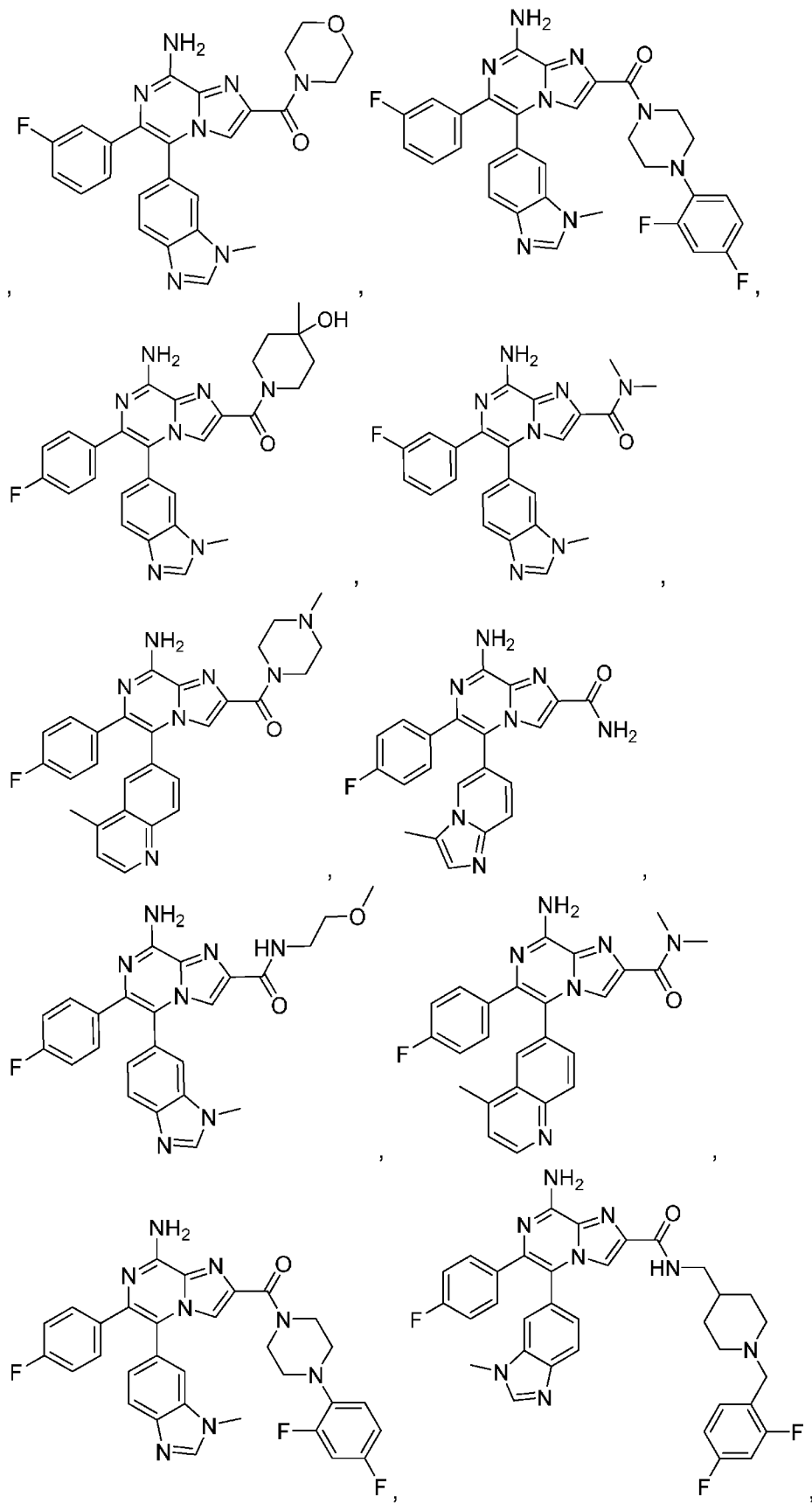


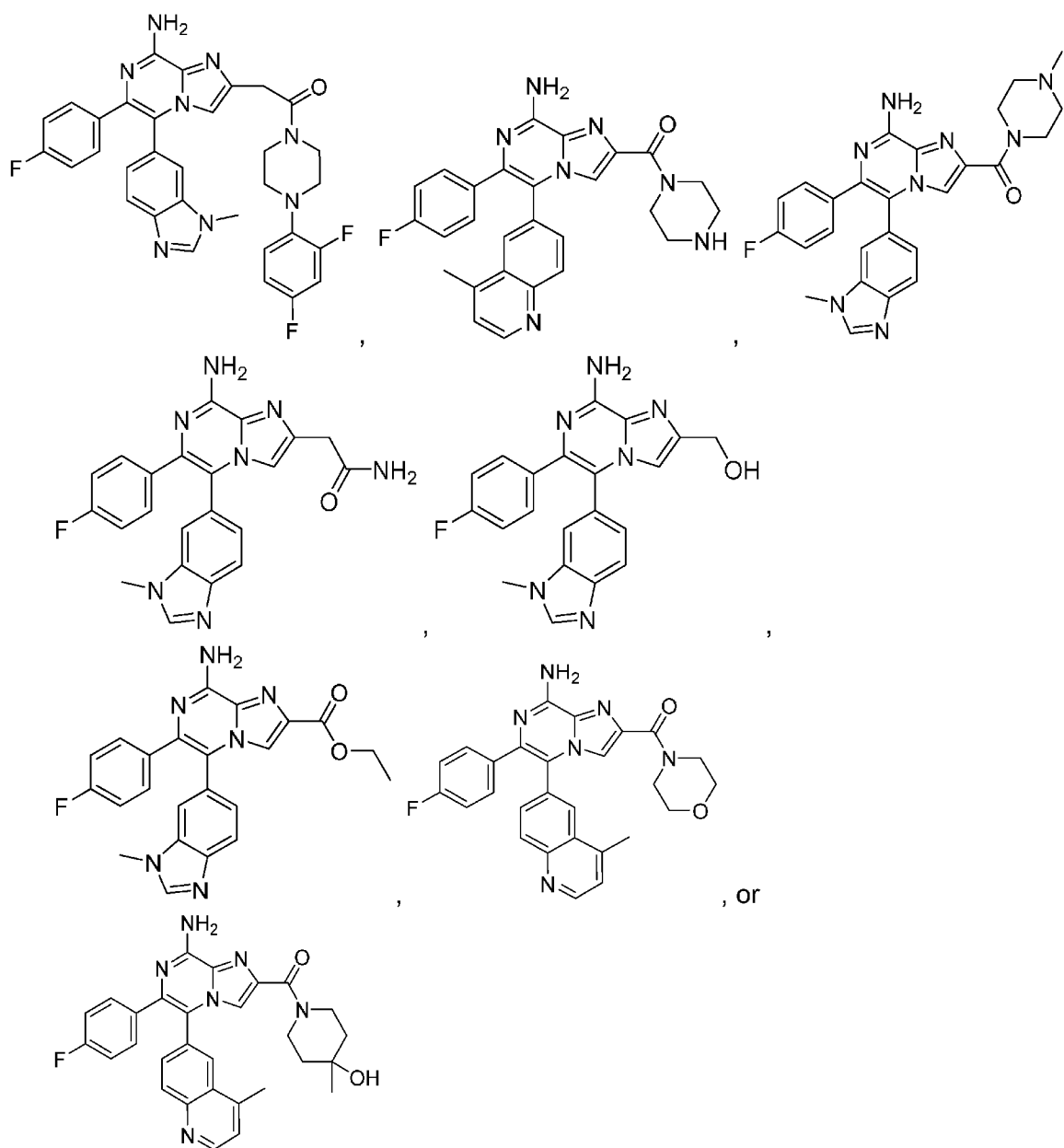


- 5 In the first aspect A1e, the present invention relates to a compound of formula (I) as defined above in the first aspect A1, wherein the compound is not:

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5

In a preferred embodiment, G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, furan-2-yl, furan-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, and pyrazol-5-yl, wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN, and wherein all other substituents have the meaning as defined above in the first aspects A1, A1a, A1b, A1c, A1d or A1e.

In another embodiment, G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-5-yl, furan-2-yl, and pyrazol-3-yl, wherein one or two of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN, and wherein all other substituents have the meaning as defined above in the first aspects A1, A1a, A1b, A1c, A1d or A1e.

In another embodiment, R^{1a} is selected from the group consisting of H and Cl; R^{1b} is selected from the group consisting of H and Cl; R^{1c} is selected from the group consisting of H and Cl; R^{2a} is CH_3 ; R^{2b} is CH_3 ; R^{2c} is CH_3 ; and wherein all other substituents have the meaning as defined above in the first aspects A1, A1a, A1b, A1c, A1d or A1e.

5 In another preferred embodiment, G^3 is selected from the group consisting of

- (i) C_1-C_6 -alkyl, a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R^3 ;
- (ii) $C(=O)R^5$, $C(=O)OR^6$, and $C(=O)N(R^{6a})(R^{6b})$;

wherein R^3 is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1-C_6 -alkyl, C_2-C_6 -alkenyl, C_2-C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^4 ;
- (ii) $C(=O)R^7$, $C(=O)OR^8$, $C(=O)N(R^{8a})(R^{8b})$, OR^8 , $N(R^{8a})(R^{8b})$, $N(R^8)C(=O)R^7$, $N(R^8)C(=O)OR^8$, and $N(R^8)C(=O)N(R^{8a})(R^{8b})$;

wherein R^4 is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1-C_6 -alkyl, C_2-C_6 -alkenyl, C_2-C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^9 ;
- (ii) $C(=O)R^{10}$, $C(=O)OR^{11}$, $C(=O)N(R^{11a})(R^{11b})$, OR^{11} , $N(R^{11a})(R^{11b})$, $N(R^{11})C(=O)R^{10}$, $N(R^{11})C(=O)OR^{11}$, $N(R^{11})C(=O)N(R^{11a})(R^{11b})$;

wherein R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1-C_6 -alkyl, C_2-C_6 -alkenyl, C_2-C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and

wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R⁷, R⁸, R^{8a}, R^{8b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹³;

wherein R⁹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁰, R¹¹, R^{11a}, R^{11b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁷;

wherein R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;
- (ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹³ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or

fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;

- (ii) C(=O)R²², C(=O)OR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b});

wherein R¹⁷ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;

- (ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b});

wherein R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and

wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

wherein R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

wherein R²⁸ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³¹;

wherein R²⁹, R³⁰, R³¹ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), and

wherein all other substituents have the meaning as defined above in the first aspects A1, A1a, A1b, A1c, A1d or A1e.

In another embodiment, G³ is selected from the group consisting of C(=O)R⁵, C(=O)OR⁶, and C(=O)N(R^{6a})(R^{6b});

wherein R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;

wherein R^{12} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ;

- (ii) $C(=O)R^{19}$, $C(=O)OR^{20}$, $C(=O)N(R^{20a})(R^{20b})$, OR^{20} , $N(R^{20a})(R^{20b})$, $N(R^{20})C(=O)R^{19}$, $N(R^{20})C(=O)OR^{20}$, $N(R^{20})C(=O)N(R^{20a})(R^{20b})$;

and/or two R^{12} present on one carbon atom together form $=O$;

wherein R^{18} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{24} ;

- (ii) $C(=O)R^{25}$, $C(=O)OR^{26}$, $C(=O)N(R^{26a})(R^{26b})$, OR^{26} , $N(R^{26a})(R^{26b})$, $N(R^{26})C(=O)R^{25}$, $N(R^{26})C(=O)OR^{26}$, $N(R^{26})C(=O)N(R^{26a})(R^{26b})$;

wherein R^{19} , R^{20} , R^{20a} , R^{20b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and

wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

wherein R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

wherein R²⁹, R³⁰ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl); and

wherein all other substituents have the meaning as defined above in the first aspects A1, A1a, A1b, A1c, A1d or A1e.

In another embodiment, said compound is selected from the group consisting of 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid; 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-{2,6-diazaspiro[3.4]octane-2-carbonyl}-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(pyridin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(4-fluoropyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[3-(difluoromethoxy)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-

[(morpholin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[2-(methylamino)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1,1-dioxo-1 λ^6 -thiolan-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2-oxopyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-hydroxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(4,4-difluoropiperidine-1-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-[4-(difluoromethyl)quinolin-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-($^2\text{H}_3$)methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(3-ethylpyrrolidin-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-[3-methylimidazo[1,2-a]pyridin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(4-aminobutyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-[4-(2,4-difluorophenyl)piperazine-1-carbonyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 6-(4-fluorophenyl)-2-[4-(2-methoxyethyl)piperazine-1-carbonyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(piperidin-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-2-(piperazine-1-carbonyl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N,N-diethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-methylpyrrolidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[3-(dimethylamino)butyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-methoxy-

ethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-(dimethylamino)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(prop-2-yn-1-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylpiperidin-4-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[[6-(2-hydroxypropan-2-yl)pyridin-2-yl]methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(3,3,3-trifluoropropyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-ethylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-(dimethylamino)ethyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(3-hydroxybutan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(4-methylmorpholin-2-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-3-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[1-(methoxymethyl)cyclopropyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methyl-2-oxopyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-{2-[(oxolan-2-yl)methoxy]ethyl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(1,1,1-trifluoro-3-hydroxypropan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]-3-methylpyrrolidin-3-ol; 8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine; 8-amino-6-(4-fluorophenyl)-N-(1-methylpyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-hydroxycyclopentyl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-dimethylpropyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methoxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2-fluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-[(1-hydroxycyclopropyl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-

chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[1-(1-hydroxycyclopropyl)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{3-chloroimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(3-hydroxypropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[1-(dimethylamino)-2-methylpropan-2-yl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-methylazetidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-({1-[(2,4-difluorophenyl)methyl]piperidin-4-yl}methyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[2-methyl-1-(propan-2-yloxy)propan-2-yl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-2-methylphenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-[1-(2,2-difluoroethyl)-1H-1,3-benzodiazol-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 6-(4-fluorophenyl)-2-[(methylamino)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[2-(pyrrolidin-1-yl)ethyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-[1-(propan-2-yl)-1H-1,3-benzodiazol-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyanophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imid-

azo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxylic acid; 8-amino-6-(3-cyanophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(2-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyanophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-4-fluorophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-2-yl]ethan-1-one; 8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-[1-(trifluoromethyl)cyclopropyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-4-fluorophenyl)-N-(2,2-difluoroethyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-[1-(trifluoromethyl)cyclopropyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 2-(4,5-dihydro-1H-imidazol-2-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1-cyanocyclopropyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1,1-difluoropropan-2-yl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-cyanoethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid; and 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide.

In a second aspect A2, the present invention relates to a pharmaceutical composition comprising a pharmaceutically effective amount of the compound according to formula (I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e, and optionally a pharmaceutically acceptable carrier, diluent or excipient. Put in different words, the present invention relates to the compound according to formula (I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e, or a pharmaceutical composition comprising a pharmaceutically effective amount of the compound according to formula (I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e, for use in medicine.

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In a third aspect A3, the present invention relates to a compound according to formula (I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e, or a pharmaceutical composition comprising a pharmaceutically effective amount of the compound according to formula

(I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e, for use in the treatment of a disease selected from the group consisting of cancer, Parkinson's disease, Huntington's disease, Alzheimer's disease, psychosis, stroke, extra pyramidal syndrome (in particular dystonia, akathisia, pseudoparkinsonism and tardive dyskinesia), attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), amyotrophic lateral sclerosis, cirrhosis, fibrosis, fatty liver, addictive behavior, dermal fibrosis (in particular dermal fibrosis in scleroderma), sleep disorders, AIDS, autoimmune diseases, infections, atherosclerosis, ischemia-reperfusion injury, idiopathic pulmonary fibrosis, systemic sclerosis, irritable bowel disease and as analgesic. Further indications are described below in the detailed description, together with preferred combinations, namely the compounds of the present invention together with check-point inhibitors, wherein such combinations are used for the treatment of cancer.

In a fourth aspect A4, the present invention is concerned with a method for antagonizing the adenosine A2A receptor, wherein said receptor is exposed to at least one compound according to formula (I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e, wherein said method is preferably performed outside the human or animal body.

In a fifth aspect A5, the present invention relates to the use of a compound according to formula (I) as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e as adenosine A2A receptor antagonist.

Detailed description relating to aspects A1, A1a, A1b, A1c, A1d, A1e, A2, A3, A4, and A5

In the following, preferred embodiments of the substituents in the above formula (I) are described in further detail.

The following embodiments relate to G¹ as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e.

In embodiment 1(A), G¹ is selected from the group consisting of phenyl and a 5- to 6-membered fully unsaturated heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN.

In a preferred embodiment 1(B), G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, furan-2-yl, furan-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, and pyrazol-5-yl, wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN.

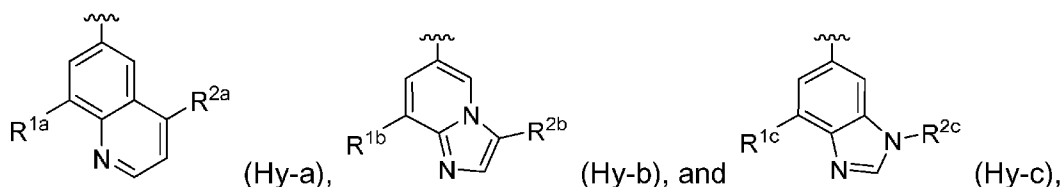
In another embodiment 1(C), G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-5-yl, furan-2-yl, and pyrazol-3-yl, wherein one or two of the

substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN.

In another embodiment 1(D), G¹ is phenyl, wherein one or two of the substitutable carbon atoms in the aforementioned phenyl is substituted with same or different substituents selected from the group consisting of CH₃, F and CN.

The following embodiments relate to G² as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e.

In embodiment 2(A), G² is selected from the group consisting of



wherein

R^{1a} is selected from the group consisting of H and Cl;

R^{1b} is selected from the group consisting of H and Cl;

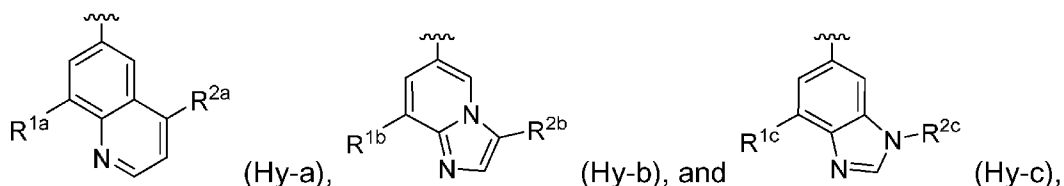
R^{1c} is selected from the group consisting of H and Cl;

R^{2a} is selected from the group consisting of Cl and C₁-C₃-alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R^{2b} is selected from the group consisting of Cl and C₁-C₃-alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F; and

R^{2c} is C₁-C₃-alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

In another embodiment 2(B), G² is selected from the group consisting of



wherein

R^{1a} is selected from the group consisting of H and Cl;

R^{1b} is selected from the group consisting of H and Cl;

R^{1c} is selected from the group consisting of H and Cl;

R^{2a} is CH₃;

R^{2b} is CH₃;

R^{2c} is CH₃;

The following embodiments relate to G³ as defined above in the first aspects A1, A1a, A1b, A1c, A1d, and A1e.

In embodiment 3(A), G³ is selected from the group consisting of

- (i) C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R³;
- (ii) C(=O)R⁵, C(=O)OR⁶, C(=O)SR⁶, C(=O)N(R^{6a})(R^{6b}), OR⁶, S(=O)_nR⁶, S(=O)_nN(R^{6a})(R^{6b}), S(=O)_mOR⁶, N(R^{6a})(R^{6b}), N(R⁶)C(=O)R⁵, N(R⁶)C(=O)OR⁶, N(R⁶)C(=O)N(R^{6a})(R^{6b}), N(R⁶)S(=O)_n(R⁶), N(R⁶)S(=O)_mN(R^{6a})(R^{6b}), and N(R⁶)S(=O)_mOR⁶;

wherein R³ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁴;
- (ii) C(=O)R⁷, C(=O)OR⁸, C(=O)SR⁸, C(=O)N(R^{8a})(R^{8b}), OR⁸, S(=O)_nR⁸, S(=O)_nN(R^{8a})(R^{8b}), S(=O)_mOR⁸, N(R^{8a})(R^{8b}), N(R⁸)C(=O)R⁷, N(R⁸)C(=O)OR⁸, N(R⁸)C(=O)N(R^{8a})(R^{8b}), N(R⁸)S(=O)_n(R⁸), N(R⁸)S(=O)_mN(R^{8a})(R^{8b}), and N(R⁸)S(=O)_mOR⁸;

wherein R⁴ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁹;
- (ii) C(=O)R¹⁰, C(=O)OR¹¹, C(=O)SR¹¹, C(=O)N(R^{11a})(R^{11b}), OR¹¹, S(=O)_nR¹¹, S(=O)_nN(R^{11a})(R^{11b}), S(=O)_mOR¹¹, N(R^{11a})(R^{11b}), N(R¹¹)C(=O)R¹⁰, N(R¹¹)C(=O)OR¹¹, N(R¹¹)C(=O)N(R^{11a})(R^{11b}), N(R¹¹)S(=O)_n(R¹¹), N(R¹¹)S(=O)_mN(R^{11a})(R^{11b}), and N(R¹¹)S(=O)_mOR¹¹;

wherein R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;

wherein R^7 , R^8 , R^{8a} , R^{8b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{13} ;

wherein R^9 is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, $C(=O)R^{14}$, $C(=O)OR^{15}$, $C(=O)SR^{15}$, $C(=O)N(R^{15a})(R^{15b})$, OR^{15} , $S(=O)_nR^{15}$, $S(=O)_nN(R^{15a})(R^{15b})$, $S(=O)_mOR^{15}$, $N(R^{15a})(R^{15b})$, $N(R^{15})C(=O)R^{14}$, $N(R^{15})C(=O)OR^{15}$, $N(R^{15})C(=O)N(R^{15a})(R^{15b})$, $N(R^{15})S(=O)_n(R^{15})$, $N(R^{15})S(=O)_mN(R^{15a})(R^{15b})$, and $N(R^{15})S(=O)_mOR^{15}$;

wherein R^{10} , R^{11} , R^{11a} , R^{11b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{17} ;

wherein R^{12} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon

or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ;

- (ii) $C(=O)R^{19}$, $C(=O)OR^{20}$, $C(=O)SR^{20}$, $C(=O)N(R^{20a})(R^{20b})$, OR^{20} , $S(=O)_nR^{20}$, $S(=O)_nN(R^{20a})(R^{20b})$, $S(=O)_mOR^{20}$, $N(R^{20a})(R^{20b})$, $N(R^{20})C(=O)R^{19}$, $N(R^{20})C(=O)OR^{20}$, $N(R^{20})C(=O)N(R^{20a})(R^{20b})$, $N(R^{20})S(=O)_n(R^{20})$, $N(R^{20})S(=O)_mN(R^{20a})(R^{20b})$, and $N(R^{20})S(=O)_mOR^{20}$;

and/or two R^{12} present on one carbon atom together form $=O$;

wherein R^{13} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{21} ;
- (ii) $C(=O)R^{22}$, $C(=O)OR^{23}$, $C(=O)SR^{23}$, $C(=O)N(R^{23a})(R^{23b})$, OR^{23} , $S(=O)_nR^{23}$, $S(=O)_nN(R^{23a})(R^{23b})$, $S(=O)_mOR^{23}$, $N(R^{23a})(R^{23b})$, $N(R^{23})C(=O)R^{22}$, $N(R^{23})C(=O)OR^{23}$, $N(R^{23})C(=O)N(R^{23a})(R^{23b})$, $N(R^{23})S(=O)_n(R^{23})$, $N(R^{23})S(=O)_mN(R^{23a})(R^{23b})$, and $N(R^{23})S(=O)_mOR^{23}$;

wherein R^{14} , R^{15} , R^{15a} , R^{15b} are independently selected from the group consisting of

- (i) H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, and C_2 - C_6 -alkynyl, wherein each substitutable carbon atom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R^{16} ;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R^{32} ;

wherein R^{16} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, $N(R^{33a})(R^{33b})$, $C(=O)NR^{33a}R^{33b}$, $S(=O)_nNR^{33a}R^{33b}$, OR^{33} and $S(=O)_nR^{33}$;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable

carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R^{32} ;

wherein R^{17} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl);

wherein R^{18} is selected from the group consisting of

(i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{24} ;

(ii) $C(=O)R^{25}$, $C(=O)OR^{26}$, $C(=O)SR^{26}$, $C(=O)N(R^{26a})(R^{26b})$, OR^{26} , $S(=O)_nR^{26}$, $S(=O)_nN(R^{26a})(R^{26b})$, $S(=O)_mOR^{26}$, $N(R^{26a})(R^{26b})$, $N(R^{26})C(=O)R^{25}$, $N(R^{26})C(=O)OR^{26}$, $N(R^{26})C(=O)N(R^{26a})(R^{26b})$, $N(R^{26})S(=O)_n(R^{26})$, $N(R^{26})S(=O)_mN(R^{26a})(R^{26b})$, and $N(R^{26})S(=O)_mOR^{26}$;

wherein R^{19} , R^{20} , R^{20a} , R^{20b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{27} ;

wherein R^{21} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl);

wherein R^{22} , R^{23} , R^{23a} , R^{23b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{28} ;

wherein R^{24} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{29} ;

wherein R^{25} , R^{26} , R^{26a} , R^{26b} are independently selected from the group consisting of H, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, and C_2 - C_4 -haloalkynyl;

wherein R^{27} is selected from the group consisting of halogen, CN, NO_2 , OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl), C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{30} ;

wherein R^{28} is selected from the group consisting of halogen, CN, NO_2 , OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl), C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{31} ;

wherein R^{29} , R^{30} , R^{31} are independently selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl);

wherein R^{32} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, C_2 - C_4 -haloalkynyl, $C(=O)R^{34}$, $C(=O)OR^{33}$, $C(=O)SR^{33}$, $C(=O)N(R^{33a})(R^{33b})$, OR^{33} , $S(=O)_nR^{33}$, $S(=O)_nN(R^{33a})(R^{33b})$, $S(=O)_mOR^{33}$, $N(R^{33a})(R^{33b})$, $N(R^{33})C(=O)R^{34}$, $N(R^{33})C(=O)OR^{33}$, $N(R^{33})C(=O)N(R^{33a})(R^{33b})$, $N(R^{33})S(=O)_n(R^{33})$, $N(R^{33})S(=O)_mN(R^{33a})(R^{33b})$, and $N(R^{33})S(=O)_mOR^{33}$;

wherein R^{33} , R^{33a} , R^{33b} , R^{34} are independently selected from the group consisting of H, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, and C_2 - C_4 -haloalkynyl;

and wherein

- 5 n is 0, 1 or 2; and
 m is 1 or 2.

In a preferred embodiment 3(B), G^3 is selected from the group consisting of

- 10 (i) C_1 - C_6 -alkyl, a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R^3 ;

- 15 (ii) $C(=O)R^5$, $C(=O)OR^6$, and $C(=O)N(R^{6a})(R^{6b})$;

wherein R^3 is selected from the group consisting of

- 20 (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^4 ;

- 25 (ii) $C(=O)R^7$, $C(=O)OR^8$, $C(=O)N(R^{8a})(R^{8b})$, OR^8 , $N(R^{8a})(R^{8b})$, $N(R^8)C(=O)R^7$, $N(R^8)C(=O)OR^8$, and $N(R^8)C(=O)N(R^{8a})(R^{8b})$;

wherein R^4 is selected from the group consisting of

- 30 (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^9 ;
- 35 (ii) $C(=O)R^{10}$, $C(=O)OR^{11}$, $C(=O)N(R^{11a})(R^{11b})$, OR^{11} , $N(R^{11a})(R^{11b})$, $N(R^{11})C(=O)R^{10}$, $N(R^{11})C(=O)OR^{11}$, $N(R^{11})C(=O)N(R^{11a})(R^{11b})$;
- 40 wherein R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or

heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R⁷, R⁸, R^{8a}, R^{8b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹³;

wherein R⁹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁰, R¹¹, R^{11a}, R^{11b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁷;

wherein R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;
- (ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹³ is selected from the group consisting of

- 5 (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;
- 10 (ii) C(=O)R²², C(=O)OR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b});
- wherein R¹⁷ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);
- 15 wherein R¹⁸ is selected from the group consisting of
- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;
- 20 (ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b});
- 25 wherein R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;
- 30 wherein R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);
- 35 wherein R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises
- 40

one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

wherein R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

wherein R²⁸ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³¹;

wherein R²⁹, R³⁰, R³¹ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

In another embodiment 3(C), G³ is selected from the group consisting of C(=O)R⁵, C(=O)OR⁶, and C(=O)N(R^{6a})(R^{6b});

wherein R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;

wherein R^{12} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ;

- (ii) $C(=O)R^{19}$, $C(=O)OR^{20}$, $C(=O)N(R^{20a})(R^{20b})$, OR^{20} , $N(R^{20a})(R^{20b})$, $N(R^{20})C(=O)R^{19}$, $N(R^{20})C(=O)OR^{20}$, $N(R^{20})C(=O)N(R^{20a})(R^{20b})$;

and/or two R^{12} present on one carbon atom together form $=O$;

wherein R^{18} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{24} ;

- (ii) $C(=O)R^{25}$, $C(=O)OR^{26}$, $C(=O)N(R^{26a})(R^{26b})$, OR^{26} , $N(R^{26a})(R^{26b})$, $N(R^{26})C(=O)R^{25}$, $N(R^{26})C(=O)OR^{26}$, $N(R^{26})C(=O)N(R^{26a})(R^{26b})$;

wherein R^{19} , R^{20} , R^{20a} , R^{20b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and

wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

wherein R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

wherein R²⁹, R³⁰ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

In another embodiment 3(D), G³ is selected from the group consisting of C(=O)R⁵, C(=O)OR⁶, and C(=O)N(R^{6a})(R^{6b});

wherein R⁵ is selected from the group consisting of a 5- to 6-membered saturated or partially unsaturated heterocyclic ring and a 7- to 10-membered saturated or partially unsaturated heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O or N, wherein said N-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents selected from the group consisting halogen, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-haloalkyl, OH, (C₁-C₄-alkyl)OH, O(C₁-C₄-alkyl), (C₁-C₄-alkyl)O(C₁-C₄-alkyl), NH₂, (C₁-C₄-alkyl)NH₂, NH(C₁-C₄-alkyl), (C₁-C₄-alkyl)NH(C₁-C₄-alkyl), N(C₁-C₄-alkyl)(C₁-C₄-alkyl), and (C₁-C₄-alkyl)N(C₁-C₄-alkyl)(C₁-C₄-alkyl) with the proviso that the point of attachment on said heterocyclic or heterobicyclic ring is N;

wherein R⁶ is selected from the group consisting of H and C₁-C₃-alkyl;

wherein R^{6a} is selected from the group consisting of H and C₁-C₃-alkyl,

wherein R^{6b} is selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkynyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;

- (ii) OR²⁰, N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;

- (ii) OR²⁶, N(R^{26a})(R^{26b});

wherein R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxi-

dized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{29} ;

wherein R^{26} , R^{26a} , R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, and C₁-C₄-haloalkyl;

wherein R^{27} is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{30} ;

wherein R^{29} , R^{30} are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

In another embodiment 3(D2), G^3 is selected from the group consisting of C(=O)N(R^{6a})(R^{6b});

wherein R^{6a} is H,

wherein R^{6b} is selected from the group consisting of C₁-C₆-alkyl, C₂-C₆-alkynyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;

wherein R^{12} is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ;

- (ii) OR²⁰, N(R^{20a})(R^{20b});

and/or two R^{12} present on one carbon atom together form =O;

wherein R^{18} is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable

carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{24} ;

(ii) OR^{26} , $N(R^{26a})(R^{26b})$;

wherein R^{20} , R^{20a} , R^{20b} are independently selected from the group consisting of H, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{27} ;

wherein R^{24} is selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{29} ;

wherein R^{26} , R^{26a} , R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, and C₁-C₄-haloalkyl;

wherein R^{27} is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{30} ;

wherein R^{29} , R^{30} are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

In another embodiment 3(E), G^3 is $C(=O)N(R^{6a})(R^{6b})$;

wherein R^{6a} is selected from the group consisting of H and C₁-C₃-alkyl;

wherein R^{6b} is selected from the group consisting of C₁-C₆-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic ring, wherein each substitutable carbon atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ; with the proviso that if R^{6b} is C₁-C₆-alkyl, said C₁-C₆-alkyl is substituted with one or more, same or different substituents R^{12} ;

wherein R^{12} is selected from the group consisting of halogen, CN, NO₂, C₁-C₃-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic

ring, wherein each substitutable carbon atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸; and

wherein R¹⁸ is selected from the group consisting of halogen, CN, NO₂, and C₁-C₃-alkyl.

In another embodiment 3(F), G³ is C(=O)N(R^{6a})(R^{6b});

wherein R^{6a} is selected from the group consisting of H and C₁-C₃-alkyl,

wherein R^{6b} is selected from the group consisting of H and C₁-C₆-alkyl, wherein each substitutable carbon in the aforementioned C₁-C₆-alkyl is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R¹² is selected from the group consisting of halogen and OR²⁰; and

wherein R²⁰ is selected from the group consisting of H and C₁-C₄-alkyl.

The following combinations of embodiments of the first aspects A1, A1a, A1b, A1c, A1d, and A1e, which are summarized in Table 1 are disclosed in combination with each other:

Table 1:

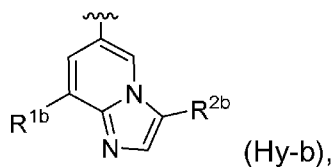
Line	G ¹	G ²	G ³
1	1(A)	2(A)	3(A)
2	1(B)	2(A)	3(A)
3	1(C)	2(A)	3(A)
4	1(D)	2(A)	3(A)
5	1(A)	2(A)	3(B)
6	1(B)	2(A)	3(B)
7	1(C)	2(A)	3(B)
8	1(D)	2(A)	3(B)
9	1(A)	2(A)	3(C)
10	1(B)	2(A)	3(C)
11	1(C)	2(A)	3(C)
12	1(D)	2(A)	3(C)
13	1(A)	2(A)	3(D)
14	1(B)	2(A)	3(D)
15	1(C)	2(A)	3(D)
16	1(D)	2(A)	3(D)
17	1(A)	2(A)	3(E)
18	1(B)	2(A)	3(E)
19	1(C)	2(A)	3(E)
20	1(D)	2(A)	3(E)
21	1(A)	2(B)	3(A)
22	1(B)	2(B)	3(A)
23	1(C)	2(B)	3(A)
24	1(D)	2(B)	3(A)
25	1(A)	2(B)	3(B)

26	1(B)	2(B)	3(B)
27	1(C)	2(B)	3(B)
28	1(D)	2(B)	3(B)
29	1(A)	2(B)	3(C)
30	1(B)	2(B)	3(C)
31	1(C)	2(B)	3(C)
32	1(D)	2(B)	3(C)
29a	1(A)	2(B)	3(D)
30a	1(B)	2(B)	3(D)
31a	1(C)	2(B)	3(D)
32a	1(D)	2(B)	3(D)
33	1(A)	2(B)	3(E)
34	1(B)	2(B)	3(E)
35	1(C)	2(B)	3(E)
36	1(D)	2(B)	3(E)
37	1(A)	2(A)	3(F)
38	1(B)	2(A)	3(F)
39	1(C)	2(A)	3(F)
40	1(D)	2(A)	3(F)
41	1(A)	2(B)	3(F)
42	1(B)	2(B)	3(F)
43	1(C)	2(B)	3(F)
44	1(D)	2(B)	3(F)

In a preferred embodiment, the present invention relates to a compound of formula (I), in particular to a compound according to embodiment 36 of Table 1, wherein

5 G^1 is phenyl, wherein one or two of the substitutable carbon atoms in the aforementioned phenyl is substituted with same or different substituents selected from the group consisting of CH_3 , F and CN;

G^2 is selected from the group consisting of



10 wherein

R^{1b} is selected from the group consisting of H and Cl;

R^{2b} is CH_3 ; and

G^3 is $C(=O)N(R^{6a})(R^{6b})$;

wherein R^{6a} is selected from the group consisting of H;

15 wherein R^{6b} is selected from the group consisting of C_1 - C_3 -alkyl, wherein each substitutable carbon atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;

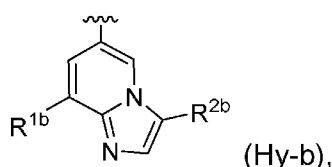
wherein R^{12} is a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic ring, wherein each substitutable carbon atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ; and

5 wherein R^{18} is selected from the group consisting of halogen, CN, NO_2 , and C_1 - C_3 -alkyl.

In a more preferred embodiment, the present invention relates to a compound of formula (I), in particular to a compound according to embodiment 36 of Table 1, wherein

10 G^1 is phenyl, wherein one or two of the substitutable carbon atoms in the aforementioned phenyl is substituted with same or different substituents selected from the group consisting of CH_3 , F and CN;

G^2 is selected from the group consisting of



15 wherein

R^{1b} is selected from the group consisting of H and Cl;

R^{2b} is CH_3 ; and

G^3 is $C(=O)N(R^{6a})(R^{6b})$;

wherein R^{6a} is selected from the group consisting of H;

20 wherein R^{6b} is C_1 -alkyl, wherein the carbon atom is substituted with one or more, same or different substituents R^{12} ;

wherein R^{12} is a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic ring, wherein each substitutable carbon atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ; and

25 wherein R^{18} is selected from the group consisting of halogen, CN, NO_2 , and C_1 - C_3 -alkyl.

Definitions relating to aspects A1a, A1b, A1c, A1d, A1e, A2, A3, A4, and A5

30 The term "compound(s) of the present invention" is to be understood as equivalent to the term "compound(s) according to the invention", therefore also comprising a salt, stereoisomer, tautomer, isotopologue, or N-oxide thereof.

The compounds according to the invention may be amorphous or may exist in one or more different crystalline states (polymorphs) which may have different macroscopic properties such as stability or show different biological properties such as activities. The present invention relates to amorphous and crystalline compounds of formula (I), mixtures of different crystalline states of the respective compound of the invention, as well as amorphous or crystalline salts thereof.

Salts of the compounds according to the invention are preferably pharmaceutically acceptable salts, such as those containing counterions present in drug products listed in the US FDA Orange Book database. They can be formed in a customary manner, e.g., by reacting the compound with an acid of the anion in question if the compounds according to the invention have a

basic functionality or by reacting acidic compounds according to the invention with a suitable base.

Suitable cationic counterions are in particular the ions of the alkali metals, preferably lithium, sodium and potassium, of the alkaline earth metals, preferably calcium, magnesium and barium, and of the transition metals, preferably manganese, copper, silver, zinc and iron, and also ammonium (NH_4^+) and substituted ammonium in which one to four of the hydrogen atoms are replaced by $\text{C}_1\text{-C}_4$ -alkyl, $\text{C}_1\text{-C}_4$ -hydroxyalkyl, $\text{C}_1\text{-C}_4$ -alkoxy, $\text{C}_1\text{-C}_4$ -alkoxy- $\text{C}_1\text{-C}_4$ -alkyl, hydroxy- $\text{C}_1\text{-C}_4$ -alkoxy- $\text{C}_1\text{-C}_4$ -alkyl, phenyl or benzyl. Examples of substituted ammonium ions comprise methylammonium, isopropylammonium, dimethylammonium, diisopropylammonium, trimethylammonium, tetramethylammonium, tetraethylammonium, tetrabutylammonium, 2-hydroxyethylammonium, 2-(2-hydroxyethoxy)ethyl-ammonium, bis(2-hydroxyethyl)ammonium, benzyltrimethylammonium and benzyltriethylammonium, furthermore the cations of 1,4-piperazine, meglumine, benzathine and lysine.

Suitable acidic counterions are in particular chloride, bromide, hydrogensulfate, sulfate, dihydrogenphosphate, hydrogenphosphate, phosphate, nitrate, bicarbonate, carbonate, hexafluorosilicate, hexafluorophosphate, benzoate, and the anions of $\text{C}_1\text{-C}_4$ -alkanoic acids, preferably formate, acetate, propionate and butyrate, furthermore lactate, gluconate, and poly acids such as succinate, oxalate, maleate, fumarate, malate, tartrate and citrate, furthermore sulfonate anions such as besylate (benzenesulfonate), tosylate (p-toluenesulfonate), napsylate (naphthalene-2-sulfonate), mesylate (methanesulfonate), esylate (ethanesulfonate), and ethanedisulfonate.

They can be formed by reacting compounds according to the invention that have a basic functionality with an acid of the corresponding anion.

Depending on the substitution pattern, the compounds according to the invention may have one or more centres of chirality, including axial chirality. The invention provides both pure enantiomers or pure diastereomers of the compounds according to the invention, and their mixtures, including racemic mixtures. Suitable compounds according to the invention also include all possible geometrical stereoisomers (cis/trans isomers or E/Z isomers) and mixtures thereof. Cis/trans isomers may be present with respect to, e.g., an alkene, carbon-nitrogen double-bond or amide group.

Tautomers may be formed, if a substituent is present at the compound of formula (I), which allows for the formation of tautomers such as keto-enol tautomers, imine-enamine tautomers, amide-imidic acid tautomers or the like.

An isotopologue is an isotopically enriched compound. The term "isotopically enriched compound" refers to a compound containing at least one atom having an isotopic composition other than the natural isotopic composition of that atom. Preferably, the isotopologue is a deuterium (i.e. D or ^2H)-enriched compound.

The term "N-oxide" includes any compound of the present invention which has at least one tertiary nitrogen atom that is oxidized to a N-oxide moiety.

The term "substituted", as used herein, means that a hydrogen atom bonded to a designated atom is replaced with a specified substituent, provided that the substitution results in a stable or chemically feasible compound. Unless otherwise indicated, a substituted atom may have one or more substituents and each substituent is independently selected.

The term "substitutable", when used in reference to a designated atom, means that attached to the atom is a hydrogen, which can be replaced with a suitable substituent.

When it is referred to certain atoms or moieties being substituted with "one or more" substituents, the term "one or more" is intended to cover at least one substituent, e.g. 1 to 10 substituents, preferably 1, 2, 3, 4, or 5 substituents, more preferably 1, 2, or 3 substituents, most preferably 1, or 2 substituents. When neither the term "unsubstituted" nor "substituted" is explicitly mentioned concerning a moiety, said moiety is to be considered as unsubstituted.

The organic moieties mentioned in the above definitions of the variables are - like the term halogen - collective terms for individual listings of the individual group members. The prefix C_n-C_m indicates in each case the possible number of carbon atoms in the group.

The term "halogen" denotes in each case fluorine, bromine, chlorine or iodine, in particular fluorine or chlorine.

The term "alkyl" as used herein denotes in each case a straight-chain or branched alkyl group having usually from 1 to 6 carbon atoms, preferably 1 to 5 or 1 to 4 carbon atoms, more preferably 1 to 3 or 1 to 2 or 1 carbon atoms. Examples of an alkyl group are methyl, ethyl, n-propyl, iso-propyl, n-butyl, 2-butyl, iso-butyl, tert-butyl, n-pentyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 2,2-dimethylpropyl, 1-ethylpropyl, n-hexyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-1-methylpropyl, and 1-ethyl-2-methylpropyl.

The term "haloalkyl" as used herein denotes in each case a straight-chain or branched alkyl group having usually from 1 to 10 carbon atoms, frequently from 1 to 6 carbon atoms, preferably from 1 to 4 carbon atoms, wherein the hydrogen atoms of this group are partially or totally replaced with halogen atoms. Preferred haloalkyl moieties are selected from C₁-C₄-haloalkyl, more preferably from C₁-C₃-haloalkyl or C₁-C₂-haloalkyl, in particular from C₁-C₂-fluoroalkyl such as fluoromethyl, difluoromethyl, trifluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, and the like.

The term "alkenyl" as used herein denotes in each case an unsaturated hydrocarbon group having usually 2 to 6, preferably 2 to 4 carbon atoms comprising at least one carbon-carbon double bond in any position, e.g. vinyl (ethenyl), allyl (2-propen-1-yl), 1-propen-1-yl, 2-propen-2-yl, methallyl (2-methylprop-2-en-1-yl), 2-buten-1-yl, 3-buten-1-yl, 2-penten-1-yl, 3-penten-1-yl, 4-penten-1-yl, 1-methylbut-2-en-1-yl, 2-ethylprop-2-en-1-yl and the like. If geometric isomers are possible with regard to the double bond, the present invention relates to both, the E- and Z-isomers. Preferred alkenyl groups according to the invention are terminal alkenyl groups. The bonding of vinyl is exemplified below.



The term "haloalkenyl" as used herein refers to an alkenyl group as defined above, wherein the hydrogen atoms are partially or totally replaced with halogen atoms.

The term "alkynyl" as used herein denotes in each case an unsaturated hydrocarbon group having usually 2 to 6, preferably 2 to 5 or 2 to 4 carbon atoms, more preferably 2 to 3 carbon atoms, comprising at least one carbon-carbon triple bond in any position, e.g. ethynyl, propargyl (2-propyn-1-yl), 1-propyn-1-yl, 1-methylprop-2-yn-1-yl, 2-butyn-1-yl, 3-butyn-1-yl, 1-pentyn-1-yl, 3-pentyn-1-yl, 4-pentyn-1-yl, 1-methylbut-2-yn-1-yl, 1-ethylprop-2-yn-1-yl and the like.

The term "haloalkynyl" as used herein refers to an alkynyl group as defined above, wherein the hydrogen atoms are partially or totally replaced with halogen atoms.

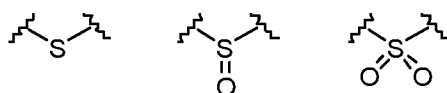
The term "alkoxy" as used herein denotes in each case a straight-chain or branched alkyl group which is bonded via an oxygen atom and has usually from 1 to 6 carbon atoms, preferably 1 to 2 carbon atoms, more preferably 1 carbon atom. Examples of an alkoxy group are methoxy, ethoxy, n-propoxy, iso-propoxy, n-butyloxy, 2-butyloxy, iso-butyloxy, tert.-butyloxy, and the like.

The term "haloalkoxy" as used herein denotes in each case a straight-chain or branched alkoxy group having from 1 to 6 carbon atoms, preferably 1 to 2 carbon atoms, more preferably 1 carbon atom, wherein the hydrogen atoms of this group are partially or totally replaced with halogen atoms, in particular fluorine atoms. Preferred haloalkoxy moieties include C₁-haloalkoxy, in particular C₁-fluoroalkoxy, such as trifluoromethoxy and the like.

The term "carbocyclic" includes, unless otherwise indicated, in general a 3- to 9-membered, preferably a 4- to 8-membered or a 5- to 7-membered, more preferably a 5- or 6-membered monocyclic ring comprising 3 to 9, preferably 4 to 8 or 5 to 7, more preferably 5 or 6 carbon atoms. The carbocycle may be saturated, partially unsaturated, or fully unsaturated. Preferably, the term "carbocycle" covers cycloalkyl and cycloalkenyl groups as defined above, for example cyclopropane, cyclobutane, cyclopentane and cyclohexane rings. When it is referred to "fully unsaturated" carbocycles, this term also includes "aromatic" carbocycles or aryls. In certain preferred embodiments, a fully unsaturated carbocycle is an aromatic carbocycle as defined below, preferably a 6-membered aromatic carbocycle. Phenyl is a preferred fully unsaturated carbocycle.

The term "carbobicyclic" includes in general bicyclic 6 to 14-membered, preferably 7- to 12-membered or 8- to 10-membered, more preferably 9- or 10-membered bicyclic rings comprising 6 to 14, preferably 7 to 12 or 8 to 10, more preferably 9 or 10 carbon atoms. The carbobicycle may be saturated, partially unsaturated, or fully unsaturated. Preferably, the term "carbobicycle" covers bicycloalkyl, bicycloalkenyl and bicyclic aromatic groups, for example bicyclohexane, bicycloheptane (such as norbornane), bicyclooctane (such as bicyclo[2.2.2]octane, bicyclo[3.2.1]octane or bicyclo[4.2.0]octane), bicyclononane (such as bicyclo[3.3.1]nonane or bicyclo[4.3.0]nonane), bicyclodecane (such as bicyclo[4.4.0]decane), bicycloundecane (such as bicyclo[3.3.3]undecane), norbornene, naphthalene and the like. Preferably, the carbobicycle is a fused carbobicycle, for example naphthalene and the like.

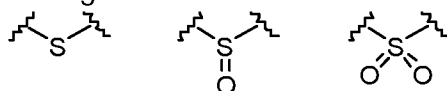
The term "heterocyclic" includes, unless otherwise indicated, in general a 3- to 9-membered, preferably a 4- to 8-membered or 5- to 7-membered, more preferably 5- or 6-membered, in particular 6-membered monocyclic ring. The heterocycle may be saturated, partially unsaturated, or fully unsaturated. As used in this context, the term "fully unsaturated" also includes "aromatic". In a preferred embodiment, a fully unsaturated heterocycle is thus an aromatic heterocycle, preferably a 5- or 6-membered aromatic heterocycle comprising one or more, e.g. 1, 2, 3, or 4, preferably 1, 2, or 3 heteroatoms selected from N, O and S as ring members, where S-atoms as ring members may be present as S, SO or SO₂. Examples of aromatic heterocycles are provided below in connection with the definition of "hetaryl". "Hetaryls" or "heteroaryls" are covered by the term "heterocycles". The saturated or partially unsaturated heterocycles usually comprise 1, 2, 3, 4 or 5, preferably 1, 2 or 3 heteroatoms selected from N, O and S as ring members, where S-atoms as ring members may be present as S, SO or SO₂. Preferably, the S atom will not be present in oxidized form in fully unsaturated compounds. In particular, the following scenarios are covered:



A skilled person is aware that resonance structures of the oxidized forms may be possible.

Saturated heterocycles include, unless otherwise indicated, in general 3- to 9-membered, preferably 4- to 8-membered or 5- to 7-membered, more preferably 5- or 6-membered monocyclic rings comprising 3 to 9, preferably 4 to 8 or 5 to 7, more preferably 5 or 6 atoms comprising at least one heteroatom, such as pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, tetrahydropyran, dioxane, morpholine or piperazine.

The term "hetaryl" or "heteroaryl" or "aromatic heterocycle" or "aromatic heterocyclic ring" includes monocyclic 5- or 6-membered aromatic heterocycles comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S, where S-atoms as ring members may be present as S, SO or SO₂. Preferably, the S atom will not be present in oxidized form in fully unsaturated compounds. In particular, the following scenarios are covered:



A skilled person is aware that resonance structures of the oxidized forms may be possible. Examples of 5- or 6-membered aromatic heterocycles include pyridyl, i.e. 2-, 3-, or 4-pyridyl, pyrimidinyl, i.e. 2-, 4- or 5-pyrimidinyl, pyrazinyl, pyridazinyl, i.e. 3- or 4-pyridazinyl, thienyl, i.e. 2- or 3-thienyl, furyl, i.e. 2- or 3-furyl, pyrrolyl, i.e. 2- or 3-pyrrolyl, oxazolyl, i.e. 2-, 3- or 5-oxazolyl, isoxazolyl, i.e. 3-, 4- or 5-isoxazolyl, thiazolyl, i.e. 2-, 3- or 5-thiazolyl, isothiazolyl, i.e. 3-, 4- or 5-isothiazolyl, pyrazolyl, i.e. 1-, 3-, 4- or 5-pyrazolyl, i.e. 1-, 2-, 4- or 5-imidazolyl, oxadiazolyl, e.g. 2- or 5-[1,3,4]oxadiazolyl, 4- or 5-(1,2,3-oxadiazol)yl, 3- or 5-(1,2,4-oxadiazol)yl, 2- or 5-(1,3,4-thiadiazol)yl, thiadiazolyl, e.g. 2- or 5-(1,3,4-thiadiazol)yl, 4- or 5-(1,2,3-thiadiazol)yl, 3- or 5-(1,2,4-thiadiazol)yl, triazolyl, e.g. 1H-, 2H- or 3H-1,2,3-triazol-4-yl, 2H-triazol-3-yl, 1H-, 2H-, or 4H-1,2,4-triazolyl and tetrazolyl, i.e. 1H- or 2H-tetrazolyl.

The term "heterobicyclic" includes in general bicyclic 6 to 14-membered, preferably 7- to 12-membered or 8- to 10-membered, more preferably 9- or 10-membered bicyclic rings comprising as ring members 1, 2, 3 or 4 heteroatoms selected from N, O and S, where S-atoms as ring members may be present as S, SO or SO₂. The heterobicycle may be saturated, partially unsaturated, or fully unsaturated. Examples of heterobicycles include benzofuranyl, benzothieryl, indolyl, indazolyl, benzimidazolyl, benzoxathiazolyl, benzoxadiazolyl, benzothiadiazolyl, benzoxazinyl, quinolinyl, isoquinolinyl, purinyl, 1,8-naphthyridyl, pteridyl, pyrido[3,2-d]pyrimidyl, pyridoimidazolyl, triethylenediamine or quinuclidine and the like. Preferably, the heterobicycle is a fused heterobicycle, for example quinolinyl and the like.

As used in the specification and the claims, the singular forms of "a" and "an" also include the corresponding plurals unless the context clearly dictates otherwise. The same applies for plural forms used herein, which also include the singular forms unless the context clearly dictates otherwise.

The terms "about" and "approximately" in the context of the present invention denotes an interval of accuracy that a person skilled in the art will understand to still ensure the technical effect of the feature in question. The term typically indicates a deviation from the indicated numerical value of $\pm 10\%$ and preferably $\pm 5\%$.

It needs to be understood that the term "comprising" is not limiting. For the purposes of the present invention, the term "consisting of" is considered to be a preferred embodiment of the

term “comprising of”. If hereinafter a group is defined to comprise at least a certain number of embodiments, this is also meant to encompass a group which preferably consists of these embodiments only.

The term “pharmaceutically acceptable excipient” as used herein refers to compounds commonly comprised in pharmaceutical compositions, which are known to the skilled person. Examples of suitable excipients are exemplary listed below. Typically, a pharmaceutically acceptable excipient can be defined as being pharmaceutically inactive.

The term “treatment” is to be understood as also including the option of “prophylaxis”. Thus, whenever reference is made herein to a “treatment” or “treating”, this is to be understood as “treatment and/or prophylaxis” or “treating and/or preventing”.

Description of pharmaceutical compositions according to the present invention

A pharmaceutical composition according to the present invention may be formulated for oral, buccal, nasal, rectal, topical, transdermal or parenteral application. Oral application may be preferred. Parenteral application can also be preferred and includes intravenous, intraarterial, intratumoral, intrathecal, intravesical, intramuscular or subcutaneous administration. The compound according to formula (I) should be applied in pharmaceutically effective amounts, for example in the amounts as set out herein below.

A pharmaceutical composition of the present invention may also be designated as formulation or dosage form. A compound of formula (I) may also be designated in the following as (pharmaceutically) active agent or active compound.

Pharmaceutical compositions may be solid or liquid dosage forms or may have an intermediate, e.g. gel-like character depending inter alia on the route of administration.

In general, the inventive dosage forms can comprise various pharmaceutically acceptable excipients, which will be selected depending on which functionality is to be achieved for the dosage form. A “pharmaceutically acceptable excipient” in the meaning of the present invention can be any substance used for the preparation of pharmaceutical dosage forms, including coating materials, film-forming materials, fillers, disintegrating agents, release-modifying materials, carrier materials, diluents, binding agents and other adjuvants. Typical pharmaceutically acceptable excipients include substances like sucrose, mannitol, sorbitol, starch and starch derivatives, lactose, and lubricating agents such as magnesium stearate, disintegrants and buffering agents.

The term “carrier” denotes pharmaceutically acceptable organic or inorganic carrier substances with which the active ingredient is combined to facilitate the application. Suitable pharmaceutically acceptable carriers include, for instance, water, aqueous salt solutions, alcohols, oils, preferably vegetable oils, propylene glycol, polyoxyethylene sorbitans, polyethylene-polypropylene block co-polymers such as poloxamer 188 or poloxamer 407, polyethylene glycols such as polyethylene glycol 200, 300, 400, 600, etc., gelatin, lactose, amylose, magnesium stearate, surfactants, perfume oil, fatty acid monoglycerides, diglycerides and triglycerides, polyoxyethylated medium or long chain fatty acids such as ricinoleic acid, and polyoxyethylated fatty acid mono-, di, and triglycerides such as capric or caprilic acids, petroethral fatty acid esters, hydroxymethyl celluloses such as hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxypropyl acetate succinate, polyvinylpyrrolidone, crosspovidone and the like. The pharmaceutical

compositions can be sterile and, if desired, mixed with auxiliary agents, like lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure, buffers, colorings, flavoring and/or aromatic substances and the like which do not deleteriously react with the active compound.

5 If liquid dosage forms are considered for the present invention, these can include pharmaceutically acceptable emulsions, solutions, suspensions and syrups containing inert diluents commonly used in the art such as water. These dosage forms may contain e.g. microcrystalline cellulose for imparting bulk, alginic acid or sodium alginate as a suspending agent, methylcellulose as a viscosity enhancer and sweeteners/flavouring agents.

10 For parenteral application, particularly suitable vehicles consist of solutions, preferably oily or aqueous solutions, as well as suspensions, emulsions, or implants. Pharmaceutical formulations for parenteral administration are particularly preferred and include aqueous solutions of the compounds of formula (I) in water-soluble form. Additionally, suspensions of the compounds of formula (I) may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, soybean oil, or tocopherols, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran.

Particularly preferred dosage forms are injectable preparations of a compound of formula (I).
20 Thus, sterile injectable aqueous or oleaginous suspensions can for example be formulated according to the known art using suitable dispersing agents, wetting agents and/or suspending agents. A sterile injectable preparation can also be a sterile injectable solution or suspension or an emulsion in a non-toxic parenterally acceptable diluant or solvent. Among the acceptable vehicles and solvents that can be used are water and isotonic sodium chloride solution. Sterile oils
25 are also conventionally used as solvent or suspending medium.

Suppositories for rectal administration of a compound of formula (I) can be prepared by e.g. mixing the compound with a suitable non-irritating excipient such as cocoa butter, synthetic triglycerides and polyethylene glycols which are solid at room temperature but liquid at rectal temperature such that they will melt in the rectum and release the compound according to formula
30 (I) from said suppositories.

For administration by inhalation, the compounds according to the present invention may be conveniently delivered in the form of an aerosol spray from pressurized packs or a nebulizer, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of e.g. gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.
35

Oral dosage forms may be liquid or solid and include e.g. tablets, troches, pills, capsules, powders, effervescent formulations, dragees and granules. Pharmaceutical preparations for oral use
40 can be obtained as solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch,

rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone (crosspovidone), agar, or alginic acid or a salt thereof such as sodium alginate. The oral dosage forms may be formulated to ensure an immediate release of the compound of formula (I) or a sustained release of the compound of formula (I).

A solid dosage form may comprise a film coating. For example, the inventive dosage form may be in the form of a so-called film tablet. A capsule of the invention may be a two-piece hard gelatin capsule, a two-piece hydroxypropylmethylcellulose capsule, a two-piece capsule made of vegetable or plant-based cellulose or a two-piece capsule made of polysaccharide.

The dosage form according to the invention may be formulated for topical application. Suitable pharmaceutical application forms for such an application may be a topical nasal spray, sublingual administration forms and controlled and/or sustained release skin patches. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

The compositions may conveniently be presented in unit dosage forms and may be prepared by any of the methods well known in the art of pharmacy. The methods can include the step of bringing the compounds into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the compounds into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product. Liquid dose units are vials or ampoules. Solid dose units are tablets, capsules and suppositories.

As regards human patients, the compound of formula (I) may be administered to a patient in an amount of about 0.001 mg to about 5000 mg per day, preferably of about 0.01 mg to about 100 mg per day, more preferably of about 0.1 mg to about 50 mg per day, which is the effective amount. The phrase "effective amount" means an amount of compound that, when administered to a mammal in need of such treatment, is sufficient to treat or prevent a particular disease or condition.

Furthermore, the pharmaceutical composition may also contain the compound of formula (I) as a prodrug such as an ester or amide thereof. A prodrug is any compound which is converted under physiological conditions or by solvolysis to any of the compounds of the invention. A prodrug may be inactive prior to administration but may be converted to an active compound of the invention *in vivo*.

Indications, for which the compounds of the present invention may be used

The compounds according to the present invention are preferably used for the treatment of a disease selected from the group consisting of cancer, Parkinson's disease, Huntington's disease, Alzheimer's disease, psychosis, stroke, extra pyramidal syndrome (in particular dystonia, akathisia, pseudoparkinsonism and tardive dyskinesia), attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), amyotrophic lateral sclerosis, cirrhosis, fibrosis, fatty liver, addictive behavior, dermal fibrosis (in particular dermal fibrosis in scleroderma), sleep disorders, AIDS, autoimmune diseases, infections, atherosclerosis and ischemia-reperfusion in-

jury. Furthermore, the compounds according to the present invention are used for idiopathic pulmonary fibrosis, systemic sclerosis, irritable bowel disease and as analgesic. The use for the treatment of cancer is particularly preferred.

More generally, the compounds according to the present invention can be used for the treatment of a disease selected from the group consisting of neurodegenerative, proliferative, inflammatory and infectious diseases, sickle cell disease, diabetic nephropathy, cognition and CNS disorders. The proliferative diseases include cancer.

Preferably, said cancer is selected from the group consisting of breast cancer, inflammatory breast cancer, ductal carcinoma, lobular carcinoma, colon cancer, pancreatic cancer, insulinomas, adenocarcinoma, ductal adenocarcinoma, adenosquamous carcinoma, acinar cell carcinoma, glucagonoma, skin cancer, melanoma, metastatic melanoma, lung cancer, small cell lung cancer, non-small cell lung cancer, squamous cell carcinoma, adenocarcinoma, large cell carcinoma, brain (gliomas), glioblastomas, astrocytomas, glioblastoma multiforme, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, Wilm's tumor, Ewing's sarcoma, Rhabdomyosarcoma, ependymoma, medulloblastoma, head and neck, kidney, liver, melanoma, ovarian, pancreatic, adenocarcinoma, ductal adenocarcinoma, adenosquamous carcinoma, acinar cell carcinoma, glucagonoma, insulinoma, prostate, sarcoma, osteosarcoma, giant cell tumor of bone, thyroid, lymphoblastic T cell leukemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, hairy-cell leukemia, acute lymphoblastic leukemia, acute myelogenous leukemia, chronic neutrophilic leukemia, acute lymphoblastic T cell leukemia, plasmacytoma, Immunoblastic large cell leukemia, mantle cell leukemia, multiple myeloma, megakaryoblastic leukemia, multiple myeloma, acute megakaryocyte leukemia, promyelocytic leukemia, erythroleukemia, malignant lymphoma, hodgkins lymphoma, non-hodgkins lymphoma, lymphoblastic T cell lymphoma, Burkitt's lymphoma, follicular lymphoma, neuroblastoma, bladder cancer, urothelial cancer, vulval cancer, cervical cancer, endometrial cancer, renal cancer, mesothelioma, esophageal cancer, salivary gland cancer, hepatocellular cancer, gastric cancer, nasopharyngeal cancer, buccal cancer, cancer of the mouth, GIST (gastrointestinal stromal tumor), neuroendocrine cancers and testicular cancer.

More preferably, said cancer is selected from the group consisting of brain (gliomas), glioblastomas, astrocytomas, glioblastoma multiforme, Bannayan-Zonana syndrome, Cowden disease, Lhermitte-Duclos disease, breast, colon, head and neck, kidney, lung, liver, melanoma, ovarian, pancreatic, adenocarcinoma, ductal adenocarcinoma, adenosquamous carcinoma, acinar cell carcinoma, glucagonoma, insulinoma, prostate, sarcoma and thyroid cancer.

Additionally, the compounds of the invention may be used to treat inflammation associated with autoimmune diseases or diseases resulting from inflammation including systemic lupus erythematosus, Addison's disease, autoimmune polyglandular disease (also known as autoimmune polyglandular syndrome), glomerulonephritis, rheumatoid arthritis scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, glomerulonephritis, rheumatoid arthritis autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, graft vs. host disease, asthma, bronchitis, acute pancreatitis, chronic pancreatitis and allergies of various types.

The compounds of the present invention may also be used to treat a neurodegenerative diseases including Alzheimer's disease (including early onset Alzheimer's disease), Parkinson's

disease, amyotrophic lateral sclerosis, Huntington's disease, senile chorea, Sydenham's chorea, frontotemporal lobar dementia, spinocerebellar ataxia, dementia with Lewy bodies, cerebral ischemia or neurodegenerative disease caused by traumatic injury, glutamate neurotoxicity, hypoxia, peripheral neuropathy, including mononeuropathy, multiple mononeuropathy or polyneuropathy. Examples of peripheral neuropathy may be found in diabetes mellitus, Lyme disease or uremia, peripheral neuropathy caused by a toxic agent, demyelinating disease such as acute or chronic inflammatory polyneuropathy, leukodystrophies, or Guillain-Barré syndrome, multiple mononeuropathy secondary to a collagen vascular disorder (e.g. polyarteritis nodosa, SLE, Sjögren's syndrome), multiple mononeuropathy secondary to sarcoidosis, multiple mononeuropathy secondary to a metabolic disease (e.g. diabetes or amyloidosis), or multiple mononeuropathy secondary to an infectious disease (e.g. Lyme disease or HIV infection).

Said pharmaceutical composition may comprise said compound as the only pharmaceutically active agent. It is to be understood that in connection with the medical uses of the invention, it can be preferred that the compounds according to the present invention are administered in combination with antibodies, radiotherapy, surgical therapy, immunotherapy, chemotherapy, toxin therapy, gene therapy, or any other therapy known to those of ordinary skill in the art for treatment of a particular disease. This is particularly relevant in connection with the treatment of cancer.

Preferably, the compounds of the present invention may be coadministered with an anti-neoplastic agent and/or an anti-neoplastic agent may be comprised in the pharmaceutical composition according to the present invention. The cancer treated by the combination of (i) a compound according to the present invention and (ii) an anti-neoplastic agent may be selected from one of the cancers listed above. It can further be preferred that said cancer is selected from the group consisting of colon, pancreatic cancer, breast cancer, prostate cancer, lung cancer including squamous non-small cell lung cancer (NSCLC) and non-squamous NSCLC, ovarian cancer, cervical cancer, renal cancer, cancer of the head and neck, lymphoma, leukemia, colorectal cancer, gastric cancer, melanoma, hepatocellular carcinoma, pancreatic carcinoma and a hematological malignancy.

An anti-neoplastic agent has activity versus a tumor and examples can be found in Cancer Principles and Practice of Oncology by V.T. Devita and S. Hellman (editors), 6th edition (February 15, 2001), Lippincott Williams & Wilkins Publishers.

Typical anti-neoplastic agents useful in the present invention include chemotherapeutic agents, topoisomerase II inhibitors, antimetabolites, topoisomerase I inhibitors, hormones and hormonal analogues, signal transduction pathway inhibitors, tyrosine kinase inhibitors, angiogenesis inhibitors, proapoptotic agents, cell cycle signaling inhibitors, proteasome inhibitors, inhibitors of cancer metabolism, and immunotherapeutic agents (such as STING pathway modulating compounds, TLR agonists and checkpoint inhibitors).

Examples for chemotherapeutic agents are anti-microtubule or anti-mitotic agents (such as paclitaxel), platinum coordination complexes (such as cisplatin), alkylating agents (such as cyclophosphamide) and antibiotic anti-neoplastics (such as doxorubicin).

It is widely known today that tumors can evade the immune system by suppressing the immune response. As discussed above, a strategy for doing so resides in the change of the micro-environment. Another (additional) strategy resides on the upregulation of receptors, which act (co-)inhibitory on the immune system (a negative "immune checkpoint" or "checkpoint"). Agents

blocking or inhibiting these receptors (thus resulting in a block of the immunosuppressive signals of the tumor) are commonly referred to as “checkpoint inhibitors” and this reference is also used herein. The corresponding receptors targeted by such agents are PD-1, PD-L1, CTLA-4, IDO, KIR, TIM-3, LAG-3, CD39, CD73, ICOS, OX40, Tim-3, Vista, BTLA, TDO, and TIGIT and such agents are typically antibodies (including variants, such as e.g. fusion proteins or the like, thereof) but may also be macrocyclic inhibitors or the like.

A checkpoint inhibitor as described herein can in particular be an antibody, a small molecule inhibitor or an antisense oligonucleotide selected from the group consisting of an anti-PD-1, anti-PD-L1, anti-CTLA-4, anti-IDO, anti-KIR, anti-TIM-3, anti-LAG-3, anti-CD39, anti-CD73, anti-ICOS, anti-OX40, anti-Tim-3, anti-Vista, anti-BTLA, anti-TDO, and anti-TIGIT-agent. Specific examples are BMS-936559, MPDL3280A and MEDI4736 (anti-PD-L1 antibodies), MK-3475 and pembrolizumab (anti-PD-1 antibodies) as well as ipilimumab (anti-CTLA-4 antibodies).

Preferably, the compounds of the present invention are administered in combination with antibodies. Preferred antibodies include anti-PD-1, anti-PD-L1, anti-CTLA-4, anti-IDO, anti-KIR, anti-TIM-3, anti-Vista, anti-TIGIT, anti-BTLA and anti-LAG3 antibody. Non-limiting examples are BMS-936559, MPDL3280A and MEDI4736 or avelumab (anti-PD-L1 antibodies), MK-3475, pembrolizumab or pidilizumab (anti-PD-1 antibodies) as well as ipilimumab (anti-CTLA-4 antibodies). Preferably, the compounds of the present invention are administered in a pharmaceutical composition comprising one or more of adjuvants, inactivated or attenuated bacteria (e.g., inactivated or attenuated *Listeria monocytogenes*), modulators of innate immune activation, preferably agonists of Toll-like Receptors (TLRs, preferably TLR7 or TLR9 agonists, e.g. SM360320, AZD8848), (NOD)-like receptors (NLRs, preferably NOD2 agonist), retinoic acid inducible gene-based (RIG)-I-like receptors (RLRs), C-type lectin receptors (CLRs), or pathogen-associated molecular patterns (“PAMPs”), cytokines (not limiting examples e.g. IL-2, IL-12, IL-6), interferons (including, but not limited to IFN alpha, IFN beta, IFN gamma, IFN lambda) or chemotherapeutic agents. The medical use may further comprise administering at least one HBV vaccine, a nucleoside HBV inhibitor or any combination thereof (e.g. RECOMBIVAX HB, ENGERIX-B, GENEVAC-B).

Combination therapy may be achieved by use of a single pharmaceutical composition that includes both agents, or by administering two distinct compositions at the same time, wherein one composition includes a compound of the present invention, and the other includes the second agent(s).

The two therapies may be given in either order and may precede or follow the other treatment by intervals ranging from minutes to weeks. In embodiments where the other agents are applied separately, one would generally ensure that a significant period of time did not expire between the time of each delivery, such that the agents would still be able to exert an advantageously combined effect on the patient. In such instances, it is contemplated that one may administer both modalities within about 12-24 h of each other and, more preferably, within about 6-12 h of each other. In some situations, it may be desirable to extend the time period for treatment significantly, however, where several days (2, 3, 4, 5, 6 or 7) to several weeks (1, 2, 3, 4, 5, 6, 7 or 8) lapse between the respective administrations. In some embodiments, the compound of the present invention is administered prior to administration of the distinct cancer treatment. In other embodiments, the distinct cancer treatment is administered prior to administration of the compound of the present invention.

The present invention is further illustrated by the following examples.

Examples

5 Part 1: Synthesis

General

10 Microwave heating was done using a Biotage Emrys Initiator microwave or Microwave Reactor Anton Paar Monowave 450. Column chromatography was carried out using an Isco Rf200d or an Interchim Puriflash 450. Solvent removal was carried out using either a Büchi, Heidolph or VWR rotary evaporator or a Genevac centrifugal evaporator. Preparative LC/MS was conducted using either a preparative HPLC instrument Waters (chromatography conditions 1) or preparative HPLC Instrument Shimadzu (chromatography conditions 2). NMR spectra were recorded
15 using a Bruker 300 MHz or 400MHz spectrometer. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (measurement range – 6.4 kHz). ¹H NMR data are reported as follows: chemical shift (multiplicity, coupling constants and number of hydrogens). Multiplicity is abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad).

20 When the term "inerted" is used to describe a reactor (e.g., a reaction vessel, flask, glass reactor, and the like) it is meant that the air in the reactor has been replaced with an essentially moisture-free or dry, inert gas (such as nitrogen, argon, and the like).

Preparative HPLC Conditions for the Purification of Target Compounds

25 *Chromatography Conditions 1:*

Prep HPLC Instrument: Waters 2545 pump with 2767 fraction collector

Column: Waters Xbridge C18 100mmx19mm, 5 μ m particle size

MS Detector: Waters 3100 mass detector

UV detector: Waters 2489 dual wavelength UV detector

30 Flow Rate : 30 ml/min

Example Gradient Time:

Time(min)	B%
-----------	----

0	20
---	----

1.5	20
-----	----

6.5	40
-----	----

6.55	95
------	----

8.5	95
-----	----

35 Representative Mobile Phase:

(1)

Mobile Phase: A: 0.1% formic acid in water

Mobile Phase: B: 0.1% formic acid in ACN

(2)

40 Mobile Phase: A: 0.1% NH₄OH in water

Mobile Phase: B: 0.1% NH₄OH in ACN

Chromatography conditions 2:

Prep HPLC Instrument: Shimadzu

Column: Gemini-NX 5 μ m C18 110Å, 250*21.2mm

Detector: SPD -20A/20AV UV-VIS

Flow Rate : 30 ml/min

Representative Mobile Phase:

5 (1)

Mobile Phase: A: 0.01%formic acid in water or TFA

Mobile Phase: B: 0.01% formic acid in ACN or TFA

(2)

Mobile Phase: A: 0.01%NH₄OH in water

10 Mobile Phase: B: 0.01% NH₄OH in ACN

Preparative SFC Conditions for the Purification of Target Compounds

Chromatography Conditions:

SFC Instrument: Thar SFC Prep Investigator (Waters)

15 Column: Chiral Technologies chiralpak IA 250mm x10mm,5 μ m particle size

ELS Detector: Waters 2424 detector

UV detector: Waters 2998 photodiode array detector, 254 nm

Flow Rate : 10 ml/min

Isocratic run: 40% isopropanol as a cosolvent

20

UPLC, HPLC and MS data provided in the examples described below were registered on:

LC-MS analyses on Bruker Amazon SL

Method name: lc-ms1-2-ba

25 Equipment:

- MS Bruker Amazon SL
- LC Dionex Ultimate 3000
- HPLC with UV-Vis or DAD detector
- column: Waters Acquity UPLC HSS C18, 50 mm x 2.1 mm x 1.8 μ m

30 Eluents:

(A) 0.1% formic acid in ACN

(B) 0.1% formic acid in water

Analytical method:

- Autosampler: injection volume: 1 μ L

35 - Pump:

	Flow	% B
Time [min]	[ml/min]	
0.00	0.5	95
0.00	0.5	95
4.00	0.5	5
5.00	0.5	5
5.20	0.5	95
6.00	0.5	95

- Column compartment:
column temperature: 25°C
time of analysis: 6 min

- Detector:

5 wave length: 254, 230, 270, 280 nm

LC-MS analyses Bruker Amazon SL

Method name: BCM-30

Equipment:

- 10 - MS Bruker Amazon SL
- LC Dionex Ultimate 3000
- HPLC with UV-Vis or DAD detector
- column: Waters Symmetry C18 3.9x150mm 5µm

Eluents:

- 15 (A) 0.1% formic acid-water solution
(B) 0.1% formic acid- ACN solution

Analytical method:

- Autosampler: injection volume: 3 µL
- Pump:

20 flow: 1.2 ml/min

Time [min]	[%] B
0.0	20
20.0	80
22.0	80
22.5	95
25.0	95
25.3	20
30.0	20

- Column compartment:
column temperature: 25°C
time of analysis: 30 min

- Detector:

25 wave length: 254 nm

LC-MS analyses on Shimadzu:

Method name: lc-ms1-2-ba

Equipment:

- 30 - Shimadzu LC-MS 2020
- HPLC with UV-Vis or DAD detector
- column: Waters Acquity UPLC HSS C18, 50 mm x 2.1 mm x 1.8 µm

Eluents:

- (A) 0.1% formic acid in ACN
35 (B) 0.1% formic acid in water

Analytical method:

- Autosampler: injection volume: 1 µL
- Pump:

Time [min]	Flow [ml/min]	% B
0.00	0.5	95
0.00	0.5	95
4.00	0.5	5
5.00	0.5	5
5.20	0.5	95
6.00	0.5	95

- Column compartment
column temperature: 25°C

5 time of analysis: 6 min

- Detector:
wave length: 254, 230, 270, 280 nm

LC-MS analyses on Corona ultra:

10 Method name: BCM-30

Equipment:

- Corona ultra
- LC Dionex Ultimate 3000
- column: Waters Symmetry C18 3.9x150mm 5 µm

15 Eluents:

(A) 0.1% formic acid-water solution

(B) 0.1% formic acid- ACN solution

Analytical method:

- Autosampler: injection volume: 3 µL
- Pump:
flow: 1.2 ml/min

Time [min]	[%] B
0.0	20
20.0	80
22.0	80
22.5	95
25.0	95
25.3	20
30.0	20

LC-MS analyses on Bruker Daltonik

Method name: Kinetex-Rot

25 Equipment:

- HPLC with UV-Vis or DAD detector
- column: Kinetex XB C18 4.6x50mm 2.6 µm
- MS: HCT Ion Trap Bruker Daltonik

Eluents:

- (A) 0.1% formic acid-water solution
- (B) 0.1% formic acid- ACN solution

5 Analytical method:

Autosampler:

- injection volume: 1µL

Pump:

- flow: 0.45mL/min

Time [min]	[%] B
0.0	5
2.0	5
9.5	80
10.5	80
12.0	5
14.0	5

10

Column compartment:

- column temperature: 25°C
- time of analysis: 14min

Detector:

15 - DAD

LC-MS analyses on Bruker Daltonik

Method name: Kinetex-BCM

Equipment:

- 20
- HPLC with UV-Vis or DAD detector
 - column: Kinetex XB C18 4.6x50mm 2.6µm
 - MS: HCT Ion Trap Bruker Daltonik

Eluents:

- 25
- (A) 0.1% formic acid-water solution
 - (B) 0.1% formic acid- ACN solution

Analytical method:

Autosampler:

- injection volume: 1µL

30 Pump:

- flow: 0.5mL/min

Time [min]	[%] B
0.0	20
6.7	80
7.5	80
7.8	95

9.5	95
10.0	20
12.0	20

Column compartment:

- column temperature: 25°C

- time of analysis: 12min

5 Detector:

- DAD

1. Mass spectrometer parameters

-Nebulizer: 40psi

-Dry gas flow: 9.0 l/min

10 -Temp: 365 C

-Ionization: positive and negative

-Scan range : 100- 1000 m/z

LC-MS analyses on Bruker Daltonik

15 Method name: Kinetex-BCM-NP

Equipment:

- HPLC with UV-Vis or DAD detector

- Column: Kinetex XB C18 (4.6 x 50mm, 2.6µm);

20 Eluents:

- (A) 0.1% formic acid-water solution

- (B) 0.1% formic acid- ACN solution

Analytical method:

25 Autosampler:

- injection volume: 1µL

Pump:

- flow: 0.5mL/min

Time [min]	[%] B
0.0	20
5.0	80
5.7	80
5.9	95
8.5	95
8.7	20
11.0	20

30 Column compartment:

- column temperature: 25°C

- time of analysis: 11min

Detector:

- DAD

LC-MS analyses on Waters Acquity UPLC SQD2

Column: Acquity UPLC BEH C18 (2.1 mm x 100 mm, 1.7 μ m);

- 5 Detection: DAD at 254nm and 280 nm + ESI, ESI (ESI i+APCI)- positive and negative detection

Method: Midpolar

Eluents:

- 10 - (A) 0.1% formic acid-water solution
- (B) 0.1% formic acid- ACN solution
- injection volume: 3 μ l
- flow= 0.5 ml/min

Time [min]	[%] B
0.0	20
0.1	20
1.1	100
2.0	100
2.5	20
3.0	20

Analysis time: 3 min

- 15 Method: Polar

Eluents:

- (A) 0.1% formic acid-water solution
- (B) 0.1% formic acid- ACN solution
- injection volume: 3 μ l
20 - flow= 0.5 ml/min

%B

Time [min]	[%] B
0.0	1
0.1	1
1.1	100
2.0	100
2.5	1
3.0	1

Analysis time: 3 min

- 25 The following abbreviations are used herein:

ACN: Acetonitrile

AcOK: Potassium acetate

AcOH: Acetic acid

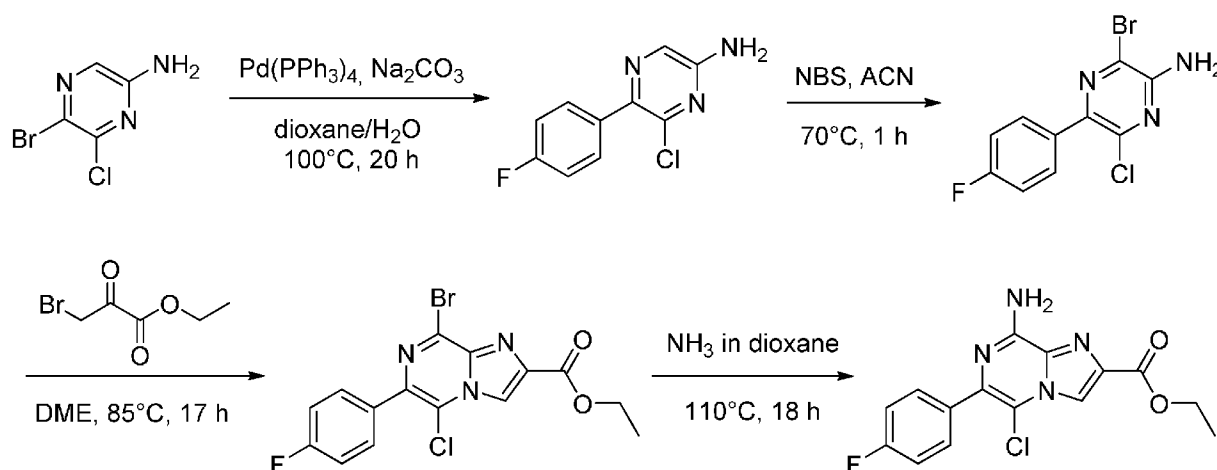
aq: Aqueous

- cAMP: Cyclic adenosine monophosphate
cod: cyclooctadiene
Conc.: Concentrated
DAST: (Diethylamino)sulfur trifluoride
- 5 DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene
DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene
DCE: 1,2-Dichloroethane
DCM: Dichloromethane
DIBAL: Diisobutylaluminium hydride
- 10 DIPEA: N-Ethyldiisopropylamine
DME: 1,2-Dimethoxyethane
DMF: Dimethylformamide
DMF: N,N-Dimethylformamide
DMSO: Dimethylsulfoxide
- 15 DPPA: Diphenyl phosphoryl azide
DPPA: Diphenylphosphoryl azide
ESI-MS: Electrospray ionization – mass spectrometry
Et₂O: Diethyl ether
Et₃N: Triethylamine
- 20 EtOAc: Ethyl acetate
EtOH: Ethanol
HATU: 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluoro-phosphate
HBTU: N,N,N',N'-Tetramethyl-O-(1H-benzotriazol-1-yl)uronium hexafluorophosphate
- 25 HTRF: Homogeneous Time Resolved Fluorescence
LCMS: Liquid chromatography – mass spectrometry
MCPBA: 3-Chloroperbenzoic acid
MeOH: Methanol
MW: Microwave
- 30 NBS: N-bromosuccinimide
NCS: N-chlorosuccinimide
NECA: 5'-(N-Ethylcarboxamido)adenosine
NMR: Nuclear magnetic resonance
on or o.n.: overnight
- 35 Pd(amphos)Cl₂: Bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II)
Pd(dppf)Cl₂: [1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II)
prep-HPLC: Preparative high-performance liquid chromatography
r.t. or rt: Room temperature
Sphos Pd G3: (2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl) [2-(2'-amino-1,1'-bi-
- 40 phenyl)]palladium(II) methanesulfonate
TFA: Trifluoroacetic acid
THF: Tetrahydrofuran

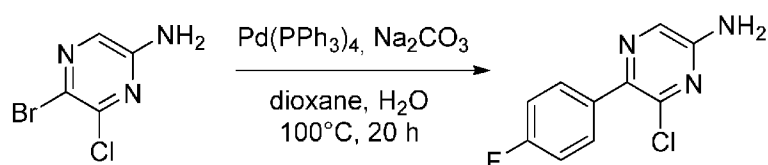
Materials: The following compounds are commercially available and/or can be prepared in a number of ways well known to one skilled in the art of organic synthesis. More specifically, disclosed compounds can be prepared using the reactions and techniques described herein. In the description of the synthetic methods described below, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment, and workup procedures, can be chosen to be the conditions standard for that reaction, unless otherwise indicated. It is understood by one skilled in the art of organic synthesis that the functionality present on various portions of the molecule should be compatible with the reagents and reactions proposed. Substituents not compatible with the reaction conditions will be apparent to one skilled in the art, and alternate methods are therefore indicated. The starting materials for the examples are either commercially available or are readily prepared by standard methods from known materials.

Procedure A:

Preparation of ethyl 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate

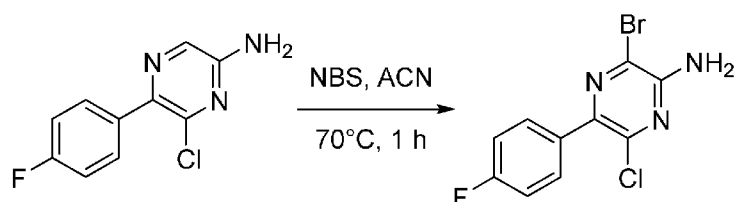


a. 6-chloro-5-(4-fluorophenyl)pyrazin-2-amine



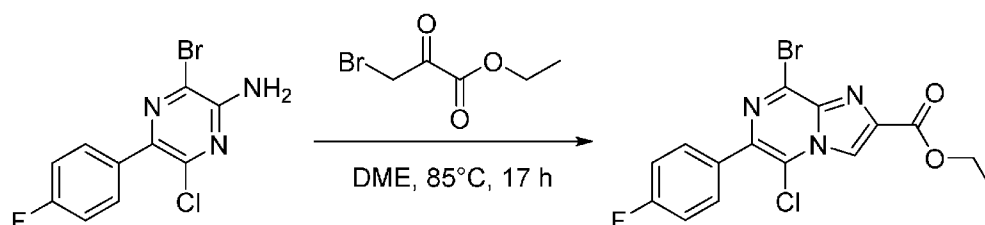
In a pressure tube were mixed 2-amino-5-bromo-6-chloropyrazine (20 g, 96.0 mmol), 4-fluorophenylboronic acid (14.8 g, 105.5 mmol), sodium carbonate (20.3 g, 191.9 mmol) in a 4:1 mixture of 1,4-dioxane : water (250 ml). The reaction mixture was sparged with argon and Pd(PPh₃)₄ (2.2 g, 2.0 mmol) was then added. The mixture was sparged with argon shortly and the vessel was sealed. The reaction mixture was heated at 100 °C for 20 h. After that time, the reaction mixture was cooled down to r.t., filtered through Celite® pad, extracted with EtOAc/NaHCO₃ solution, organic layer was washed with brine and dried over Na₂SO₄. Then the mixture was concentrated in vacuo to dryness. The obtained crude material was purified by flash chromatography on silica eluting with hexane : EtOAc (1:0 – 1:1) to lead to the title product as a light yellow solid (18.2 g, 85%). ESI-MS: 224.00 [M+H]⁺.

b. 3-bromo-6-chloro-5-(4-fluorophenyl)pyrazin-2-amine



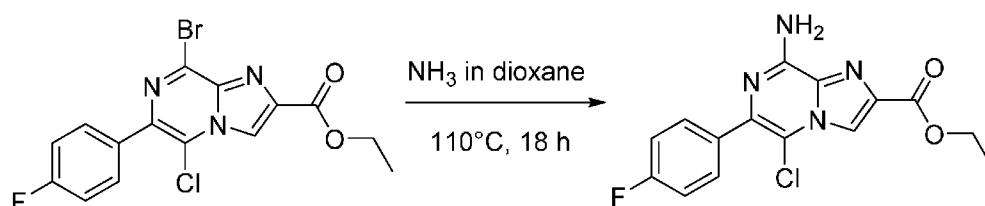
Into a pressure tube N-bromosuccinimide (12.6 g, 70.6 mmol) was added in 3 portions to the solution of 6-chloro-5-(4-fluorophenyl)pyrazin-2-amine (15 g, 64.2 mmol) in CH₃CN (100 ml). The reaction mixture was allowed to warm to room temperature then was heated at 70 °C for 1 h. After that time precipitate occurred, after cooling down the reaction mixture precipitate was filtered off to afford the title product (12.6 g, 65%) as a light yellow solid. ESI-MS: 303.70 [M+H]⁺.

c. ethyl 8-bromo-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate



To the 3-bromo-6-chloro-5-(4-fluorophenyl)pyrazin-2-amine (10 g; 33.06 mmol), dissolved in 130 ml of DME, 3-bromopyruvic acid ethyl ester (19.3 g; 99.17 mmol) was added. Reaction was stirred for 1 h at room temperature (appearance of yellow solid was observed) and then heated to 85 °C for 16 h, under an argon atmosphere. After that time extraction was performed (DCM/NaHCO₃ aq). Combined organic layers were dried over MgSO₄. Product was purified by column chromatography, eluting with DCM/EtOH (0-5%) to afford the title product as a white solid (4.5 g, 31%). ESI-MS: 400.05 [M+H]⁺.

d. ethyl 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate

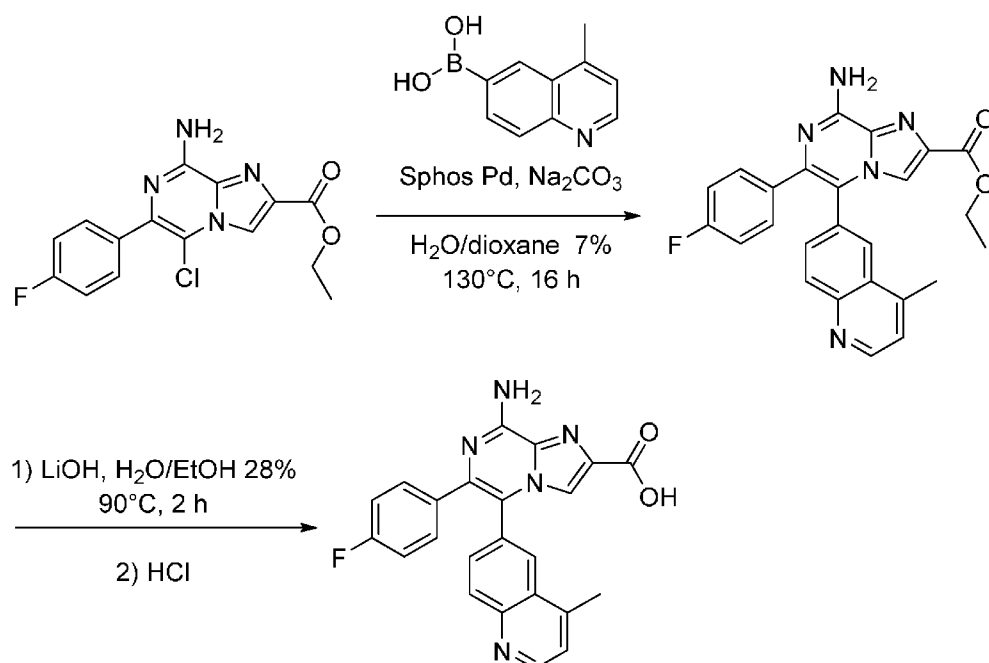


To the ethyl 8-bromo-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate (11 g; 31.06 mmol) ammonia in dioxane (140 ml) was added, reaction was heated for 20 h at 110 °C. Product was purified by column chromatography, eluting with DCM/EtOH (0-5%) to afford the title product as a white solid (10.5 g, 31.06 mmol, quant). ESI-MS: 335.15 [M+H]⁺. ¹H NMR

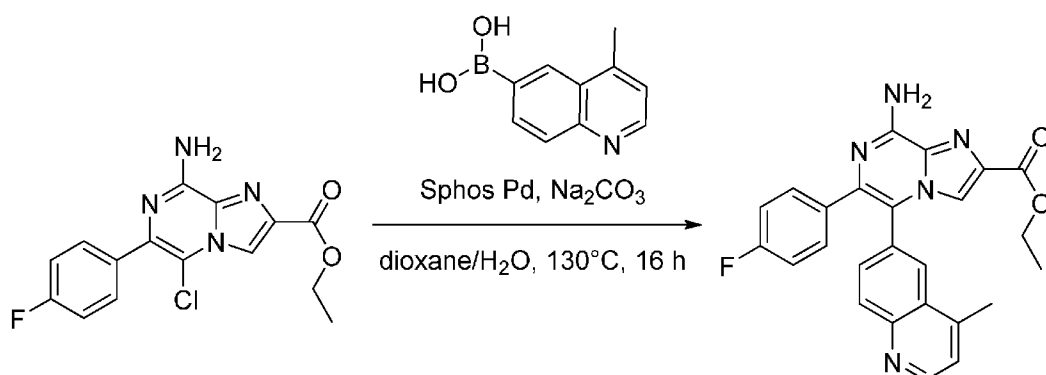
(400 MHz, DMSO-*d*₆) δ 8.48 (s, 1H), 7.77 – 7.70 (m, 2H), 7.60 (s, 2H), 7.35 – 7.28 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

Procedure B

5 Example 1: 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-*a*]pyrazine-2-carboxylic acid



10 a. ethyl 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-*a*]pyrazine-2-carboxylate



To the ethyl 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-*a*]pyrazine-2-carboxylate (Procedure A) (230 mg; 0.69 mmol) was added (4-methylquinolin-6-yl)boronic acid (380 mg, 2.06 mmol) and sodium carbonate (284 mg, 2.06 mmol) dissolved in 10ml of mixture dioxane/water 13:1 and then Sphos Pd G3 (27 mg; 0.034 mmol) was added after argon purge (15 min). Reaction mixture was heated at 130°C for 16 h. After that time the reaction mixture was cooled down to r.t., filtered and concentrated under reduced pressure. Product was purified by flash chromatography (NH₂ modified silica, DCM/EtOAc (0-50%)) to afford the title product (306 mg, 34%) as a white solid. ESI-MS: 442.40 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.04 (d, *J* = 5.0 Hz, 1H), 8.39 (s, 1H), 8.24 – 8.20 (m, 1H), 7.96 – 7.90 (m, 2H), 7.74 (d, *J* = 4.7 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.09 – 7.01 (m, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.71 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

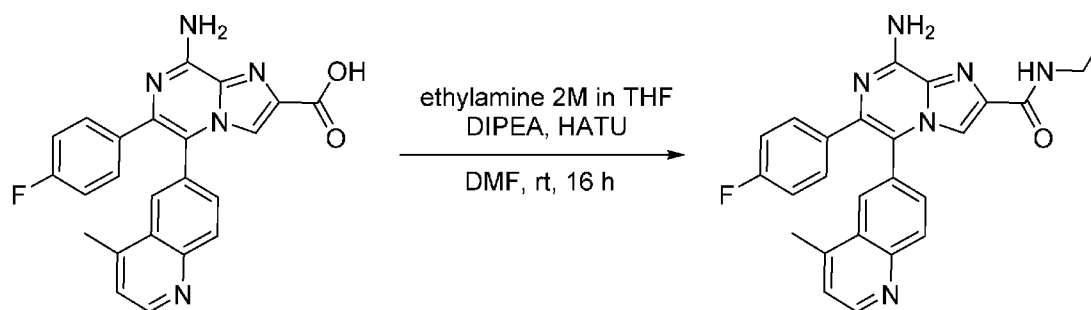
b. *8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid*



- 5 Pressure tube was charged with ethyl 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate (240 mg, 0.54 mmol) and dissolved in ethanol (5 ml) then LiOH (34 mg, 0.82 mmol) in water (2 ml) was added and reaction mixture was stirred at 90°C for 2h. Then the mixture was concentrated in vacuo to dryness and transformed into hydrochloride salt to afford the title product (230 mg, quant) as a yellow solid. ESI-MS: 414.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (d, J = 5.2 Hz, 1H), 8.49 (d, J = 1.9 Hz, 1H), 8.30 (d, J = 8.7 Hz, 1H), 8.02 – 7.92 (m, 2H), 7.85 (d, J = 5.2 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.11 (dd, J = 10.0, 7.8 Hz, 2H), 2.78 (s, 3H).
- 10

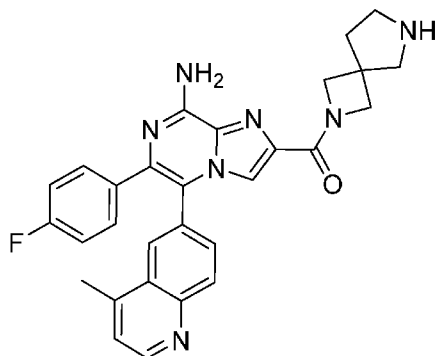
Procedure C

- 15 **Example 2: 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide**



- 20 To a solution of 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid (**Example 1**, 25 mg, 0.06 mmol) in DMF (3 ml) were added: HATU (28mg, 0.07mmol), DIPEA (0.021 ml, 0.12 mmol) and ethylamine 2M in THF (0.036 ml). The mixture was stirred at room temperature for 16 h. The mixture was evaporated. Extracted with EtOAc/H₂O, organic layer was washed with brine and dried over Na₂SO₄. Then the mixture was concentrated in vacuo to dryness. The obtained crude material was purified by flash chromatog-
- 25 raphy (silica gel, DCM, MeOH 0-7%), then transformed into hydrochloride salt to give the title compound (18 mg, 68%) as white solid, hydrochloride salt. ESI-MS: 441.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.03 (d, J = 5.0 Hz, 1H), 8.39 (s, 1H), 8.23 – 8.14 (m, 2H), 7.89 (d, J = 7.6 Hz, 2H), 7.72 (s, 1H), 7.38 (dd, J = 8.3, 5.7 Hz, 2H), 7.07 (t, J = 8.8 Hz, 2H), 3.33 – 3.25 (m, 2H), 2.71 (s, 3H), 1.11 (t, J = 7.2 Hz, 3H).

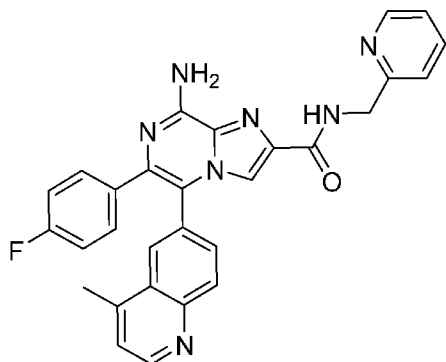
Example 3: 2-{2,6-diazaspiro[3.4]octane-2-carbonyl}-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine



- 5 The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2,6-diaza-spiro[3.4]octane-6-carboxylic acid tert-butyl ester for ethylamine to lead to the title compound (2 mg, 69%) as white solid. ESI-MS: 508.40 [M+H]⁺. ¹H NMR (400 MHz, Deuterium Oxide) δ 9.16 (d, J = 4.6 Hz, 1H), 8.89 (s, 1H), 8.47 (d, J = 8.5 Hz, 1H), 8.43 (d, J = 1.9 Hz, 1H), 8.27 (s, 1H), 8.16 (dd, J = 8.7, 1.9 Hz, 1H), 7.83 (d, J = 4.9 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.40 – 7.34 (m, 2H), 5.13 (s, 3H), 4.02 (d, J = 4.1 Hz, 2H), 3.88 – 3.82 (m, 2H), 2.92 (s, 3H), 2.83 – 2.77 (m, 2H), 2.64 (s, 1H).

Example 4:

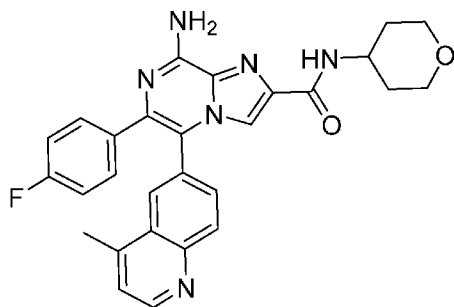
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(pyridin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide



- 20 The title compound was synthesized following the approach outlined in **Procedure C**, substituting pyridin-2-ylmethanamine for ethylamine and substituting Et₃N for DIPEA and substituting HBTU for HATU to lead to the title compound (36 mg, 17%) as yellow solid, hydrochloride salt. ESI-MS: 502.10 [M+H]⁺. ¹H NMR (400 MHz, Methanol-*d*₄) δ 9.11 (d, J = 5.5 Hz, 1H), 8.77 (d, J = 5.7 Hz, 1H), 8.67 (s, 1H), 8.50 (td, J = 8.0, 1.5 Hz, 1H), 8.28 (d, J = 8.8 Hz, 1H), 8.19 (s, 1H), 8.11 (dd, J = 8.8, 1.5 Hz, 1H), 8.00 (dd, J = 15.4, 6.8 Hz, 2H), 7.96 – 7.87 (m, 1H), 7.52 (dt, J = 14.3, 7.2 Hz, 2H), 7.10 (t, J = 8.7 Hz, 2H), 4.97 (s, 2H), 2.96 (s, 3H).

Example 5:

8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide

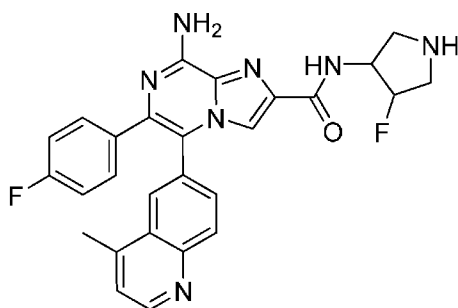


5

The title compound was synthesized following the approach outlined in **Procedure C**, substituting 4-aminotetrahydropyran for ethylamine and conducting this step for 3 h to lead to the title compound (18 mg, 87%) as yellow solid, hydrochloride salt. ESI-MS: 497.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.2 Hz, 1H), 8.47 (d, J = 1.8 Hz, 1H), 8.30 (d, J = 8.7 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 7.99 (s, 1H), 7.95 (dd, J = 8.7, 1.8 Hz, 1H), 7.83 (d, J = 5.1 Hz, 1H), 7.44 – 7.35 (m, 2H), 7.15 – 7.04 (m, 2H), 4.05 – 3.92 (m, 1H), 3.90 – 3.80 (m, 2H), 3.38 (m, J = 11.8, 2.1 Hz, 2H), 2.77 (s, 3H), 1.81 – 1.68 (m, 2H), 1.63 – 1.49 (m, 2H).

Example 6:

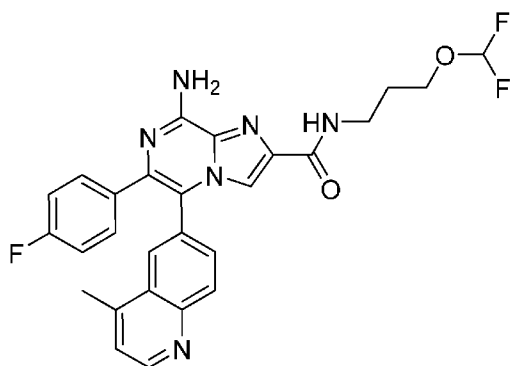
8-amino-6-(4-fluorophenyl)-N-(4-fluoropyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting tert-butyl 3-amino-4-fluoropyrrolidine-1-carboxylate for ethylamine and substituting Et₃N for DIPEA and substituting HBTU for HATU to lead to the title compound (27.5 mg, 52%) as yellow solid, hydrochloride salt. ESI-MS: 500.20 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.71 (s, 2H), 9.12 (d, J = 5.2 Hz, 1H), 9.03 (d, J = 7.3 Hz, 1H), 8.53 (s, 1H), 8.34 – 8.21 (m, 2H), 7.95 – 7.79 (m, 2H), 7.45 – 7.33 (m, 2H), 7.16 – 7.03 (m, 2H), 5.42 – 5.16 (m, 1H), 4.76 – 4.62 (m, 1H), 3.63 – 3.55 (m, 2H), 3.44 – 3.30 (m, 2H), 2.84 (s, 3H).

Example 7:

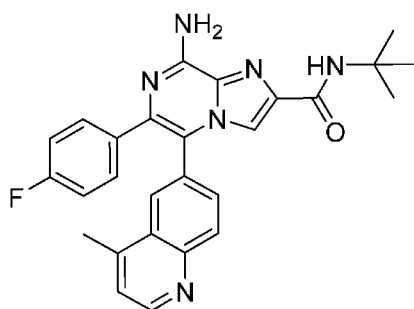
8-amino-N-[3-(difluoromethoxy)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-(difluoromethoxy)propan-1-amine for ethylamine and performing this step for 1.5 h to lead to the title compound (26 mg, 17%) as yellow solid, hydrochloride salt. ESI-MS: 521.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.08 (d, J = 5.1 Hz, 1H), 8.45 (s, 1H), 8.33 (t, J = 6.0 Hz, 1H), 8.25 (d, J = 8.7 Hz, 1H), 7.96 – 7.89 (m, 2H), 7.81 – 7.76 (m, 1H), 7.42 – 7.36 (m, 2H), 7.12 – 7.05 (m, 2H), 6.66 (t, J = 76.2 Hz, 1H), 3.86 (t, J = 6.4 Hz, 2H), 3.34 (q, J = 6.7 Hz, 2H), 2.75 (s, 3H), 1.87-1.80 (m, J = 6.6 Hz, 2H).

Example 8:

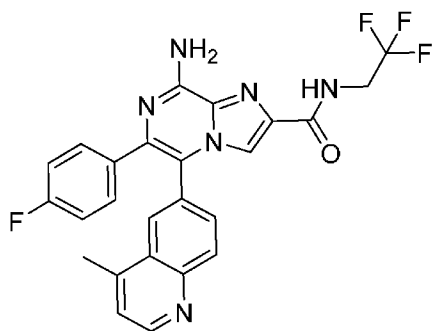
8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting tert-butylamine for ethylamine to lead to the title compound (19 mg, 28%) as yellow solid, hydrochloride salt. ESI-MS: 469.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (d, J = 5.2 Hz, 1H), 8.49 (s, 1H), 8.32 (d, J = 8.7 Hz, 1H), 7.95 (dd, J = 8.8, 1.8 Hz, 1H), 7.91 – 7.82 (m, 2H), 7.48 (s, 1H), 7.43 – 7.36 (m, 2H), 7.10 (t, J = 8.9 Hz, 2H), 2.79 (s, 3H), 1.39 (s, 9H).

Example 9:

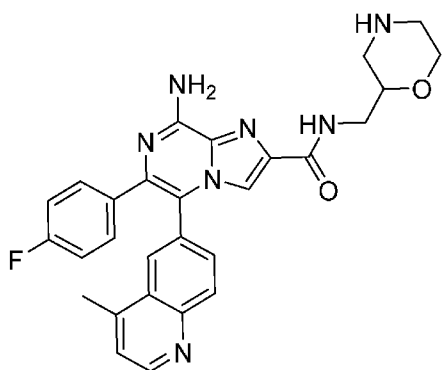
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2,2,2-trifluoroethylamine for ethylamine to lead to the title compound (23 mg, 99%) as yellow solid, hydrochloride salt. ESI-MS: 495.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.04 (d, J = 5.0 Hz, 1H), 8.75 (t, J = 6.6 Hz, 1H), 8.42 (s, 1H), 8.22 (d, J = 8.6 Hz, 1H), 8.02 (s, 1H), 7.90 (d, J = 8.8 Hz, 1H), 7.74 (s, 1H), 7.41 – 7.34 (m, 2H), 7.06 (t, J = 8.9 Hz, 2H), 4.09 (dd, J = 9.8, 6.8 Hz, 2H), 2.73 (d, J = 1.7 Hz, 3H).

Example 10:

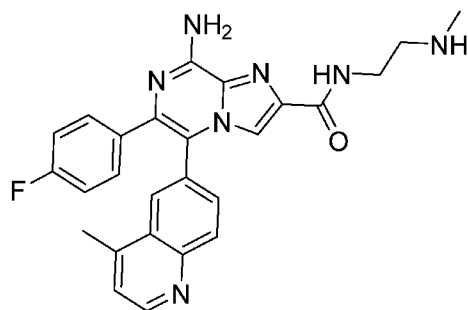
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(morpholin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 4-Boc-2-aminomethylmorpholine for ethylamine to lead to the title compound (19 mg, 34%) as yellow solid, hydrochloride salt. ESI-MS: 512.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.41 – 9.23 (m, 2H), 9.06 (d, J = 5.1 Hz, 1H), 8.43 (s, 1H), 8.33 (t, J = 6.2 Hz, 1H), 8.26 (d, J = 8.7 Hz, 1H), 7.97 (s, 1H), 7.91 (d, J = 8.7 Hz, 1H), 7.77 (s, 1H), 7.42 – 7.35 (m, 2H), 7.08 (t, J = 8.9 Hz, 2H), 3.99 – 3.93 (m, 2H), 3.89 – 3.83 (m, 2H), 3.42 – 3.35 (m, 2H), 3.23 (d, J = 12.5 Hz, 1H), 3.16 (d, J = 12.9 Hz, 1H), 3.01 – 2.89 (m, 1H), 2.74 (s, 3H).

Example 11:

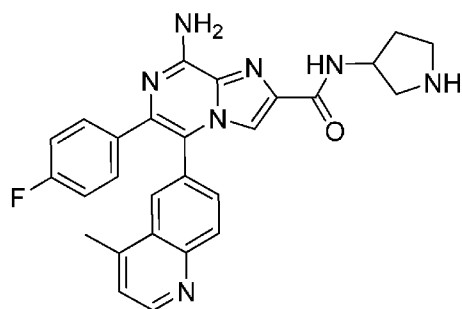
8-amino-6-(4-fluorophenyl)-N-[2-(methylamino)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting N-methylenediamine for ethylamine to lead to the title compound (14 mg, 19%) as yellow solid, hydrochloride salt. ESI-MS: 470.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.00 (d, J = 4.9 Hz, 1H), 8.67 (s, 2H), 8.58 (t, J = 6.0 Hz, 1H), 8.36 (s, 1H), 8.20 (d, J = 8.7 Hz, 1H), 7.97 (s, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.68 (s, 2H), 7.41 – 7.35 (m, 2H), 7.09 – 7.02 (m, 2H), 3.58 – 3.52 (m, 2H), 3.10 – 3.02 (m, 2H), 2.70 (s, 3H), 2.56 (t, J = 5.4 Hz, 3H).

10 Example 12:

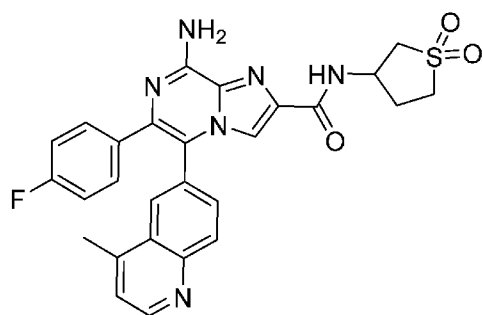
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide



15 The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-Boc-3-aminopyrrolidine for ethylamine to lead to the title compound (9 mg, 21%) as yellow solid, hydrochloride salt. ESI-MS: 482.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.25 (s, 1H), 9.15 (s, 1H), 9.07 (d, J = 5.1 Hz, 1H), 8.71 (d, J = 7.2 Hz, 1H), 8.45 (s, 1H), 8.26 (d, J = 8.8 Hz, 1H), 8.10 (s, 1H), 7.98 (s, 1H), 7.92 – 7.86 (m, 1H), 7.78 (s, 1H), 7.42 – 7.34 (m, 2H), 7.08 (t, J = 8.9 Hz, 2H), 4.57 (h, J = 6.4 Hz, 1H), 3.43 – 3.29 (m, 2H), 3.21 (q, J = 6.3 Hz, 1H), 3.14 (dq, J = 11.5, 5.7 Hz, 1H), 2.78 (s, 3H), 2.26 – 2.15 (m, 1H), 2.01 – 1.89 (m, 1H).

Example 13:

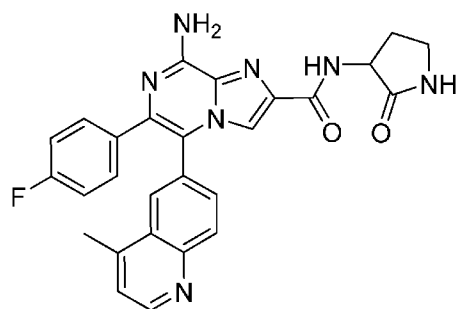
25 *8-amino-N-(1,1-dioxo-1λ⁶-thiolan-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide*



The title compound was synthesized following the approach outlined in **Procedure C**, substituting tetrahydro-3-thiophenamine 1,1-dioxide hydrochloride for ethylamine and substituting HBTU
 5 for HATU to lead to the title compound (65 mg, 19%) as yellow solid, hydrochloride salt. ESI-MS: 531.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (d, J = 5.2 Hz, 1H), 8.71 (d, J = 7.7 Hz, 1H), 8.50 (d, J = 1.9 Hz, 1H), 8.31 (d, J = 8.7 Hz, 1H), 8.06 (s, 1H), 7.95 (dd, J = 8.7, 1.8 Hz, 1H), 7.85 (d, J = 5.3 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.14 – 7.06 (m, 2H), 4.70 (h, J = 8.0 Hz, 1H), 3.47 (dd, J = 13.2, 7.8 Hz, 1H), 3.35 (ddd, J = 12.9, 8.2, 4.3 Hz, 1H), 3.24 – 3.16 (m, 1H),
 10 3.16 – 3.08 (m, 1H), 2.79 (s, 3H), 2.43 (dq, J = 13.1, 7.1, 6.7 Hz, 1H), 2.27 – 2.17 (m, 1H).

Example 14:

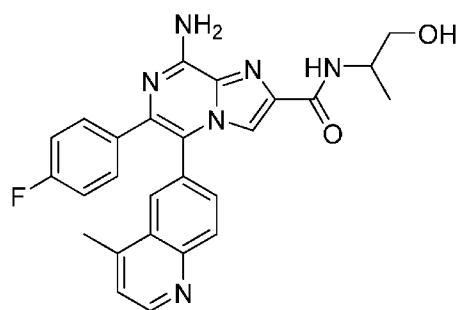
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2-oxopyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-amino-2-pyrrolidinone for ethylamine 2M in THF and substituting HBTU for HATU to lead
 20 to the title compound (16 mg, 20%) as yellow solid, hydrochloride salt. ESI-MS: 496.30 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.12 (d, J = 5.2 Hz, 1H), 8.51 (s, 1H), 8.36 (dd, J = 13.2, 5.2 Hz, 2H), 8.02 (s, 1H), 7.95 (s, 1H), 7.86 (d, J = 5.3 Hz, 1H), 7.42 (dd, J = 8.6, 5.6 Hz, 2H), 7.11 (t, J = 8.8 Hz, 2H), 4.52 (q, J = 9.0 Hz, 1H), 3.28 – 3.20 (m, 2H), 2.79 (s, 3H), 2.06–1.85 (m, 1H), 2.06 – 1.85 (m, 1H).

Example 15:

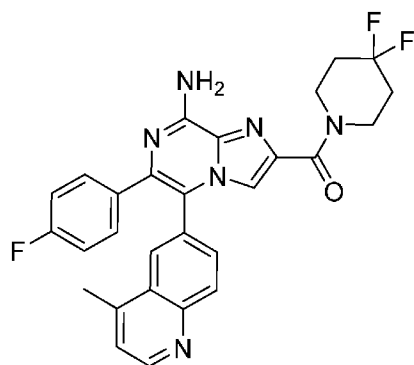
8-amino-6-(4-fluorophenyl)-N-(1-hydroxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-aminopropan-1-ol for ethylamine and substituting HBTU for HATU to lead to the title compound (12 mg, 13%) as yellow solid, hydrochloride salt. ESI-MS: 471.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.2 Hz, 1H), 8.47 (d, J = 1.9 Hz, 1H), 8.29 (d, J = 8.7 Hz, 1H), 8.00 – 7.90 (m, 2H), 7.84 (dd, J = 10.7, 6.8 Hz, 2H), 7.44 – 7.36 (m, 2H), 7.10 (t, J = 8.9 Hz, 2H), 4.04-3.98 (m, 2H), 3.47-3.39 (m, 2H), 2.77 (s, 3H), 1.14 (d, J = 6.7 Hz, 3H).

10 Example 16:

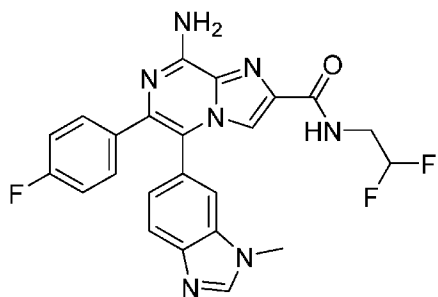
2-(4,4-difluoropiperidine-1-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 4,4-difluoropiperidine for ethylamine to lead to the title compound (43 mg, 48%) as yellow solid, hydrochloride salt. ESI-MS: 517.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.09 (d, J = 5.1 Hz, 1H), 8.48 (s, 1H), 8.27 (d, J = 8.8 Hz, 1H), 8.10 (s, 2H), 7.92 (dd, J = 8.7, 1.8 Hz, 1H), 7.88 (s, 1H), 7.82 (d, J = 5.1 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.14 – 7.06 (m, 2H), 4.17 (s, 2H), 3.73 (s, 2H), 2.76 (s, 3H), 2.06 (s, 4H).

Example 17:

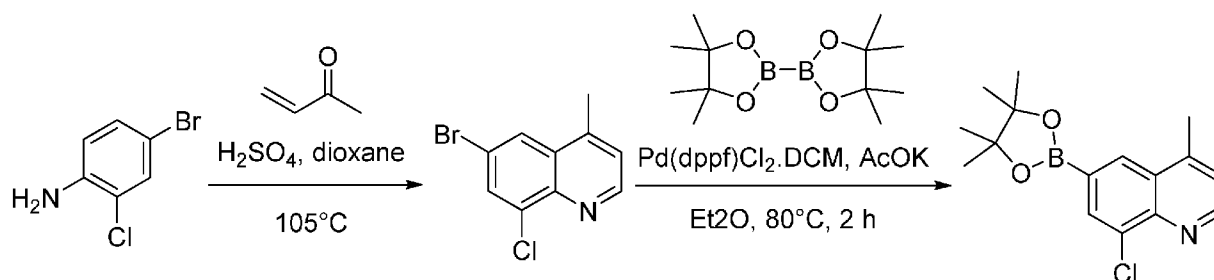
8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine and substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in this step and performing this step for 2 h at 100°C to lead to the title compound (24.2 mg, 91%) as beige solid, hydrochloride salt. ESI-MS: 466.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.61 (s, 1H), 8.64 (t, J = 6.2 Hz, 1H), 8.21 (d, J = 1.4 Hz, 1H), 8.02 (s, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.51 – 7.36 (m, 3H), 7.13 (t, J = 8.9 Hz, 2H), 6.13 (tt, J = 55.9, 3.8 Hz, 1H), 4.05 (s, 3H), 3.69 (tt, J = 15.7, 3.8 Hz, 2H).

Procedure D

Preparation of 8-chloro-4-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline



a. 6-bromo-8-chloro-4-methylquinoline

In a 3-necked flask 4-bromo-2-chloroaniline (6.6 g, 32 mmol) and 1,4-dioxane (450 ml) were stirred at 12°C, into it sulfuric acid (3.4 ml, 64 mmol) was added slowly and the mixture was heated to reflux. Into this refluxing mixture 3-buten-2-one (3.89 ml, 48 mmol) was added dropwise. Reaction was heated for 6 h at reflux and then another portion of 3-buten-2-one (3.89 ml, 48 mmol) was added and reaction was carried for additional 4 h. The reaction mixture was cooled to r.t. and the solvent was evaporated, the residue was dissolved in DCM, 1M solution of sodium carbonate (aq) was added until pH 8. Organic layer was washed with water, dried with Na₂SO₄, filtered and concentrated. Product was purified by flash chromatography (silica gel, hexane/DCM 50-100% of DCM) to afford a title product (3.82 g, 47%) as a yellow solid. ESI-MS: 257.80 [M+H]⁺.

b. 8-chloro-4-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline

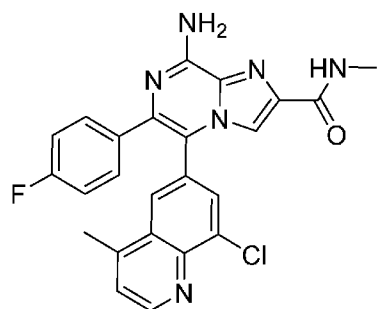
A pressure tube was charged with 6-bromo-8-chloro-4-methylquinoline (500 mg, 1.95 mmol), bis(pinacolato)diboron (643 mg, 2.53 mmol) and KOAc (574 mg, 5.85 mmol) and 75 mL of diethyl ether and sparged with argon for 10 min. Pd(dppf)Cl₂ • DCM (71 mg, 0.1 mmol) was added in one portion and the reaction mixture was sparged with argon for additional 5 min. The

pressure tube was capped and the reaction mixture was stirred at 80°C for 2 h. Then the reaction mixture was cooled to r.t., filtered through Celite® and the filtrate was concentrated under reduced pressure. Product was purified by flash chromatography (silica gel, hexane/EtOAc) to afford the title compound (0.518g, 87.5%) as a yellowish solid. ESI-MS: 304.20 [M+H]⁺.

5

Example 18:

8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



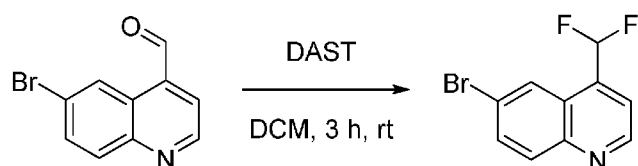
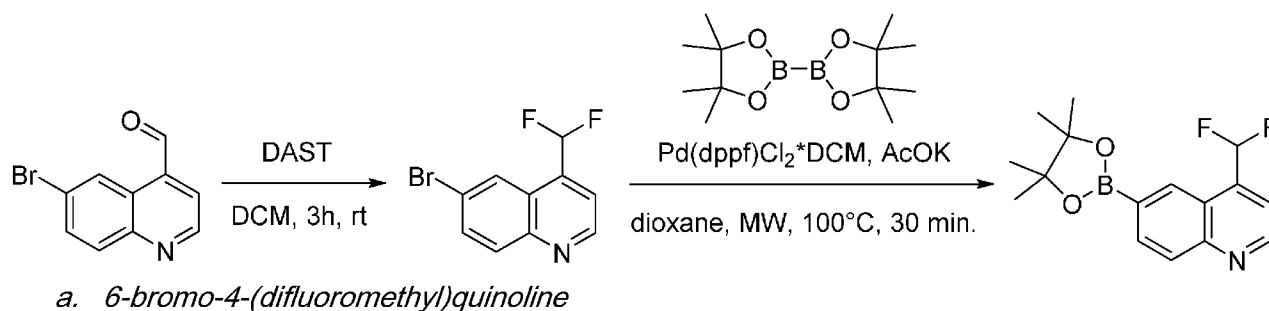
10

The title compound was synthesized following the approach outlined in **Procedure F**, substituting 8-chloro-4-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (**Procedure D**) for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **Procedure F**, **step b** substituting SPhos Pd G3 for Pd(amphos)Cl₂ in **step b** and performing this step for 2 h at 120°C on oil bath to lead to the title compound (24.5 mg, 6.5%) as yellow solid, hydrochloride salt. ESI-MS: 461.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.94 (d, J = 4.4 Hz, 1H), 8.23 – 8.17 (m, 2H), 8.04 (bs, 1H), 7.97 (d, J = 1.8 Hz, 1H), 7.56 (d, J = 4.3 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.17 – 7.10 (m, 2H), 2.78 (d, J = 4.7 Hz, 3H), 2.60 (s, 3H).

15

20 Procedure E:

Preparation of 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline

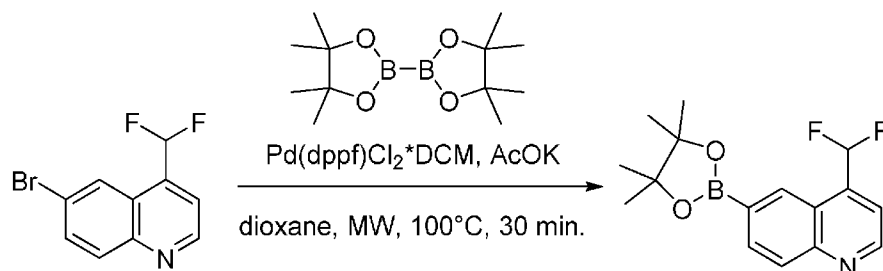


25

Into the flask 6-bromoquinoline-4-carbaldehyde (500 mg, 2.21 mmol) was added and dissolved in DCM (5 ml) to this (diethylamino)sulfur trifluoride (DAST) (0.705ml, 4.24mmol) was added. The mixture was stirred for 3 h at room temperature. The mixture was carefully

quenched with saturated sodium bicarbonate and extracted with DCM. Combined organic layers were dried with magnesium sulfate and evaporated to provide the product (446 mg, 82%) as a brown solid. ESI-MS: 257.90 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.10 (d, J = 4.3 Hz, 1H), 8.38 (q, J = 1.6 Hz, 1H), 8.11 (d, J = 8.9 Hz, 1H), 8.02 (dd, J = 9.0, 2.1 Hz, 1H), 7.82 (d, J = 4.4 Hz, 1H), 7.74 (t, J = 53.6 Hz, 1H).

b. 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline

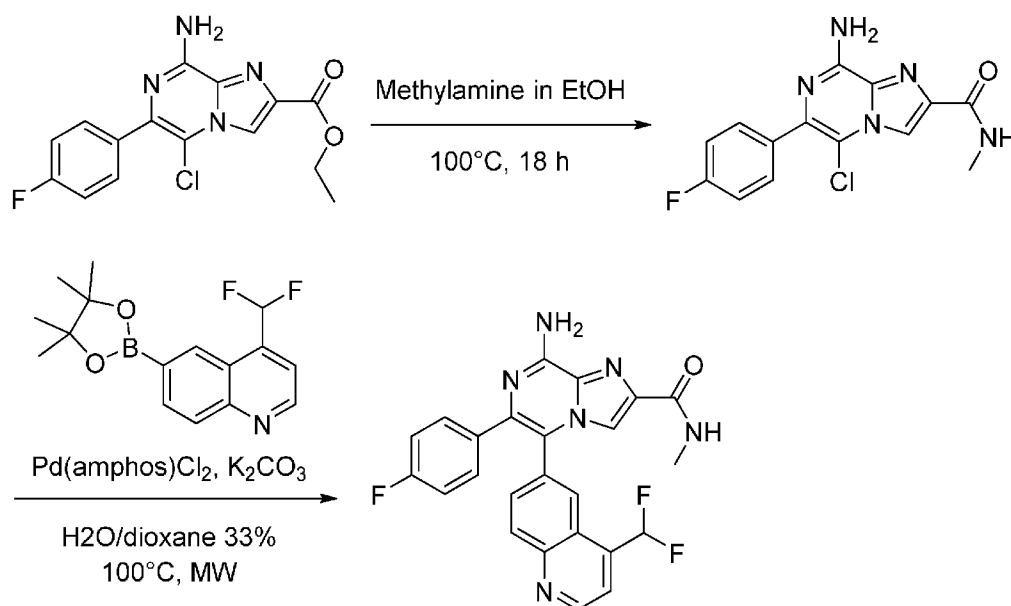


Microwave tube was charged with 6-bromo-4-(difluoromethyl)quinoline (0.100 g, 0.39 mmol), bis(pinacolate)diboron (167 mg, 0.66 mmol), potassium acetate (0.076 g, 0.77 mmol) and dioxane (2 ml) and sparged with argon for 15 min. Pd(dppf)Cl₂*DCM (0.085 g, 0.12 mmol) was added and argon was bubbled through the suspension for another 5 minutes. Subsequently the tube was closed and the reaction mixture was heated at 100°C for 30 minutes under microwave irradiation. Then reaction mixture was cooled to r.t. then diluted with EtOAc, washed with brine. Organic layer was dried over magnesium sulfate, filtered and concentrated to give crude product as a yellowish oil. The product containing a mixture of the acid and ester was used for the next step without further purification. ESI-MS: 223.0, 306.3 [M+H]⁺.

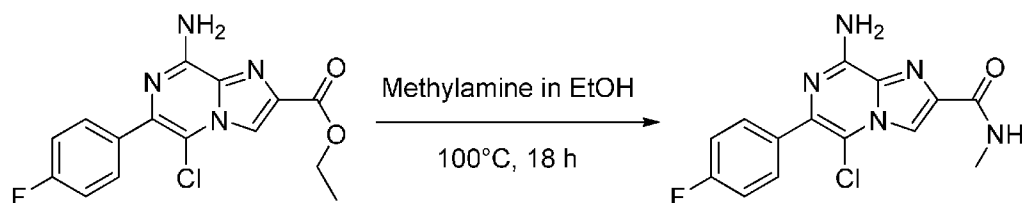
Example 19:

Procedure F

8-amino-5-[4-(difluoromethyl)quinolin-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide

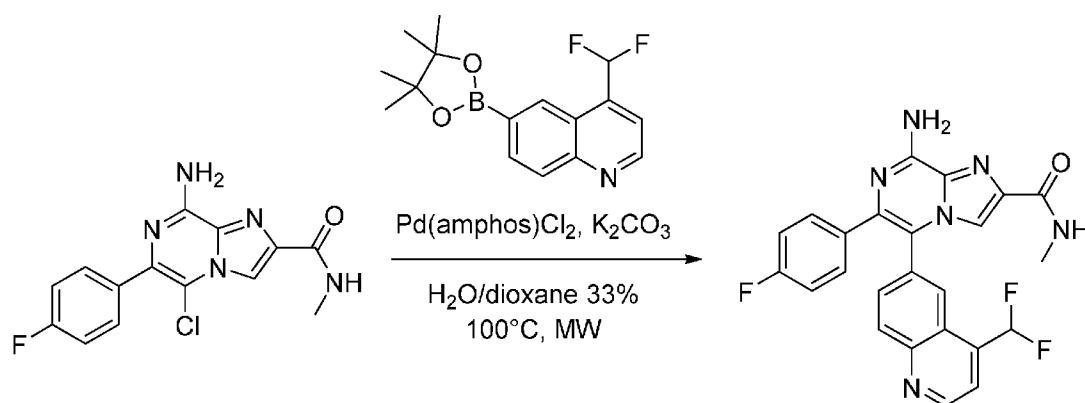


a. 8-amino-5-chloro-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



Into the pressure tube ethyl 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate (1 g, 2.64 mmol), absolute ethanol (4 ml) and methylamine 33%(w) in absolute ethanol (1.64 ml, 13.2 mmol) were added. Reaction was heated for 16 h at 100°C. The mixture was evaporated to lead to the title compound as yellowish solid (0.81 g, 96%). ESI-MS: 321.30 [M+H]⁺.

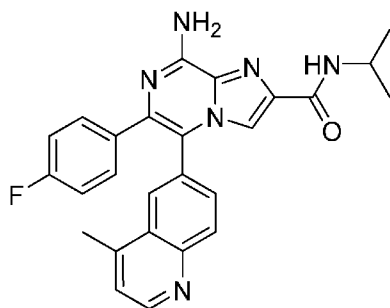
b. 8-amino-5-[4-(difluoromethyl)quinolin-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



Microwave tube was charged with 8-amino-5-chloro-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide (40 mg, 0.125 mmol), 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (Procedure E, 40 mg, 0.15mmol) potassium carbonate (43 mg, 0.31 mmol) and dioxane/water 2:1 (1 ml) and sparged with argon for 15 min. Pd(amphos)Cl₂ (4 mg, 0.05 eq) was added in one portion and argon was bubbled through the suspension for another 5 minutes. Subsequently the tube was closed and the reaction mixture was heated for 1 h at 100°C under microwave irradiation. After that time reaction mixture was diluted with EtOAc and water. Water phase was washed with EtOAc. The combined organic phases were dried over MgSO₄, filtered and evaporated. Product was purified by flash chromatography (diol-modified silica gel, EtOAc, Hexane 20-80%) to lead to the title compound (27 mg, 47%) as yellow solid, hydrochloride salt. ESI-MS: 463.25 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (d, J = 4.4 Hz, 1H), 8.55 (s, 2H), 8.28 – 8.17 (m, 3H), 7.97 (s, 1H), 7.88 (dd, J = 8.7, 1.9 Hz, 1H), 7.81 (d, J = 4.4 Hz, 1H), 7.55 (t, J = 53.7 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.19 – 7.04 (m, 2H), 2.77 (d, J = 4.7 Hz, 3H)

Example 20:

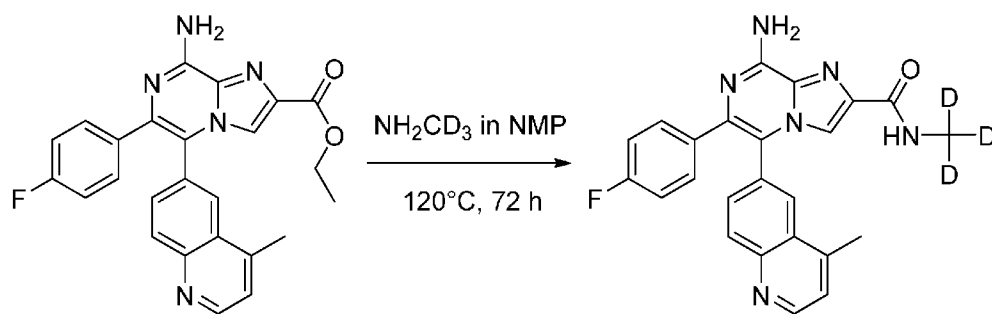
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting isopropylamine for ethylamine to lead to the title compound (30.5 mg, 30%) as yellow solid, hydrochloride salt. ESI-MS: 455.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.09 (d, J = 5.2 Hz, 1H), 8.45 (s, 1H), 8.28 (d, J = 8.7 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.90 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 5.0 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.09 (t, J = 8.9 Hz, 2H), 4.07 (dt, J = 7.9, 6.4 Hz, 1H), 2.76 (s, 3H), 1.16 (d, J = 6.6 Hz, 6H).

Example 21:

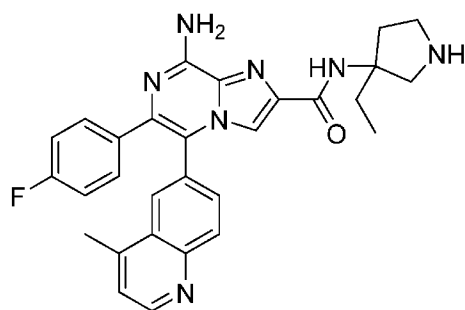
8-amino-6-(4-fluorophenyl)-N-(²H₃)methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



In a pressure tube ethyl 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate (**Procedure B, step a**) (30 mg, 0.07 mmol) was suspended in a solution of NH₂CD₃ in NMP (5 ml, 0.07 mmol) and stirred for 72 h at 120°C. Then solvent was evaporated and product was purified by flash chromatography (DCM/MeOH 0-10%) to lead to the title compound (22 mg, 75%) as yellow solid, hydrochloride salt. ESI-MS: 430.30 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.15 (d, J = 5.2 Hz, 1H), 8.54 (d, J = 1.7 Hz, 1H), 8.36 (d, J = 8.7 Hz, 1H), 8.26 (s, 1H), 8.06 (s, 1H), 7.99 – 7.86 (m, 2H), 7.47 – 7.37 (m, 2H), 7.19 – 7.07 (m, 2H), 2.82 (s, 3H).

Example 22:

8-amino-N-(3-ethylpyrrolidin-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

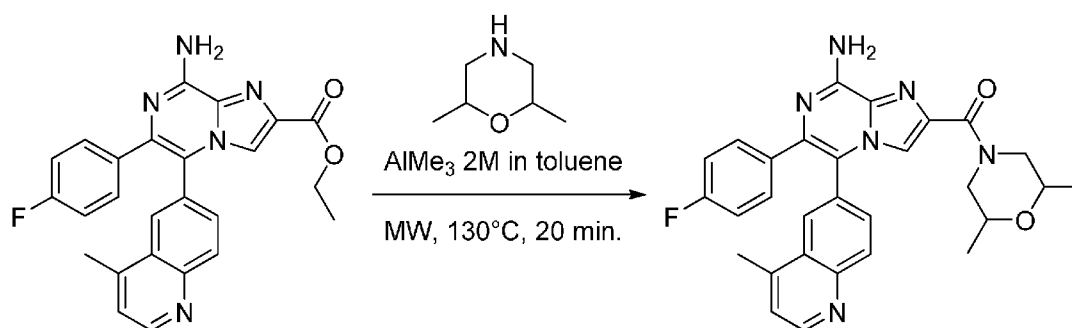


The title compound was synthesized following the approach outlined in **Procedure C**, substituting tert-butyl 3-amino-3-ethylpyrrolidine-1-carboxylate for ethylamine and substituting Et₃N for DIPEA and substituting HBTU for HATU to lead to the title compound (22 mg, 50%) as yellow solid, hydrochloride salt. ESI-MS: 510.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.31 (s, 2H), 9.06 (d, J = 4.9 Hz, 1H), 8.43 (s, 1H), 8.26 (d, J = 8.7 Hz, 1H), 8.14 (s, 1H), 8.07 (s, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.77 (s, 1H), 7.38 (dd, J = 8.7, 5.6 Hz, 2H), 7.08 (t, J = 8.9 Hz, 2H), 3.76 (s, 1H), 3.28 (s, 2H), 3.17 – 3.08 (m, 1H), 2.76 (s, 3H), 2.47 – 2.36 (m, 1H), 2.17 – 2.03 (m, 1H), 2.00 – 1.87 (m, 1H), 1.83 – 1.69 (m, 1H), 0.83 (t, J = 7.4 Hz, 3H).

Procedure G

Example 23:

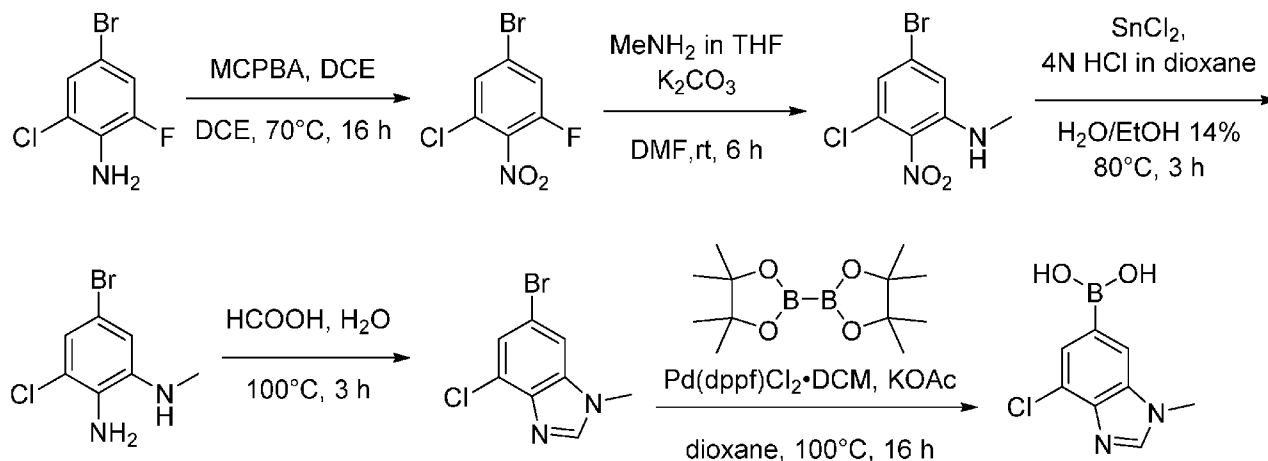
2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine



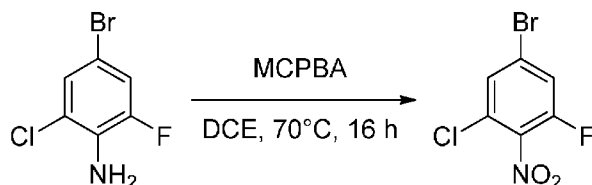
In the microwave reactor ethyl 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate (**Procedure B, step a**, 40 mg, 0.091 mmol) and 2,6-dimethylmorpholine (0.11 ml, 0.91 mmol) were dissolved in THF (2.3 ml). Then 2M AlMe₃ in toluene (0.18 ml, 0.36 mmol) was added slowly under argon atmosphere. The resulted mixture was heated to 130°C under microwave irradiation for 20 min. Then reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. Product was purified by HPLC (with TFA addition) to lead to the title compound (10 mg, 19%) as yellow solid, hydrochloride salt. ESI-MS: 511.30 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.07 (d, J = 5.1 Hz, 1H), 8.50 – 8.42 (m, 1H), 8.23 (d, J = 8.7 Hz, 1H), 7.97 – 7.71 (m, 3H), 7.45 – 7.34 (m, 2H), 7.19 – 6.98 (m, 2H), 5.05 – 4.89 (m, 1H), 4.41 – 4.30 (m, 1H), 3.22 – 3.07 (m, 2H), 2.96 – 2.79 (m, 2H), 2.75 (s, 3H), 1.13 (d, J = 5.8 Hz, 6H).

Procedure H

Preparation of (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid

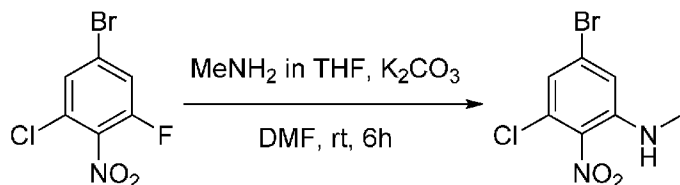


5 *a. 5-bromo-1-chloro-3-fluoro-2-nitrobenzene*



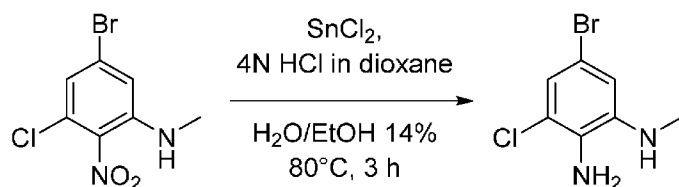
10 In a pressure tube 4-bromo-2-chloro-6-fluoroaniline (1 g, 4.45 mmol) was dissolved in 1,2-dichloroethane (20 ml) into it 3-chloroperbenzoic acid (3.12 ml, 17.15 mmol) was added. Reaction was heated for 12 h at 70°C. Resulting mixture was diluted with DCM and washed with water followed by saturated solution of NaHCO₃. Organic phase was dried over MgSO₄, filtrated and concentrated. Crude reaction mixture was used to the next step without further purification.

b. 5-bromo-3-chloro-N-methyl-2-nitroaniline



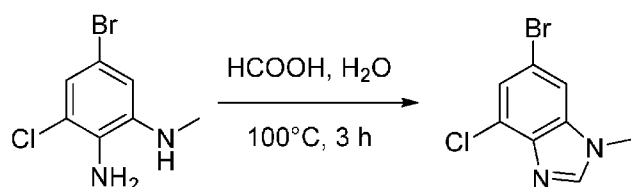
15 Round bottom flask was charged with 5-bromo-1-chloro-3-fluoro-2-nitrobenzene (100 mg, 0.4 mmol), K₂CO₃ (81.5 mg, 0.59 mmol) and DMF (2 ml), the mixture was cooled to 0°C and methylamine 2M in THF (0.3 ml, 0.59 mmol) was added. Reaction was left at r.t. for 6 h. Then the solvent was evaporated and product was purified by flash chromatography (silica gel, hexane/chloroform 0-20%) to afford the title product as orange solid (26 mg, 25%).

c. 5-bromo-3-chloro-N1-methylbenzene-1,2-diamine



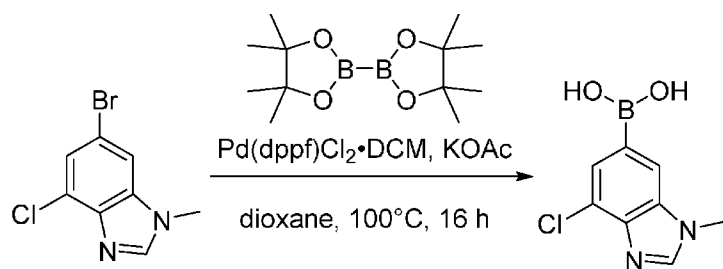
A pressure tube was charged with 5-bromo-3-chloro-N-methyl-2-nitroaniline (966 mg, 3.64 mmol), EtOH (30 ml), water (5 ml), 4N HCl in dioxane (4.55 ml, 18.2 mmol) and then tin(II) chloride was added and the mixture was stirred at 80°C for 3 h. After that time, the mixture was cooled to room temperature and concentrated under reduced pressure. The mixture was cautiously treated with an excess of 12.5M NaOH. The mixture was diluted with EtOAc and washed with water. Organic phase was dried over MgSO₄, filtered, and concentrated. Resulting brown oil was used for the next step without further purification (0.82 g, 96%). ESI-MS: 236.00[M+H]⁺.

d. 6-bromo-4-chloro-1-methyl-1H-1,3-benzodiazole



Into a pressure tube suspension of 5-bromo-3-chloro-N-methylbenzene-1,2-diamine (822 mg, 3.5 mmol) in water (5 ml) was added followed by formic acid (1.32 ml, 35 mmol). Reaction was heated for 3 h at 100°C. After that time reaction mixture was cooled, flask was put into an ice bath and 0.5M NaOH solution was added until pH 9-10. White precipitate was filtered off and a filtrate was washed with EtOAc and DCM. Organic phase was dried over MgSO₄ and evaporated. Product was purified by flash chromatography (silica gel, DCM/MeOH 95:5) to afford the title product as a brown solid (0.622 g, 73%). ESI-MS: 246.95 [M+H]⁺.

e. (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid

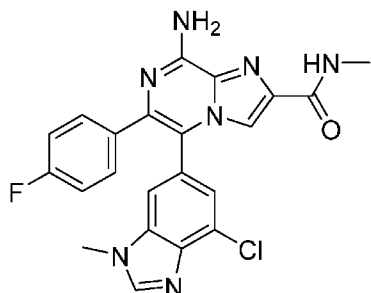


In a pressure tube, 6-bromo-4-chloro-1-methyl-1H-1,3-benzodiazole (200 mg, 0.85 mmol), bis(pinacolato)diboron (280 mg, 1.10 mmol) and KOAc (104 mg, 1.06 mmol) were dissolved in 15 mL of dry 1,4-dioxane and sparged with argon for 10 min. Pd(dppf)Cl₂ · DCM (34.7 mg, 0.04 mmol) was added in one portion and the reaction mixture was sparged with argon for additional 5 min. The pressure tube was capped and the reaction mixture was stirred at 100°C for 16 h. Then the reaction mixture was filtered through Celite® and the filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc and precipitated with hexane to afford

the title product as a mixture of acid and ester, a beige solid (0.480 g, 0.2 mmol, 79%). ESI-MS: 293.10; 211.05[M+H]⁺.

Example 24:

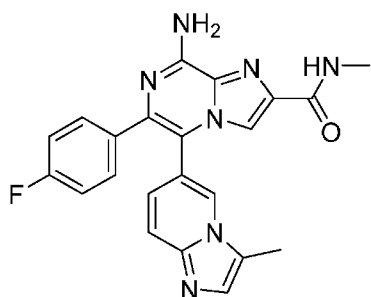
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure F**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **step b** to lead to the title compound (25 mg, 34%) as off-white solid, hydrochloride salt. ESI-MS: 450.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.49 (s, 1H), 8.20 (d, J = 4.9 Hz, 1H), 7.85 (s, 1H), 7.79 (d, J = 1.4 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.33 (d, J = 1.4 Hz, 1H), 7.13 (t, J = 8.9 Hz, 2H), 3.85 (s, 3H), 2.78 (d, J = 4.6 Hz, 3H).

Example 25:

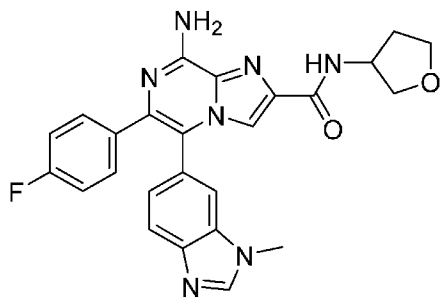
8-amino-6-(4-fluorophenyl)-N-methyl-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure F**, substituting {3-methylimidazo[1,2-a]pyridin-6-yl}boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **step b** and substituting Pd(PPh₃)₄ for Pd(amphos)Cl₂ and performing this step at 130°C for 16 h to lead to the title compound (25.6 mg, 20%) as yellow solid, hydrochloride salt. ESI-MS: 416.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.14 (s, 1H), 8.22 (s, 1H), 8.13 (q, J = 4.2, 3.7 Hz, 1H), 8.07 (d, J = 1.3 Hz, 1H), 7.98 (dd, J = 9.3, 0.9 Hz, 1H), 7.73 (dd, J = 9.2, 1.5 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.15 – 7.07 (m, 2H), 2.80 (d, J = 4.8 Hz, 3H), 2.54 (d, J = 1.1 Hz, 3H).

Example 26:

8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide

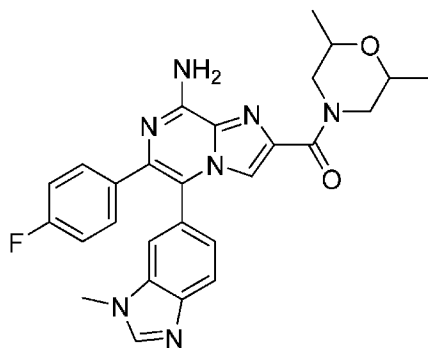


5

The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure C**, substituting 3-amino-
10 tetrahydrofuran for ethylamine to lead to the title compound (19 mg, 17%) as off-white solid, hydrochloride salt. ESI-MS: 472.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.23 (s, 1H), 8.19 (d, J = 7.2 Hz, 1H), 8.10 (s, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.76 (s, 1H), 7.42 (dd, J = 8.4, 1.5 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.11 – 7.01 (m, 2H), 4.51 – 4.44 (m, 1H), 3.98 (s, 3H), 3.88 – 3.83 (m, 1H), 3.82 – 3.78 (m, 1H), 3.74 – 3.68 (m, 1H), 3.62 – 3.57 (m, 1H), 2.23 – 2.12 (m, 1H), 1.94 –
15 1.82 (m, 1H).

Example 27:

2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazin-8-amine



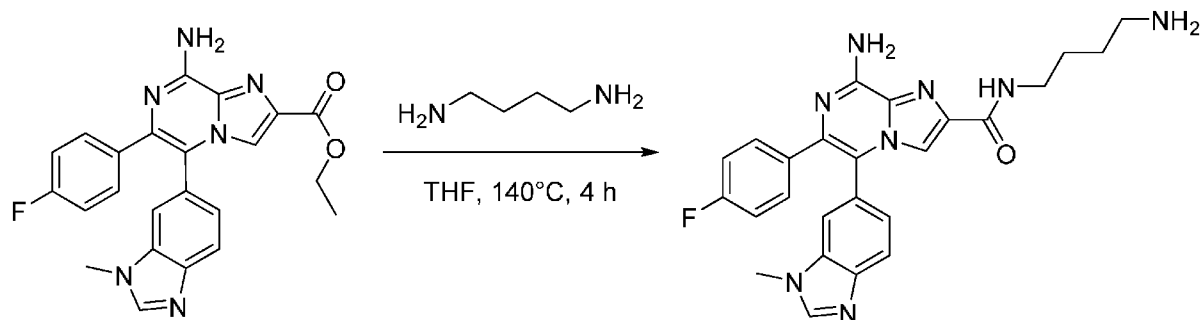
20

The title compound was synthesized following the approach outlined in **Procedure B**, substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2h at 100°C and then following **Procedure G**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic
25 acid for (4-methylquinolin-6-yl)boronic acid to lead to the title compound (28 mg, 43%) as yellow solid, hydrochloride salt. ESI-MS: 500.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.34 (s, 1H), 8.13 (s, 1H), 7.87 (d, J = 8.5 Hz, 1H), 7.66 (s, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.08 (t, J = 8.9 Hz, 2H), 5.08 (s, 1H), 4.36 (d, J = 13.2 Hz, 1H), 3.99 (s, 3H), 2.85 (s, 1H), 2.47 – 2.41 (m, 3H), 1.14 (d, J = 6.2 Hz, 6H).

30

Example 28:

8-amino-N-(4-aminobutyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



5

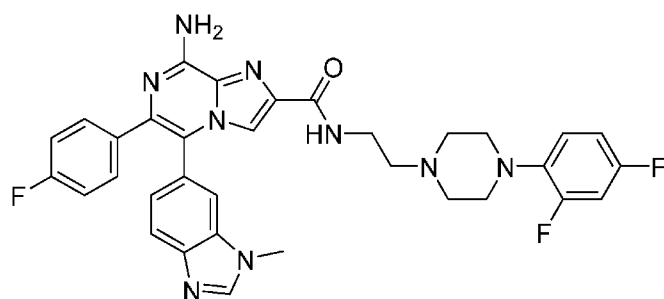
In a pressure tube ethyl 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate (described in Procedure B, step a substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in this step and performing this step for 2 h at 100°C) (20 mg, 0.05 mmol) was suspended in THF (2.5 ml) and 1,4-diaminobutane (0.14 ml, 1.4 mmol) was added into it, reaction was stirred for 4 h at 140°C. To the resulting mixture water was added and EtOAc. Organic layer was washed with brine, dried over Na₂SO₄, filtered and concentrated to lead to the title compound (10 mg, 19%) as beige solid, hydrochloride salt. ESI-MS: 473.50 [M+H]⁺. ¹H NMR (300 MHz, Deuterium Oxide) δ 9.02 (s, 1H), 7.84 (s, 1H), 7.84 – 7.75 (m, 2H), 7.51 (dd, J = 8.6, 1.4 Hz, 1H), 7.31 – 7.20 (m, 2H), 6.99 – 6.86 (m, 2H), 3.90 (s, 3H), 3.40 – 3.32 (m, 2H), 3.00 – 2.87 (m, 2H), 1.72 – 1.53 (m, 4H).

15

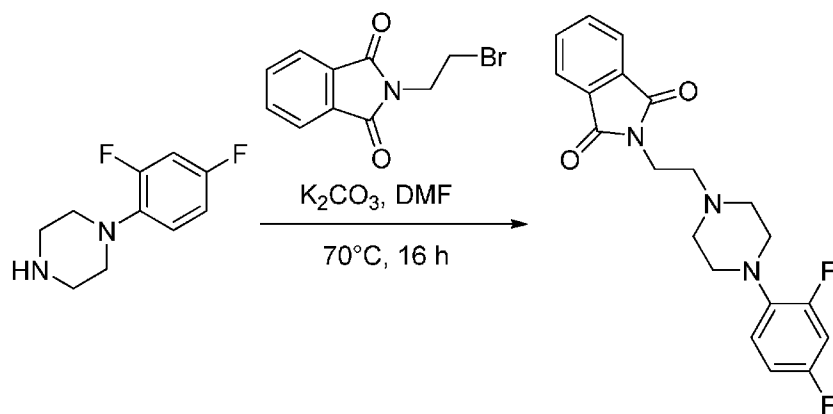
Example 29:

8-amino-N-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

20

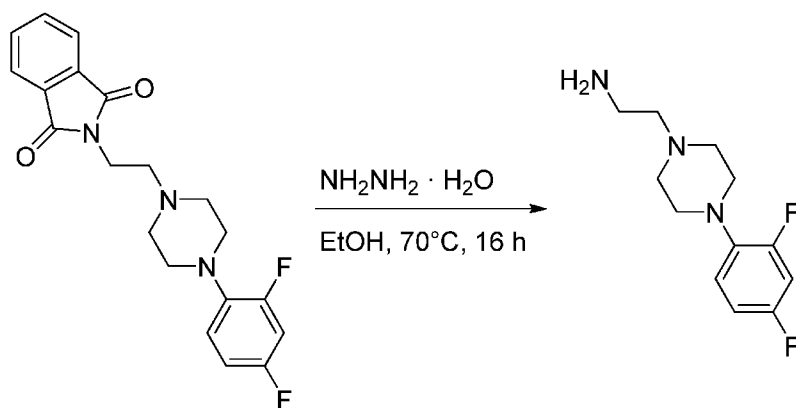


a. 2-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}-2,3-dihydro-1H-isoindole-1,3-dione



A pressure tube was charged with 1-(2,4-difluorophenyl)piperazine (250 mg, 1.3 mmol), 2-(2-bromoethyl)-1H-isoindole-1,3(2H)-dione (384 mg, 1.5 mmol), K_2CO_3 (349 mg, 2.5 mmol) and DMF (4ml). Reaction was heated for 16 h at 70°C. The reaction mixture was diluted with water, extracted with EtOAc. Combined organic layers were washed with brine dried over Na_2SO_4 , filtered and concentrated. Product was isolated by flash chromatography (silica gel, Hexane/EtOAc 0% to 50%) to afford the title product as light beige solid (300 mg, 64%). ESI-MS: 372.7 $[M+H]^+$.

b. 2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethan-1-amine



In a pressure tube were placed 2-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl]-2,3-dihydro-1H-isoindole-1,3-dione (300 mg, 0.8 mmol) and hydrazinium hydroxide (N_2H_2 64-65%) (0.40 ml, 0.8 mmol) in EtOH (3 ml). The vessel was sealed and the mixture was stirred at 70°C for 16 h. Volatiles were distilled off in vacuo to afford the title product as a white solid (0.185 g, quant). ESI-MS: 242.10 $[M+H]^+$.

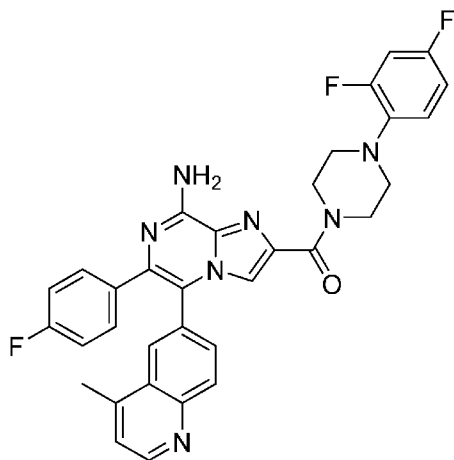
c. 8-amino-N-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

The title compound was synthesized following the approach outlined in Procedure B, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in Procedure B, step a and substituting $Pd(amphos)Cl_2$ for Sphos Pd G3 in step a and performing this step for 2 h at 100°C and the following Procedure G, substituting 2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethan-1-amine for 2,6-dimethylmorpholine to lead to the title compound (10 mg,

13%) as yellow solid, hydrochloride salt. ESI-MS: 626.25 [M+H]⁺. ¹H NMR (300 MHz, Deuterium Oxide) δ 9.03 (s, 1H), 7.90 (s, 1H), 7.85 (s, 1H), 7.79 (d, J = 8.6 Hz, 1H), 7.52 (dd, J = 8.5, 1.4 Hz, 1H), 7.31 – 7.23 (m, 2H), 7.13 – 7.03 (m, 2H), 7.00 – 6.86 (m, 4H), 3.91 (s, 3H), 3.81 (t, J = 5.9 Hz, 2H), 3.79 – 3.60 (m, 2H), 3.63 – 3.47 (m, 2H), 3.45 (t, J = 6.0 Hz, 2H), 3.40 – 3.19 (m, 2H), 3.20 – 3.00 (m, 2H).

Example 30:

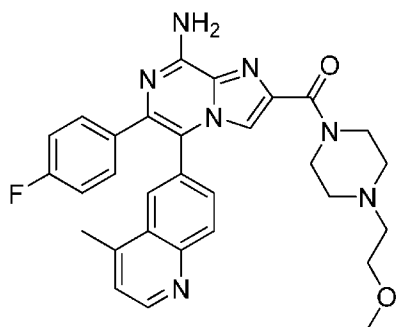
2-[4-(2,4-difluorophenyl)piperazine-1-carbonyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-(2,4-difluorophenyl)piperazine for ethylamine to lead to the title compound (19 mg, 40%) as yellow solid, hydrochloride salt. ESI-MS: 594.35 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.11 (d, J = 5.1 Hz, 1H), 8.49 (d, J = 1.8 Hz, 1H), 8.29 (d, J = 8.7 Hz, 1H), 7.94 (dd, J = 8.8, 1.8 Hz, 1H), 7.90 (s, 1H), 7.84 (d, J = 5.2 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.24 (ddd, J = 12.2, 9.0, 2.9 Hz, 1H), 7.16 – 7.07 (m, 3H), 7.02 (td, J = 8.4, 2.8 Hz, 1H), 4.32 – 4.23 (m, 2H), 3.81 – 3.77 (m, 2H), 3.02 (t, J = 4.8 Hz, 4H), 2.78 (s, 3H).

Example 31:

6-(4-fluorophenyl)-2-[4-(2-methoxyethyl)piperazine-1-carbonyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine

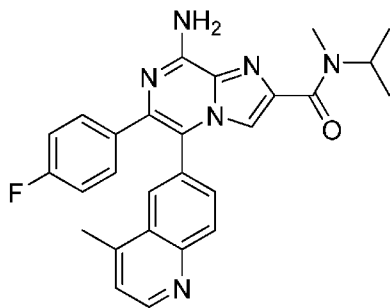


The title compound was synthesized following the approach outlined in **Procedure C**, substituting N-(2-methoxyethyl)piperazine for ethylamine and performing this step at room temperature

for 2 h to lead to the title compound (24 mg, 9%) as yellow solid, hydrochloride salt. ESI-MS: 540.00 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.27 (s, 1H), 9.14 (d, J = 5.3 Hz, 1H), 8.52 (s, 2H), 8.37 (d, J = 8.8 Hz, 1H), 8.03 – 7.83 (m, 3H), 7.40 (dd, J = 8.7, 5.5 Hz, 2H), 7.10 (t, J = 8.9 Hz, 2H), 5.43 (s, 1H), 4.59 – 4.49 (m, 1H), 3.82 – 3.71 (m, 2H), 3.61 – 3.52 (m, 2H), 3.41 – 3.27 (m, 5H), 3.26 – 3.03 (m, 4H), 2.80 (s, 3H).

Example 32:

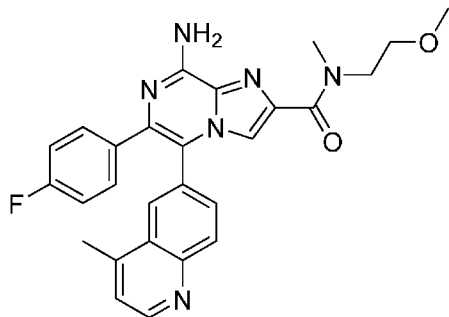
*8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-*a*]pyrazine-2-carboxamide*



The title compound was synthesized following the approach outlined in **Procedure C**, substituting N-isopropylmethylamine for ethylamine to lead to the title compound (18 mg, 13%) as yellow solid, hydrochloride salt. ESI-MS: 469.00 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.15 (d, J = 5.3 Hz, 1H), 8.94 (s, 1H), 8.55 (s, 1H), 8.38 (d, J = 8.7 Hz, 1H), 8.01 – 7.87 (m, 3H), 7.48 – 7.38 (m, 2H), 7.21 – 7.08 (m, 2H), 4.78 – 4.63 (m, 1H), 3.09 (s, 3H), 2.81 (s, 3H), 1.22 – 1.06 (m, 6H).

Example 33:

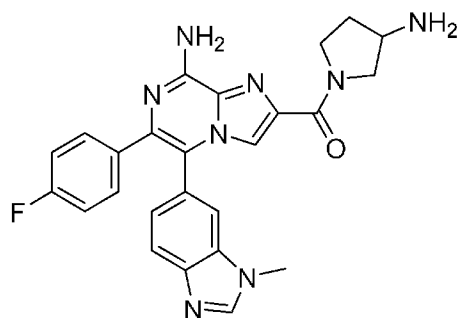
*8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-*a*]pyrazine-2-carboxamide*



The title compound was synthesized following the approach outlined in **Procedure C**, substituting (2-methoxyethyl)methylamine for ethylamine to lead to the title compound (11 mg, 8%) as yellow solid, hydrochloride salt. ESI-MS: 485.00 [M+H]⁺. ¹H NMR (300 MHz, Deuterium Oxide) δ 8.90 (d, J = 5.7 Hz, 1H), 8.43 (s, 1H), 8.15 (dd, J = 8.8, 1.7 Hz, 1H), 8.02 – 7.82 (m, 3H), 7.37 – 7.26 (m, 2H), 7.02 – 6.90 (m, 2H), 3.94 (t, J = 5.2 Hz, 1H), 3.67 (s, 2H), 3.59 (t, J = 5.2 Hz, 1H), 3.32 – 3.22 (m, 3H), 3.10 – 2.98 (m, 3H), 2.78 (s, 3H).

Example 34:

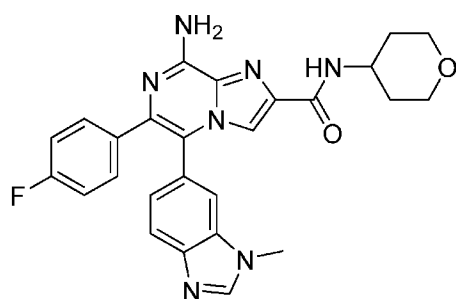
1-[8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine



- 5 The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure G**, substituting 3-(Boc-amino)pyrrolidine for 2,6-dimethylmorpholine to lead to the title compound (26 mg, 75%) as
 10 beige solid, hydrochloride salt. ESI-MS: 471.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.43 (s, 1H), 9.35 (s, 1H), 9.27 (s, 1H), 8.80 (d, J = 7.2 Hz, 1H), 8.18 (s, 1H), 8.06 (s, 1H), 7.86 (d, J = 8.5 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.09 (t, J = 8.9 Hz, 2H), 4.57 (q, J = 6.2 Hz, 1H), 4.06 (s, 3H), 3.39 – 3.31 (m, 2H), 3.26 – 3.15 (m, 2H), 2.19 (dq, J = 14.5, 7.3, 6.6 Hz, 1H), 1.97 (s, 1H).

15 **Example 35:**

8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide

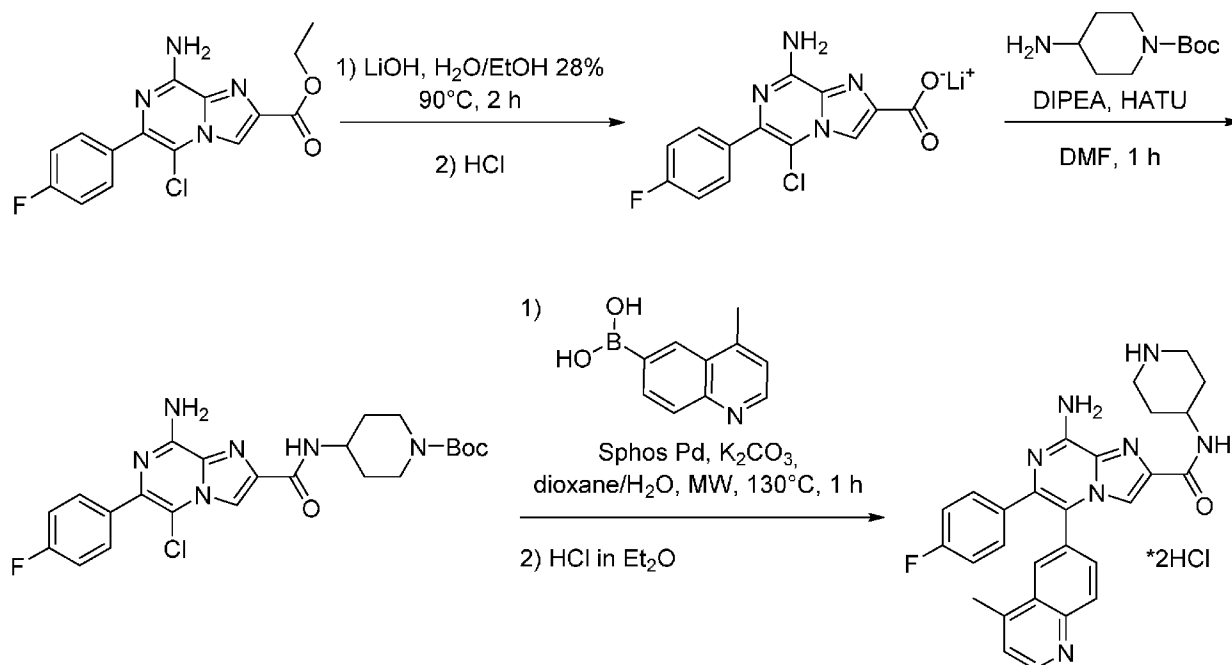


- 20 The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **step a** and performing this step for 2h at 100°C and then following **Procedure G**, substituting 4-aminotetrahydropyran
 25 for 2,6-dimethylmorpholine to lead to the title compound (19 mg, 25%) as yellow solid, hydrochloride salt. ESI-MS: 486.60 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.41 (s, 1H), 8.16 (s, 1H), 8.10 (d, J = 4.9 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.79 (s, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.42 – 7.35 (m, 2H), 7.08 (t, J = 8.6 Hz, 2H), 4.01 (s, 3H), 4.00 – 3.94 (m, 1H), 3.90 – 3.83 (m, 2H), 3.43 – 3.33 (m, 2H), 1.80 – 1.70 (m, 2H), 1.66 – 1.50 (m, 2H).

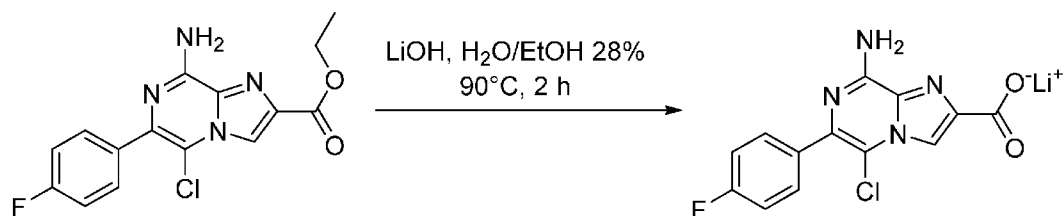
30

Procedure I

Example 36:

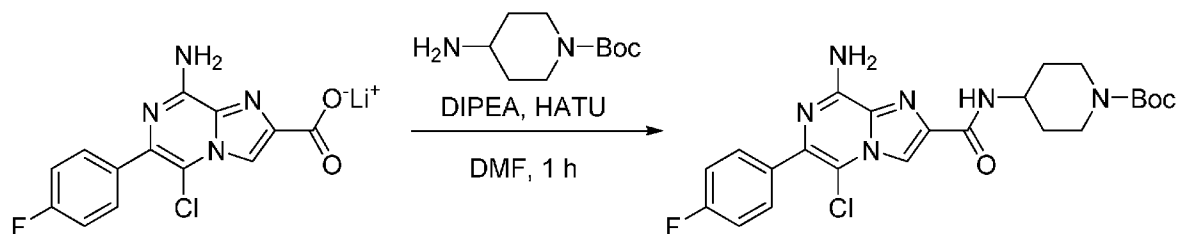
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(piperidin-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide

5

a. lithium 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate

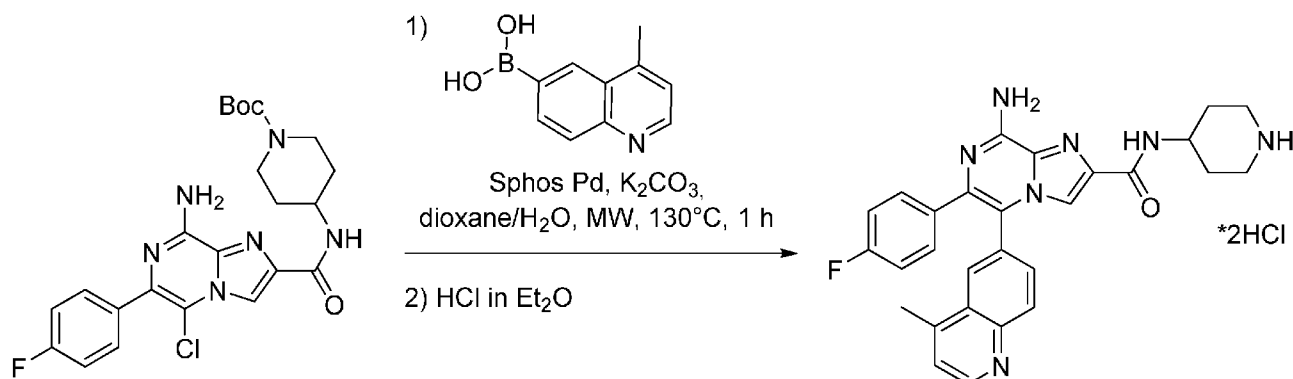
In a pressure tube was placed ethyl 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate (**Procedure A**, 200 mg, 0.6 mmol) and dissolved in ethanol (10 ml), then LiOH (75 mg, 1.8 mmol) in water (4 ml) was added and reaction mixture was stirred at 90°C for 2h. Product precipitated from the mixture after cooling down. Product was filtered off to afford the title product (187 mg, quant yield) as a yellow solid. ESI-MS: 308.90 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.95 (d, J = 9.4 Hz, 1H), 7.69 – 7.73 (m, 2H), 7.38 – 7.24 (m, 2H).

15

b. tert-butyl 4-[8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-amido]piperidine-1-carboxylate

Into a flask lithium 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate (35 mg, 0.11 mmol) was dissolved in DMF (3 ml) and then HATU (51 g, 0.13 mmol), DIPEA (0.06 mL, 0.37 mmol) and 1-Boc-4-aminopiperidine (47.8 mg, 0.12 mmol) and reaction was stirred at room temperature for 1 h. Then reaction mixture was extracted with EtOAc/H₂O, organic layer was washed with brine and dried over Na₂SO₄, filtered and concentrated in vacuo to dryness. Resulting solid was used for the next step without further purification (55 mg, quant) ESI-MS: 487.3 [M-H]⁺.

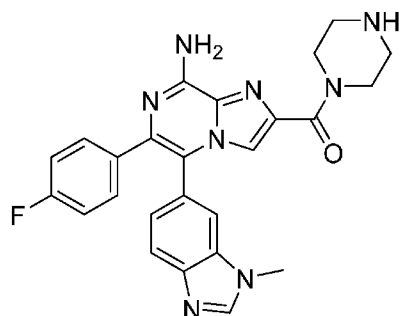
c. 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(piperidin-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide



In a pressure tube was placed tert-butyl 4-[8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-amido]piperidine-1-carboxylate (55 mg, 0.11 mmol), (4-methylquinolin-6-yl)boronic acid (42 mg, 0.22 mmol) and potassium carbonate (46.5 mg, 0.34 mmol) dissolved in 3.5 ml of mixture dioxane/water 6:1; then Sphos Pd G3 (4.4 mg; 0.006 mmol) was added after argon purge (15 min). Product was purified by flash chromatography (silica gel, DCM/EtOAc 1:1, then DCM/MeOH (0-5%)) and transformed into hydrochloride salt to afford the title product (10 mg, 15%) as yellow solid. ESI-MS: 496.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.07 (d, J = 5.0 Hz, 1H), 8.87 (d, J = 37.9 Hz, 3H), 8.43 (s, 1H), 8.26 (dd, J = 12.8, 8.3 Hz, 2H), 8.01 (s, 1H), 7.96 – 7.91 (m, 1H), 7.79 (s, 1H), 7.42 – 7.35 (m, 2H), 7.08 (t, J = 8.9 Hz, 2H), 4.07 – 4.04 (m, 1H), 3.28 (d, J = 12.6 Hz, 2H), 3.00 (t, J = 11.8 Hz, 2H), 2.75 (s, 3H), 1.95 (d, J = 13.0 Hz, 2H), 1.76 (d, J = 13.2 Hz, 2H).

Example 37:

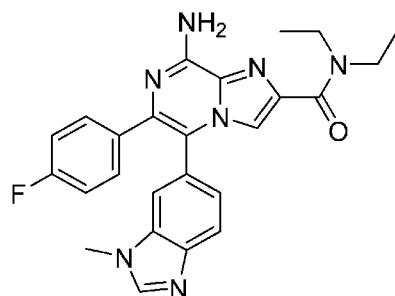
6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-2-(piperazine-1-carbonyl)imidazo[1,2-a]pyrazin-8-amine



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure G**, substituting *tert*-butylpiperazine-1-carboxylate for 2,6-dimethylmorpholine to lead to the title compound (26 mg, 33%) as white solid, hydrochloride salt. ESI-MS: 471.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.40 (s, 1H), 9.34 (s, 3H), 8.13 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 1H), 7.69 (s, 1H), 7.43 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.07 (t, *J* = 8.9 Hz, 2H), 4.51 (d, *J* = 20.3 Hz, 4H), 3.99 (s, 3H), 3.83 (s, 2H), 3.32 (s, 1H), 3.17 (s, 1H).

Example 38:

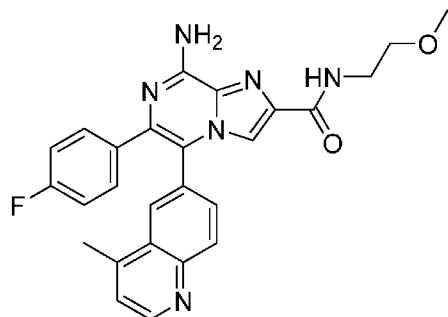
8-amino-N,N-diethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure C**, substituting N,N-diethylamine for ethylamine to lead to the title compound (6.2 mg, 21%) as off-white solid, hydrochloride salt. ESI-MS: 458.20 [M+H]⁺. ¹H NMR (300 MHz, Deuterium Oxide) δ 9.23 (s, 1H), 8.00 (d, *J* = 1.3 Hz, 1H), 7.96 – 7.89 (m, 1H), 7.83 (s, 1H), 7.67 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.49 – 7.33 (m, 2H), 7.14 – 7.00 (m, 2H), 4.03 (s, 3H), 3.68 (q, *J* = 7.1 Hz, 2H), 3.55 (q, *J* = 7.2 Hz, 2H), 1.30 – 1.10 (m, 6H).

Example 39:

8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



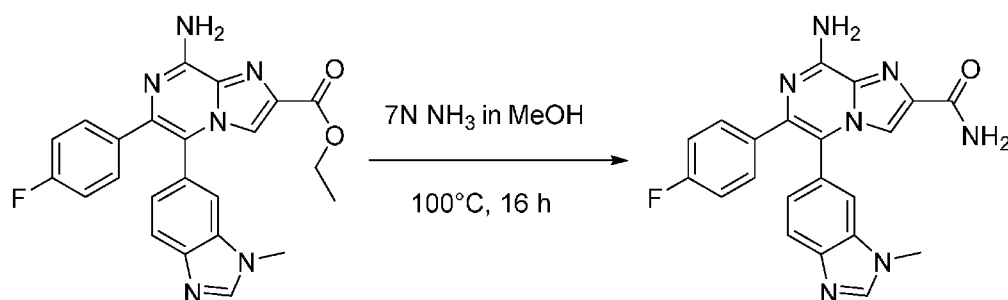
The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-methoxyethylamine for ethylamine to lead to the title compound (36 mg, 55%) as yellow solid, hydrochloride salt. ESI-MS: 471.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.08 (d, J = 5.1 Hz, 1H), 8.50 – 8.42 (m, 1H), 8.26 (d, J = 8.7 Hz, 1H), 8.12 (s, 1H), 7.98 – 7.88 (m, 2H), 7.80 (d, J = 5.1 Hz, 1H), 7.44 – 7.33 (m, 2H), 7.09 (t, J = 8.9 Hz, 2H), 3.47 – 3.43 (m, 4H), 3.26 (s, 3H), 2.76 (s, 3H).

Procedure J

Example 40:

8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

The title compound was synthesized following the approach outlined in **Procedure A**, subsequently **Procedure B, step a**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in this step and substituting Pd(amphos)Cl₂ for Sphos Pd G3 and performing this step for 2 h at 100°C to yield the (ethyl 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate).



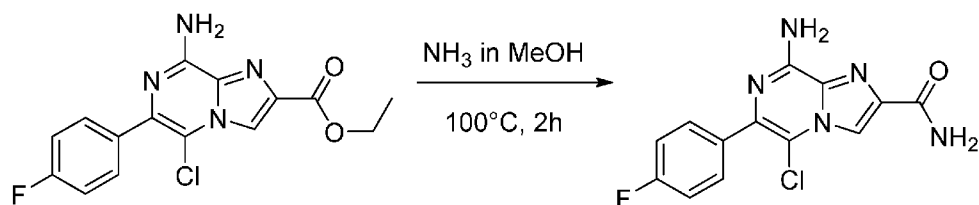
Into the pressure tube ethyl 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate (25 mg, 0.06 mmol) and NH₃ in methanol (7N, 5 ml) were added. Reaction was heated for 16 h at 100°C. Solvent was evaporated. Product was purified by flash chromatography (NH₂ modified silica gel, eluted with DCM/hexane from 10% hexane to 0% hexane then DCM/MeOH from 0% MeOH to 4% MeOH) to lead to the title compound (15 mg, 54%) as white solid, hydrochloride salt. ESI-MS: 402.40 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.44 (s, 1H), 8.16 (s, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.83 (s, 1H), 7.58 (s, 2H), 7.45 (dd, J = 8.5, 1.5 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.10 (t, J = 8.8 Hz, 2H).

Procedure K

Example 41 (not according to the invention):

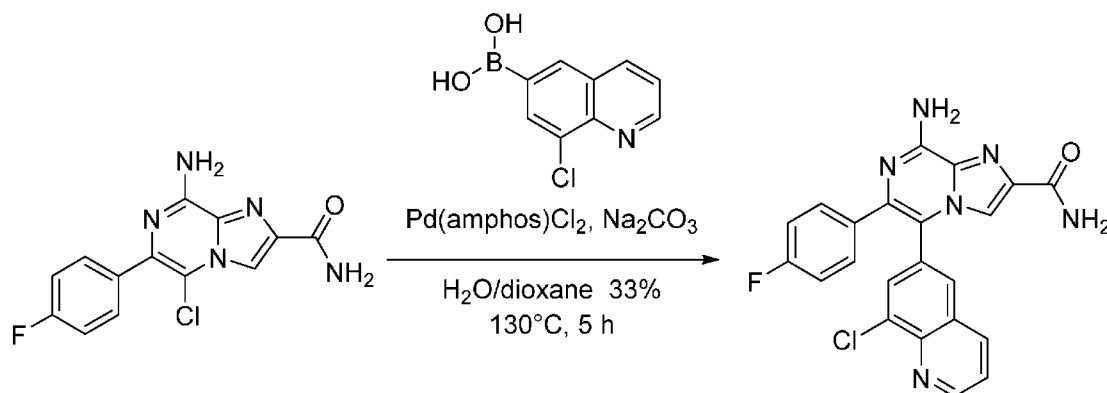
8-amino-5-(8-chloroquinolin-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide

a. 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamid



To the ethyl 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxylate (0.84 g; 2.51 mmol) 7N ammonia in methanol (100 ml) was added, reaction was heated for 2 h in 100°C . Product was purified by column chromatography, eluting with DCM/MeOH (0-10%) to afford the title product as a pale yellow solid (0.78 g, 2.51 mmol, quant). ESI-MS: 305.85; $[\text{M}+\text{H}]^+$.

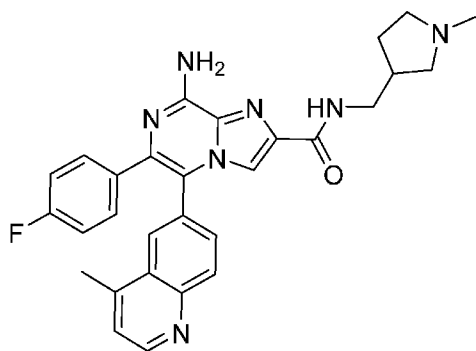
b. 8-amino-5-(8-chloroquinolin-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide



A pressure tube was charged with 8-amino-5-chloro-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide (110 mg, 0.36 mmol), (8-chloroquinolin-6-yl)boronic acid (95 mg, 0.54 mmol), sodium carbonate (114 mg, 0.054 mmol) and dioxane/water 2/1 (1 ml) and sparged with argon for 15 min. $\text{Pd}(\text{amphos})\text{Cl}_2$ (25 mg, 0.04 mmol) was added in one portion and argon was bubbled through the suspension for another 5 minutes. Subsequently the tube was closed and the reaction mixture was heated for 5 h at 130°C . After cooling reaction mixture was diluted with EtOAc and water. Water phase was washed with EtOAc. The combined organic phases were dried over MgSO_4 , filtered and concentrated. Product was purified by flash chromatography (NH₂ modified silica gel, Hexane/EtOAc/EtOH from 1/1/0 to 0/95/5) to lead to the title compound (11 mg, 7%) as yellowish solid. ESI-MS: 433.20 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, DMSO-*d*₆) δ 9.09 (dd, $J = 4.2, 1.7$ Hz, 1H), 8.45 (dd, $J = 8.4, 1.7$ Hz, 1H), 8.11 (d, $J = 1.8$ Hz, 1H), 7.99 (d, $J = 1.9$ Hz, 1H), 7.86 (s, 1H), 7.70 (dd, $J = 8.3, 4.2$ Hz, 1H), 7.49 (d, $J = 25.5$ Hz, 2H), 7.43 – 7.27 (m, 4H), 7.13 – 6.98 (m, 2H).

Example 42:

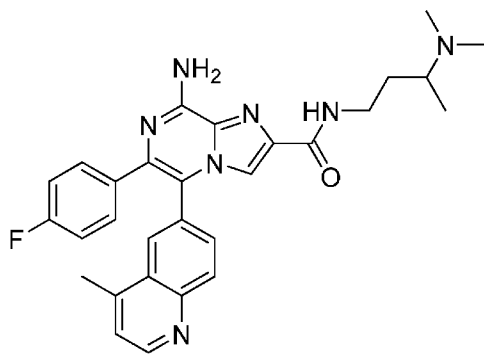
8-amino-6-(4-fluorophenyl)-N-[(1-methylpyrrolidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting (1-methylpyrrolidin-3-yl)-methanamine hydrochloride for ethylamine to lead to the title compound (25 mg, 49%) as yellow solid, hydrochloride salt. ESI-MS: 510.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.33 (s, 1H), 9.00 (d, J = 4.8 Hz, 1H), 8.56 – 8.47 (m, 1H), 8.34 (d, J = 8.6 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.89 (dd, J = 14.1, 7.6 Hz, 2H), 7.67 (s, 2H), 7.41 – 7.34 (m, 2H), 7.06 (dd, J = 10.0, 7.8 Hz, 2H), 3.37 – 3.31 (m, 2H), 3.16 – 2.92 (m, 3H), 2.84 – 2.76 (m, 4H), 2.69 (s, 4H), 2.20 – 1.93 (m, 1H), 1.90 – 1.59 (m, 1H).

Example 43:

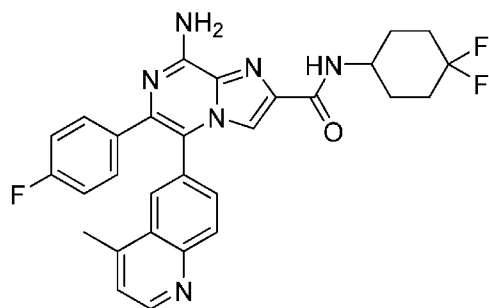
8-amino-N-[3-(dimethylamino)butyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting (4-aminobutan-2-yl)dimethylamine for ethylamine to lead to the title compound (27 mg, 35%) as yellow solid, hydrochloride salt. ESI-MS: 512.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.96 (s, 1H), 9.01 (d, J = 4.8 Hz, 1H), 8.45 (t, J = 5.8 Hz, 1H), 8.37 (d, J = 1.7 Hz, 1H), 8.20 (d, J = 8.7 Hz, 1H), 7.91 (s, 1H), 7.87 (dd, J = 8.7, 1.8 Hz, 1H), 7.69 (d, J = 4.8 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.06 (t, J = 8.9 Hz, 2H), 3.39 – 3.31 (m, 2H), 2.70 (d, J = 1.8 Hz, 3H), 2.68 (d, J = 5.0 Hz, 4H), 2.63 (d, J = 5.0 Hz, 3H), 2.08 – 1.97 (m, 1H), 1.72 – 1.60 (m, 1H), 1.26 (d, J = 6.6 Hz, 3H).

Example 44:

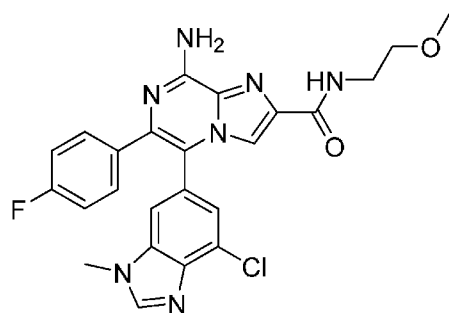
8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 4,4-difluorocyclohexan-1-amine for ethylamine to lead to the title compound (26 mg, 42%) as yellow solid, hydrochloride salt. ESI-MS: 531.50 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.08 (d, J = 5.1 Hz, 1H), 8.44 (d, J = 1.8 Hz, 1H), 8.27 (d, J = 8.7 Hz, 1H), 8.13 (d, J = 8.1 Hz, 1H), 8.01 – 7.88 (m, 2H), 7.80 (d, J = 5.2 Hz, 1H), 7.44 – 7.32 (m, 2H), 7.09 (t, J = 8.9 Hz, 2H), 3.95 (m, 1H), 2.75 (s, 3H), 2.12 – 1.76 (m, 6H), 1.65 (d, J = 16.5 Hz, 2H)

Example 45:

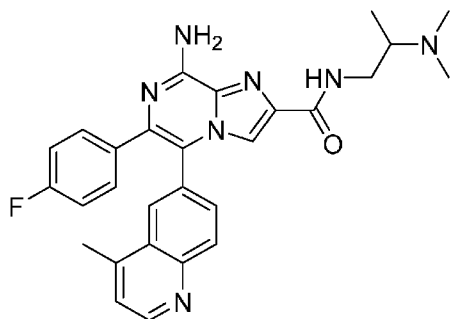
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **step a** and performing this step at 100°C for 1 h and performing **step b** in **Procedure B** at 80°C for 1 h and then following **Procedure C**, substituting 2-methoxyethyl-1-amine for ethylamine to lead to the title compound (19 mg, 33%) as yellow solid, hydrochloride salt. ESI-MS: 494.20 [M+H]⁺. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.11 (s, 1H), 7.96 (s, 1H), 7.45 (dd, J = 8.8, 5.0 Hz, 2H), 7.33 (d, J = 1.4 Hz, 1H), 7.25 (d, J = 1.5 Hz, 1H), 7.08 – 7.00 (m, 2H), 3.85 (s, 3H), 3.74 – 3.65 (m, 2H), 3.61 (t, J = 4.9 Hz, 2H), 3.46 (s, 3H).

Example 46:

8-amino-N-[2-(dimethylamino)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

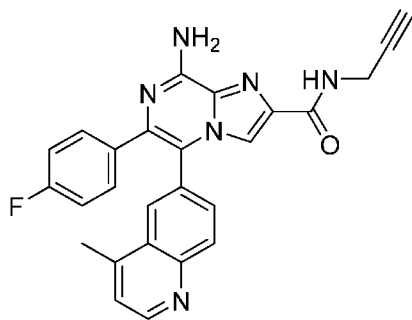


The title compound was synthesized following the approach outlined in **Procedure C**, substituting (1-aminopropan-2-yl)dimethylamine for ethylamine and substituting Et₃N for DIPEA and substituting HBTU for HATU in this step to lead to the title compound (5 mg, 32%) as white solid.

ESI-MS: 498.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.81 (d, J = 4.4 Hz, 1H), 8.17 (d, J = 1.6 Hz, 1H), 8.07 (d, J = 8.6 Hz, 1H), 7.93 (s, 1H), 7.79 – 7.68 (m, 2H), 7.42 (d, J = 4.3 Hz, 1H), 7.35 (dd, J = 8.8, 5.6 Hz, 4H), 7.01 (t, J = 8.9 Hz, 2H), 3.26 – 3.15 (m, 2H), 2.77 (s, 1H), 2.55 (s, 3H), 2.20 (s, 6H), 0.90 (d, J = 6.4 Hz, 3H).

Example 47:

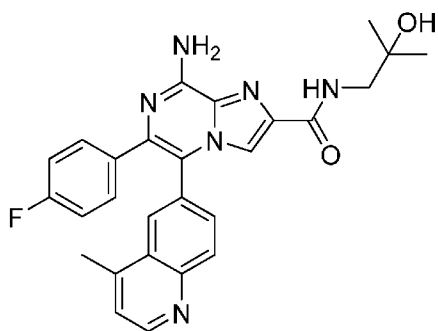
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(prop-2-yn-1-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-amino-1-propyne for ethylamine to lead to the title compound (12 mg, 17%) as yellow solid, hydrochloride salt. ESI-MS: 451.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.04 (d, J = 4.8 Hz, 1H), 8.56 (t, J = 5.8 Hz, 1H), 8.43 – 8.39 (m, 1H), 8.21 (d, J = 8.7 Hz, 1H), 7.99 (s, 1H), 7.89 (d, J = 8.7 Hz, 1H), 7.73 (s, 1H), 7.41 – 7.35 (m, 2H), 7.08 (t, J = 8.8 Hz, 2H), 4.06 (dd, J = 5.8, 2.5 Hz, 2H), 3.15 (t, J = 2.5 Hz, 1H), 2.73 (s, 3H).

Example 48:

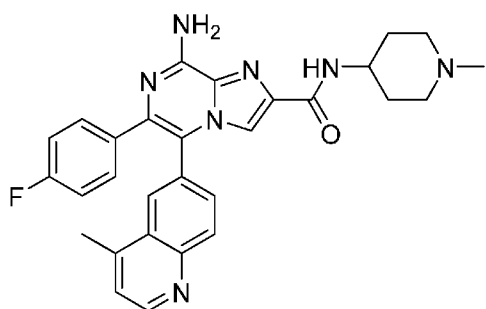
8-amino-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-amino-2-methyl-2-propanol for ethylamine to lead to the title compound (37.5 mg, 37%) as yellow solid, hydrochloride salt. ESI-MS: 485.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (d, J = 5.2 Hz, 1H), 8.50 (s, 1H), 8.32 (d, J = 8.8 Hz, 1H), 8.00 – 7.93 (m, 2H), 7.92 – 7.83 (m, 2H), 7.44 – 7.37 (m, 2H), 7.15 – 7.07 (m, 2H), 3.27 (d, J = 6.1 Hz, 2H), 2.79 (s, 3H), 1.11 (s, 6H).

10 **Example 49:**

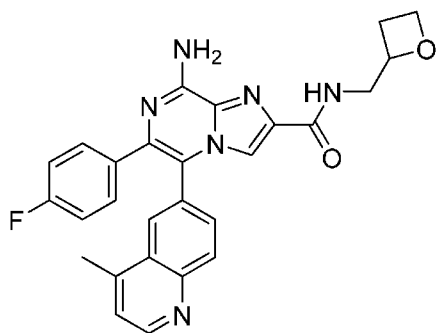
8-amino-6-(4-fluorophenyl)-N-(1-methylpiperidin-4-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



15 The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-methylpiperidin-4-amine for ethylamine to lead to the title compound (17 mg, 38%) as yellow solid, hydrochloride salt. ESI-MS: 510.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.51 (s, 1H), 9.05 (d, J = 5.0 Hz, 1H), 8.42 (d, J = 11.6 Hz, 1H), 8.26 (d, J = 8.7 Hz, 2H), 8.20 (d, J = 7.9 Hz, 1H), 7.98 (s, 1H), 7.91 (d, J = 8.5 Hz, 1H), 7.76 (s, 1H), 7.41 – 7.34 (m, 2H), 7.07 (t, J = 8.8 Hz, 2H), 4.03 – 3.98 (m, 1H), 3.39 (s, 1H), 3.28 (d, J = 5.9 Hz, 1H), 3.06 (d, J = 12.0 Hz, 2H), 2.74 (d, J = 13.2 Hz, 3H), 2.71 – 2.67 (m, 3H), 1.99 (d, J = 13.9 Hz, 2H), 1.90 (t, J = 12.6 Hz, 2H).

25 **Example 50:**

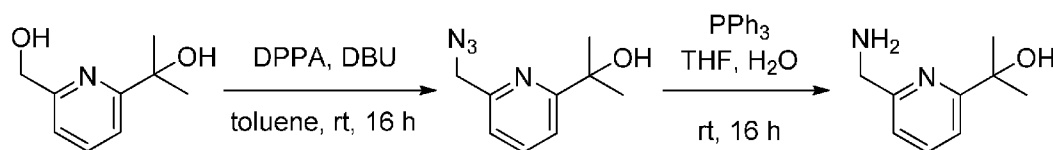
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting oxetan-2-ylmethanamine for ethylamine and substituting Et₃N for DIPEA and substituting HBTU for HATU in this step to lead to the title compound (14 mg, 30%) as white solid. ESI-MS: 483.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.81 (d, J = 4.4 Hz, 1H), 8.26 – 8.15 (m, 2H), 8.07 (d, J = 8.6 Hz, 1H), 7.83 (s, 1H), 7.74 (dd, J = 8.7, 1.9 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.41 – 7.30 (m, 4H), 7.02 (t, J = 8.9 Hz, 2H), 4.81 (dt, J = 12.3, 6.2 Hz, 1H), 4.51 (dd, J = 13.7, 7.9 Hz, 1H), 4.42 (dt, J = 9.0, 5.9 Hz, 1H), 3.62 – 3.53 (m, 1H), 3.53 – 3.45 (m, 1H), 2.61 (dd, J = 11.6, 5.5 Hz, 1H), 2.56 (s, 3H), 2.39 (dd, J = 16.8, 8.1 Hz, 1H).

Example 51:

8-amino-6-(4-fluorophenyl)-N-[[6-(2-hydroxypropan-2-yl)pyridin-2-yl]methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

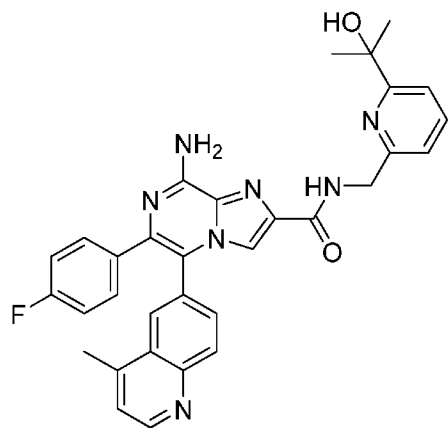


a. 2-[6-(azidomethyl)pyridin-2-yl]propan-2-ol

In a flask was placed solution of 2-[6-(hydroxymethyl)pyridin-2-yl]propan-2-ol (371 mg, 2.2 mmol) in toluene (5 mL) and mixture was cooled to 0°C and then diphenylphosphoryl azide (0.6 ml, 2.66 mmol) was added followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (0.4 ml, 2.66 mmol). Resulting mixture was allowed to warm to room temperature and stirred for 16 h. Crude mixture was diluted with EtOAc and washed with water. Organic layer was dried over MgSO₄, filtered and concentrated. The residue was dissolved in 1M HCl (2 eq) and extracted with a mixture of methyl *tert*-butyl ether/hexane (3:7). Organic layer was washed with water and combined aqueous phase was neutralized with 2M NaOH aq and extracted with ethyl acetate. Organic phase was dried over MgSO₄, filtered and concentrated to afford yellow oil (210 mg, 49%) that was used for the next step without further purification. ESI-MS: 193.1 [M+H]⁺.

b. 2-[6-(aminomethyl)pyridin-2-yl]propan-2-ol

In a flask 2-[6-(azidomethyl)pyridin-2-yl]propan-2-ol (70 mg, 0.36 mmol) in THF (5 ml) and water (0.5 ml) and PPh₃ in 10% aqueous THF (190 mg, 0.73 mmol) were stirred for 16 h at room temperature. Resulting mixture was evaporated into dynes and used for the next step without further purification. ESI-MS: 167.2 [M+H]⁺.

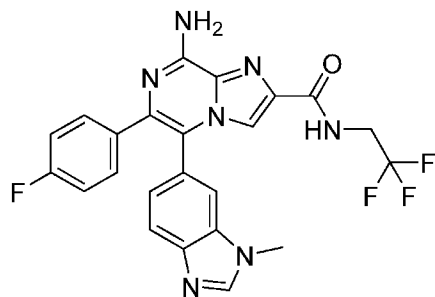


c. 8-amino-6-(4-fluorophenyl)-N-([6-(2-hydroxypropan-2-yl)pyridin-2-yl]methyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

5 The title compound was synthesized following the approach outlined in **Procedure I**, substituting 2-[6-(aminomethyl)pyridin-2-yl]propan-2-ol [prepared following the approach outlined in step A and B] for 1-Boc-4-aminopiperidine in **Procedure I**, **step b** to lead to the title compound (7 mg, 7%) as yellow solid, hydrochloride salt. ESI-MS: 562.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.09 (d, J = 5.1 Hz, 1H), 8.94 (s, 1H), 8.48 (s, 1H), 8.27 (d, J = 8.7 Hz, 1H), 8.05 (s, 1H), 7.93 (dd, J = 8.7, 1.8 Hz, 2H), 7.82 (t, J = 6.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.32 (s, 1H), 7.09 (t, J = 8.8 Hz, 2H), 4.67 (d, J = 5.9 Hz, 2H), 2.77 (s, 3H), 1.47 (s, 6H).

Example 52:

15 *8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide*

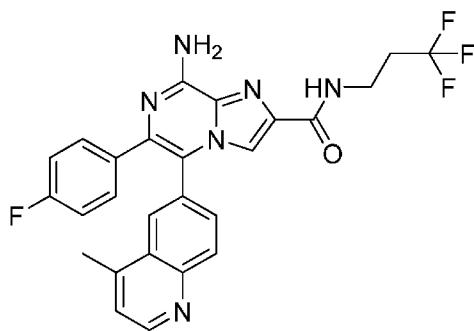


20 The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, **step a** and performing this step for 2 h at 100°C and then following **Procedure C**, substituting 2,2,2-trifluoroethylamine for ethylamine to lead

to the title compound (10 mg, 15%) as white solid, hydrochloride salt. ESI-MS: 484.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.39 (s, 1H), 8.76 (t, J = 6.6 Hz, 1H), 8.15 (d, J = 7.6 Hz, 1H), 7.92 – 7.83 (m, 2H), 7.46 (dd, J = 8.4, 1.5 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.07 (t, J = 8.9 Hz, 2H), 4.13 – 4.06 (m, 2H), 4.01 (s, 3H).

Example 53:

8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(3,3,3-trifluoropropyl)imidazo[1,2-a]pyrazine-2-carboxamide

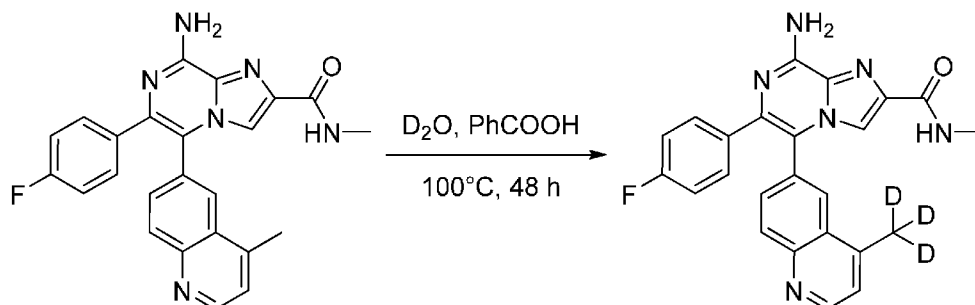


- 5 The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3,3,3-trifluoropropylamine for ethylamine to lead to the title compound (26 mg, 17%) as yellow solid, hydrochloride salt. ESI-MS: 509.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (s, 1H), 8.44 (s, 2H), 8.22 (d, J = 9.2 Hz, 1H), 7.91 (d, J = 7.1 Hz, 2H), 7.77 (s, 1H), 7.38 (dd, J = 8.6, 5.7 Hz, 2H), 7.08 (t, J = 8.7 Hz, 2H), 3.52 (q, J = 6.7 Hz, 2H), 2.59 – 2.54 (m, 2H), 2.74 (s, 3H).

Procedure L

Example 54:

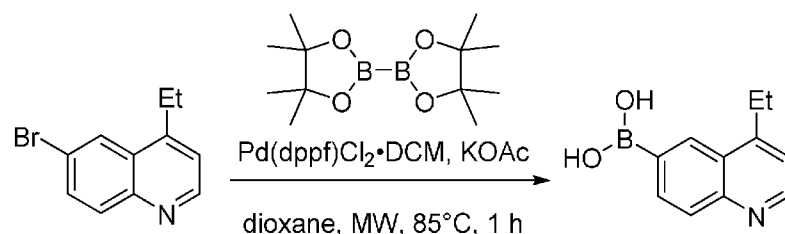
- 15 *8-amino-6-(4-fluorophenyl)-N-methyl-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide*



- 20 The title compound was synthesized following the approach outlined in **Procedure F**, substituting (4-methylquinolin-6-yl)boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **step b**, and performing additional **step – Procedure L**:

- Into a pressure tube 8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide hydrochloride (25 mg, 0.05 mmol), benzoic acid (66 mg, 0.5 mmol) and 1 ml of D₂O were added. The reaction was stirred for 48 h at 100°C. Then the solvent was evaporated and product was purified by flash chromatography (NH₂ modified silica gel, hexane/DCM 0-100%) to lead to the title compound (25 mg, quant) as yellow solid, hydrochloride salt. ESI-MS: 430.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.07 (d, J = 5.0 Hz, 1H), 8.44 (d, J = 2.0 Hz, 1H), 8.25 – 8.18 (m, 2H), 7.96 – 7.87 (m, 2H), 7.78 (d, J = 5.0 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.14 – 7.03 (m, 2H), 2.78 (d, J = 4.7 Hz, 3H).

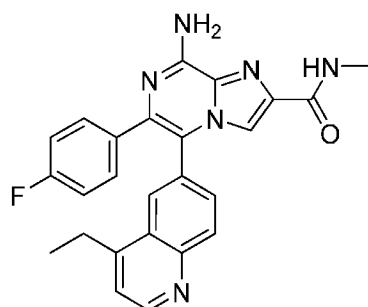
- 30 **Procedure M**

Preparation of (4-ethylquinolin-6-yl)boronic acid

A microwave reaction tube was charged with 6-bromo-4-ethylquinoline (411 mg, 1.74 mmol), bis(pinacolato)diboron (663 mg, 2.61 mmol) and KOAc (342 mg, 3.48 mmol) and 5 mL of 1,4-dioxane. This suspension was then sparged with argon for 10 min. Pd(dppf)Cl₂·DCM (28 mg, 0.03 mmol) was added in one portion and the reaction mixture was sparged with argon for additional 5 min. The pressure tube was capped and the reaction mixture was stirred at 80°C for 1 h under microwave irradiation. Then the reaction mixture was filtered through Celite® and the filtrate was concentrated under reduced pressure. Resulting mixture was used for the next step without further purification to lead to the title compound (0.200 g, 57%). ESI-MS: 201.90 [M+H]⁺.

Example 55:

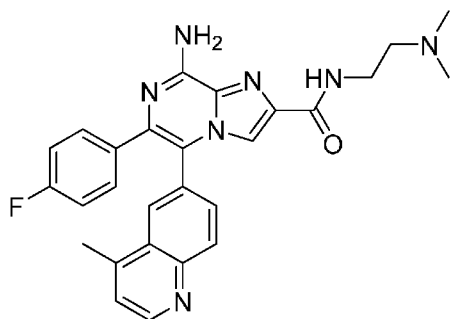
8-amino-5-(4-ethylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure F**, substituting (4-ethylquinolin-6-yl)boronic acid (**Procedure M**) for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **step b** and substituting Pd Sphos G3 for Pd(amphos)Cl₂ and performing this step at 130°C on oil bath for 3 h to lead to the title compound (87 mg, 52%) as yellow solid, hydrochloride salt. ESI-MS: 441.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.14 (d, J = 5.2 Hz, 1H), 8.45 (d, J = 1.8 Hz, 1H), 8.35 (d, J = 8.7 Hz, 1H), 8.22 (d, J = 4.8 Hz, 1H), 8.03 (dd, J = 8.7, 1.7 Hz, 1H), 7.98 (s, 1H), 7.82 (d, J = 5.2 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.16 – 7.06 (m, 2H), 3.23 – 3.07 (m, 2H), 2.79 (d, J = 4.7 Hz, 3H), 1.16 (t, J = 7.5 Hz, 3H).

Example 56:

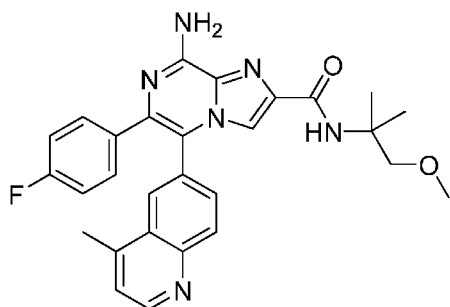
8-amino-N-[2-(dimethylamino)ethyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting N,N-dimethylenediamine for ethylamine to lead to the title compound (32 mg, 24%) as yellow solid, hydrochloride salt. ESI-MS: 484.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.90 (s, 1H), 9.04 (d, J = 4.8 Hz, 1H), 8.66 – 8.59 (m, 1H), 8.41 (s, 1H), 8.23 (d, J = 8.6 Hz, 1H), 8.04 – 8.00 (m, 1H), 7.87 (d, J = 8.9 Hz, 1H), 7.75 (s, 2H), 7.41 – 7.35 (m, 2H), 7.11 – 7.04 (m, 2H), 3.63 (q, J = 6.1 Hz, 2H), 3.23 (q, J = 6.0 Hz, 2H), 2.81 (s, 3H), 2.80 (s, 3H), 2.74 (s, 3H).

Example 57:

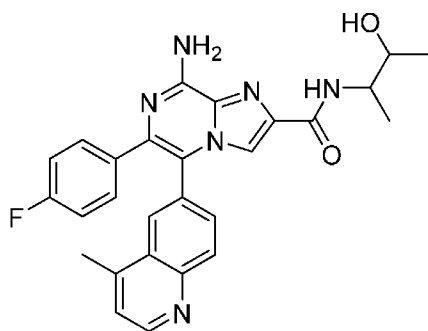
8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-methoxy-2-methylpropan-2-amine for ethylamine to lead to the title compound (27 mg, 30%) as yellow solid, hydrochloride salt. ESI-MS: 499.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.12 (d, J = 5.1 Hz, 1H), 8.48 (s, 1H), 8.29 (d, J = 8.8 Hz, 1H), 7.95 (dd, J = 8.9, 1.8 Hz, 1H), 7.84 (s, 2H), 7.45 (s, 1H), 7.42 – 7.35 (m, 2H), 7.13 – 7.05 (m, 2H), 3.47 (s, 2H), 3.31 (s, 3H), 2.78 (s, 3H), 1.36 (s, 6H).

Example 58:

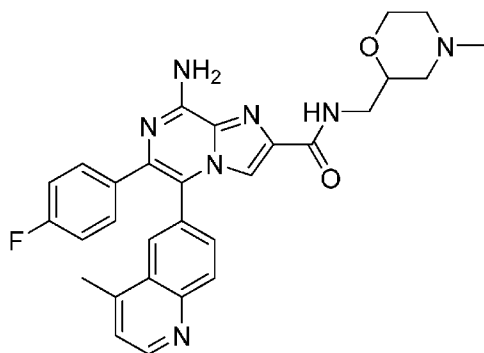
8-amino-6-(4-fluorophenyl)-N-(3-hydroxybutan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-aminobutan-2-ol for ethylamine to lead to the title compound (10 mg, 9%) as yellow solid, hydrochloride salt. ESI-MS: 485.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.07 (d, J = 4.9 Hz, 1H), 8.44 (s, 1H), 8.28 – 8.21 (m, 1H), 7.96 – 7.76 (m, 4H), 7.43 – 7.35 (m, 2H), 7.12 – 7.04 (m, 2H), 3.95 – 3.85 (m, 1H), 3.73 – 3.66 (m, 1H), 2.75 (s, 3H), 1.16 – 1.01 (m, 6H).

Example 59:

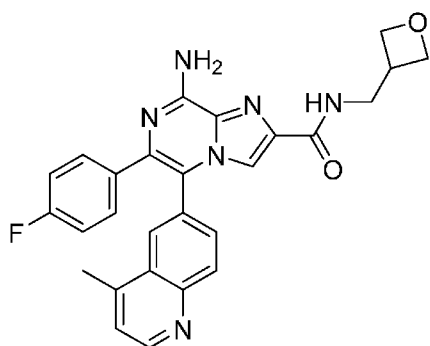
8-amino-6-(4-fluorophenyl)-N-[(4-methylmorpholin-2-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting (4-methylmorpholin-2-yl)methanamine for ethylamine to lead to the title compound (22 mg, 32%) as yellow solid, hydrochloride salt. ESI-MS: 526.20 [M+H]⁺. ¹H NMR (400 MHz, Methanol-*d*₄) δ 9.14 (d, J = 5.7 Hz, 1H), 8.75 (t, J = 6.3 Hz, 1H), 8.68 (s, 1H), 8.29 (d, J = 8.8 Hz, 1H), 8.16 – 8.10 (m, 2H), 8.02 (d, J = 5.6 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.11 (t, J = 8.6 Hz, 2H), 4.18 (dd, J = 13.3, 3.7 Hz, 1H), 4.02 – 3.95 (m, 1H), 3.89 – 3.79 (m, 1H), 3.71 – 3.63 (m, 1H), 3.63 – 3.54 (m, 2H), 3.52 – 3.42 (m, 1H), 3.20 – 3.11 (m, 1H), 2.97 (s, 4H), 2.94 (s, 3H).

Example 60:

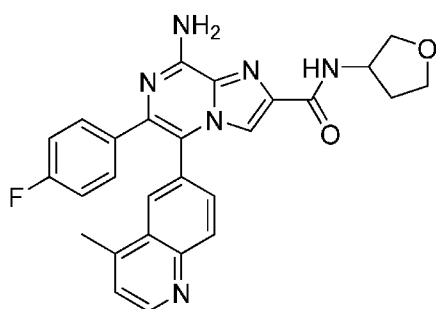
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-3-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-oxetanemethanamine for ethylamine to lead to the title compound (11 mg, 19%) as white solid. ESI-MS: 483.20 [M+H]⁺. ¹H NMR (400 MHz, Methanol-*d*₄) δ 8.77 (d, J = 4.5 Hz, 1H), 8.17 (d, J = 1.9 Hz, 1H), 8.10 (d, J = 8.7 Hz, 1H), 7.97 (s, 1H), 7.77 (dd, J = 8.7, 1.9 Hz, 1H), 7.45 (d, J = 4.6 Hz, 1H), 7.38 (dd, J = 8.7, 5.5 Hz, 2H), 6.93 (t, J = 8.8 Hz, 2H), 4.83 (dd, J = 7.8, 6.2 Hz, 2H), 4.62 (s, 1H), 4.54 (t, J = 6.1 Hz, 2H), 3.71 (d, J = 6.8 Hz, 2H), 2.63 (s, 3H).

Example 61:

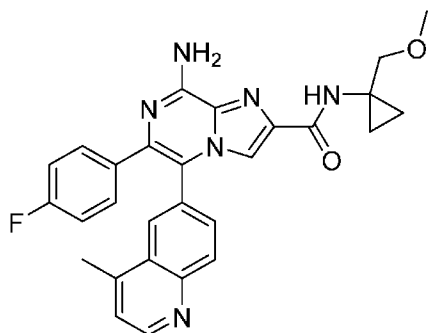
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting tetrahydrofuran-3-amine for ethylamine to lead to the title compound (37 mg, 46%) as yellow solid, hydrochloride salt. ESI-MS: 483.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.0 Hz, 1H), 8.47 (s, 1H), 8.27 (dd, J = 16.5, 8.0 Hz, 2H), 8.03 (s, 1H), 7.94 (d, J = 8.6 Hz, 1H), 7.83 (s, 1H), 7.39 (dd, J = 8.7, 5.6 Hz, 2H), 7.10 (t, J = 8.7 Hz, 2H), 3.84 (dd, J = 15.2, 7.9 Hz, 2H), 3.80 – 3.76 (m, 1H), 3.69 (td, J = 8.3, 5.8 Hz, 1H), 3.58 (dd, J = 9.0, 3.8 Hz, 1H), 2.77 (s, 3H), 2.22 – 2.12 (m, 1H), 1.91 – 1.83 (m, 1H).

Example 62:

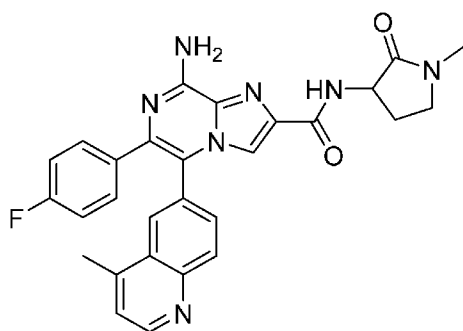
8-amino-6-(4-fluorophenyl)-N-[1-(methoxymethyl)cyclopropyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-methoxymethyl-cyclopropylamine for ethylamine to lead to the title compound (14 mg, 14%) as yellow solid, hydrochloride salt. ESI-MS: 495.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (d, *J* = 5.0 Hz, 1H), 8.41 (s, 1H), 8.32 (s, 1H), 8.24 (d, *J* = 8.7 Hz, 1H), 7.97 (s, 1H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.77 (s, 1H), 7.43 – 7.34 (m, 2H), 7.13 – 7.04 (m, 2H), 3.42 (s, 2H), 3.24 (s, 4H), 2.74 (s, 3H), 0.77 (s, 3H).

Example 63:

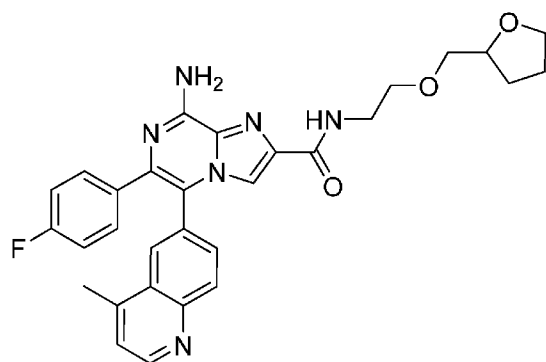
8-amino-6-(4-fluorophenyl)-N-(1-methyl-2-oxopyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-amino-N-methyl-2-pyrrolidinone for ethylamine to lead to the title compound (21 mg, 33%) as yellow solid, hydrochloride salt. ESI-MS: 510.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.11 (d, *J* = 5.1 Hz, 1H), 8.49 (d, *J* = 1.8 Hz, 1H), 8.42 (d, *J* = 8.2 Hz, 1H), 8.30 (d, *J* = 8.7 Hz, 1H), 8.00 (s, 1H), 7.96 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.84 (d, *J* = 5.2 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.10 (t, *J* = 8.9 Hz, 2H), 4.59 (q, *J* = 9.0 Hz, 1H), 3.35 – 3.26 (m, 2H), 2.78 (s, 3H), 2.76 (s, 3H), 2.37 (td, *J* = 6.9, 5.7, 3.9 Hz, 1H), 1.90 (dq, *J* = 12.1, 9.3 Hz, 1H).

Example 64:

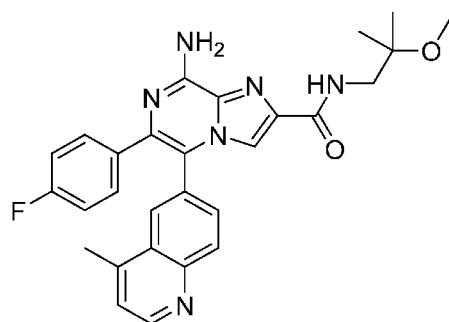
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-{2-[(oxolan-2-yl)methoxy]ethyl}imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-[(oxolan-2-yl)methoxy]ethan-1-amine for ethylamine to lead to the title compound (21 mg, 29%) as yellow solid, hydrochloride salt. ESI-MS: 541.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.07 (d, J = 5.0 Hz, 1H), 8.45 (s, 1H), 8.24 (d, J = 8.8 Hz, 1H), 8.14 (t, J = 5.9 Hz, 1H), 7.92 (d, J = 13.2 Hz, 2H), 7.79 (s, 1H), 7.42 – 7.35 (m, 2H), 7.09 (t, J = 8.8 Hz, 2H), 3.93 – 3.89 (m, 1H), 3.73 – 3.68 (m, 1H), 3.63 – 3.57 (m, 1H), 3.54 (dd, J = 6.0, 4.5 Hz, 2H), 3.46 – 3.41 (m, 2H), 3.40 – 3.34 (m, 2H), 2.75 (s, 3H), 1.91 – 1.81 (m, 1H), 1.81 – 1.70 (m, 2H), 1.54 – 1.44 (m, 1H).

Example 65:

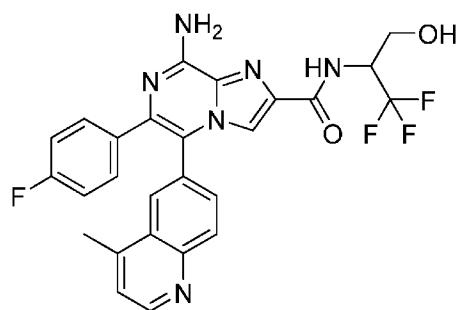
8-amino-6-(4-fluorophenyl)-N-(2-methoxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-methoxy-2-methyl-1-propanamine for ethylamine to lead to the title compound (40 mg, 32%) as yellow solid, hydrochloride salt. ESI-MS: 499.70 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.2 Hz, 1H), 8.47 (s, 1H), 8.28 (d, J = 8.8 Hz, 1H), 7.95 (d, J = 8.9 Hz, 2H), 7.83 (s, 1H), 7.77 (t, J = 6.2 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.09 (t, J = 8.8 Hz, 2H), 3.36 (d, J = 6.2 Hz, 2H), 3.16 (s, 3H), 2.77 (s, 3H), 1.12 (s, 6H).

Example 66:

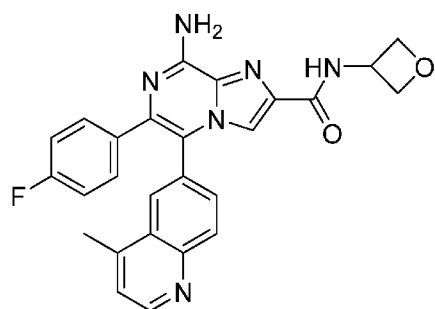
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(1,1,1-trifluoro-3-hydroxypropan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-amino-3,3,3-trifluoropropan-1-ol hydrochloride for ethylamine to lead to the title compound (9 mg, 1%) as yellow solid, hydrochloride salt. ESI-MS: 525.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.05 (d, J = 5.0 Hz, 1H), 8.43 (s, 1H), 8.37 (d, J = 9.5 Hz, 1H), 8.23 (d, J = 8.7 Hz, 1H), 8.01 (s, 1H), 7.95 – 7.90 (m, 1H), 7.76 (s, 1H), 7.41 – 7.35 (m, 2H), 7.07 (t, J = 8.9 Hz, 2H), 4.79 (s, 2H), 2.74 (s, 3H), 2.53 (s, 1H).

10 Example 67:

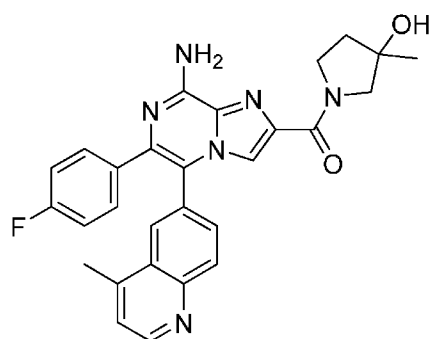
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide



15 The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-oxetaneamine for ethylamine to lead to the title compound (3.5 mg, 11%) as white solid. ESI-MS: 469.20 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.91 (d, J = 6.9 Hz, 1H), 8.82 (d, J = 4.3 Hz, 1H), 8.18 (d, J = 1.5 Hz, 1H), 8.08 (d, J = 8.6 Hz, 1H), 7.89 (s, 1H), 7.75 (dd, J = 8.6, 1.8 Hz, 1H), 7.48 – 7.22 (m, 5H), 7.02 (t, J = 8.9 Hz, 2H), 5.08 – 4.95 (m, 1H), 4.75 (t, J = 6.9 Hz, 2H), 4.58 (t, J = 6.4 Hz, 2H), 2.56 (s, 3H).

Example 68:

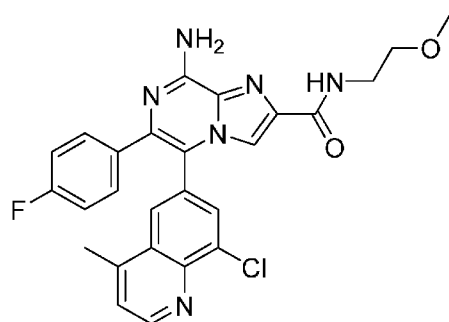
1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]-3-methylpyrrolidin-3-ol



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-hydroxy-3-methylpyrrolidine for ethylamine to lead to the title compound (19 mg, 28%) as yellow solid, hydrochloride salt. ESI-MS: 497.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.09 (d, *J* = 5.0 Hz, 1H), 8.46 (s, 1H), 8.26 (d, *J* = 8.7 Hz, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.83 (s, 2H), 7.45 – 7.36 (m, 2H), 7.10 (t, *J* = 8.7 Hz, 2H), 4.21 (s, 1H), 3.81 (d, *J* = 12.1 Hz, 1H), 3.60 – 3.54 (m, 1H), 3.54 – 3.49 (m, 1H), 2.76 (s, 3H), 1.97 – 1.74 (m, 2H), 1.34 (d, *J* = 1.6 Hz, 3H).

10 Example 69:

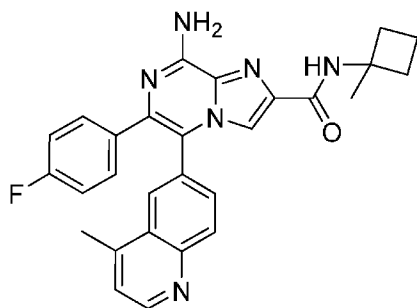
8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting 8-chloro-4-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (**Procedure D**) for (4-methylquinolin-6-yl)boronic acid and substituting Pd(PPh₃)₄ for Sphos Pd G3 in **Procedure B**, **step b** and performing this step for 1.5 h at 90°C and then following **Procedure C**, substituting 2-methoxyethylamine for ethylamine to lead to the title compound (16 mg, 23%) as yellow solid, hydrochloride salt. ESI-MS: 505.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.93 (d, *J* = 4.3 Hz, 1H), 8.19 (d, *J* = 1.8 Hz, 1H), 8.14 (s, 1H), 8.04 (s, 1H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.55 (dd, *J* = 4.3, 1.1 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.12 (t, *J* = 8.8 Hz, 2H), 3.44 (d, *J* = 2.6 Hz, 4H), 3.25 (s, 3H), 2.59 (d, *J* = 0.9 Hz, 3H).

25 Example 70:

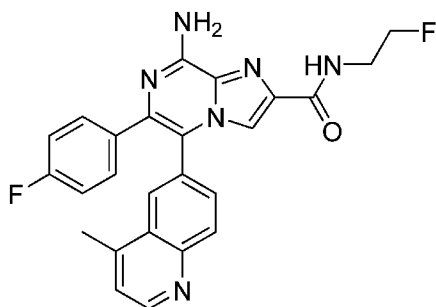
8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-methylcyclobutan-1-amine for ethylamine to lead to the title compound (7 mg, 15%) as yellow solid, hydrochloride salt. ESI-MS: 481.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.07 (d, J = 5.1 Hz, 1H), 8.44 – 8.41 (m, 1H), 8.24 (d, J = 8.7 Hz, 1H), 8.01 (s, 1H), 7.94 – 7.88 (m, 2H), 7.78 (d, J = 5.1 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.08 (t, J = 8.9 Hz, 2H), 2.74 (s, 3H), 2.30 (s, 2H), 2.02 – 1.95 (m, 2H), 1.81 (td, J = 10.1, 9.1, 5.1 Hz, 2H), 1.46 (s, 3H).

10 Example 71:

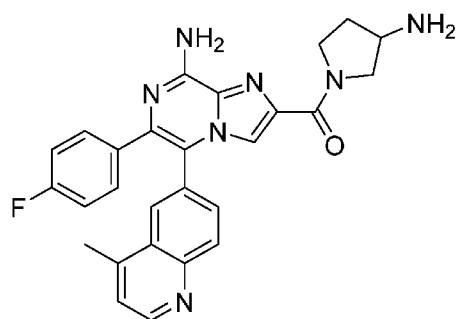
8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-fluoroethylamine hydrochloride for ethylamine to lead to the title compound (66 mg, 59%) as yellow solid, hydrochloride salt. ESI-MS: 459.20 [M+H]⁺. ¹H NMR (Deuterium Oxide): 9.00 (d, J = 5.8 Hz, 1H), 8.53 (d, J = 1.7 Hz, 1H), 8.24 (d, J = 8.9 Hz, 1H), 8.12 (s, 1H), 8.06 (dd, J = 8.9, 1.8 Hz, 1H), 7.96 (dd, J = 5.8 Hz, 1.0 Hz, 1H), 7.46-7.38 (m, 2H), 7.10-7.02 (m, 2H), 4.65 (dt, J = 47.0, 4.9 Hz, 1H), 3.75 (dt, J = 28.3, 4.9 Hz, 1H), 3.79 – 3.77 (m, 1H), 3.72 – 3.70 (m, 1H), 2.88 (s, 3H).

Example 72:

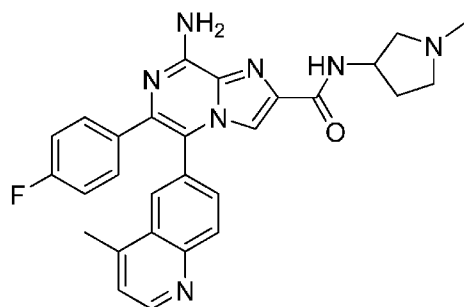
1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-(Boc-amino)pyrrolidine for ethylamine to lead to the title compound (18 mg, 47%) as yellow solid, hydrochloride salt. ESI-MS: 482.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.11 (d, J = 5.2 Hz, 1H), 8.52 – 8.46 (m, 1H), 8.41 (s, 2H), 8.31 (d, J = 8.7 Hz, 1H), 7.93 (dd, J = 8.6, 1.9 Hz, 1H), 7.86 (dd, J = 14.5, 4.4 Hz, 2H), 7.44 – 7.35 (m, 2H), 7.10 (td, J = 8.9, 1.7 Hz, 2H), 4.25 (d, J = 7.3 Hz, 3H), 3.08 – 3.05 (m, 1H), 2.77 (s, 3H), 2.31 – 1.98 (m, 3H).

Example 73:

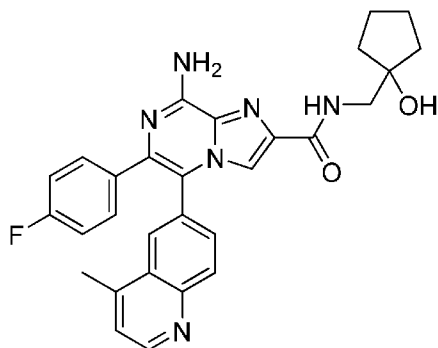
8-amino-6-(4-fluorophenyl)-N-(1-methylpyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-methylpyrrolidin-3-amine for ethylamine and substituting Et₃N for DIPEA and substituting HBTU for HATU in this step to lead to the title compound (13 mg, 21%) as yellow solid, hydrochloride salt. ESI-MS: 496.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.05 (s, 1H), 8.89 (dd, J = 11.4, 5.9 Hz, 1H), 8.70 (d, J = 7.3 Hz, 1H), 8.28 (s, 1H), 8.14 (dd, J = 8.6, 3.6 Hz, 1H), 7.99 (d, J = 13.8 Hz, 1H), 7.86 – 7.71 (m, 1H), 7.55 (d, J = 4.6 Hz, 2H), 7.41 – 7.27 (m, 2H), 7.03 (t, J = 8.9 Hz, 2H), 4.80 – 4.50 (m, 1H), 3.81 (dt, J = 12.1, 7.2 Hz, 1H), 3.04 (dq, J = 18.6, 9.8, 9.1 Hz, 2H), 2.82 (dd, J = 13.8, 4.8 Hz, 3H), 2.65 (d, J = 5.8 Hz, 3H), 2.26 (dt, J = 16.7, 8.5 Hz, 1H), 1.98 (s, 2H).

Example 74:

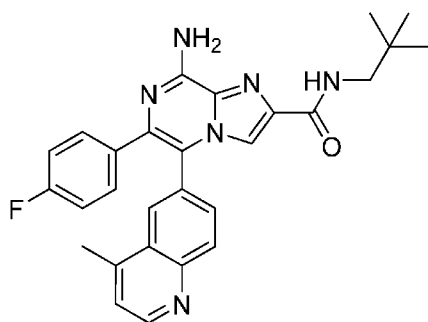
8-amino-6-(4-fluorophenyl)-N-[(1-hydroxycyclopentyl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-(aminomethyl)cyclopentanol hydrochloride for ethylamine to lead to the title compound (10 mg, 15%) as yellow solid, hydrochloride salt. ESI-MS: 511.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.07 (d, J = 5.7 Hz, 1H), 8.44 (s, 1H), 8.24 (d, J = 9.1 Hz, 1H), 7.97 – 7.86 (m, 3H), 7.79 (d, J = 4.2 Hz, 1H), 7.38 (dd, J = 8.6, 5.4 Hz, 2H), 7.08 (t, J = 8.1 Hz, 2H), 3.37 (d, J = 6.0 Hz, 3H), 2.75 (s, 3H), 1.69 (s, 2H), 1.52 (s, 6H).

Example 75:

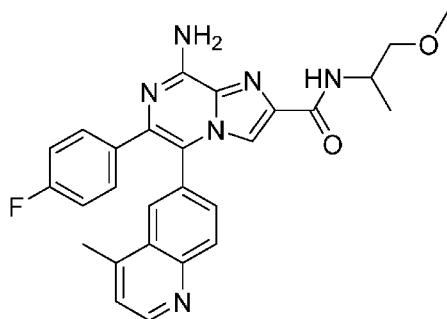
8-amino-N-(2,2-dimethylpropyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2,2-dimethyl-1-propanamine for ethylamine to lead to the title compound (10 mg, 10%) as yellow solid, hydrochloride salt. ESI-MS: 483.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.03 (d, J = 4.5 Hz, 1H), 8.40 (s, 1H), 8.20 (d, J = 8.6 Hz, 1H), 7.99 – 7.93 (m, 1H), 7.91 (d, J = 5.2 Hz, 2H), 7.73 (s, 1H), 7.42 – 7.33 (m, 2H), 7.07 (t, J = 8.8 Hz, 2H), 3.13 (d, J = 5.3 Hz, 2H), 2.72 (s, 3H), 0.90 (s, 9H).

Example 76:

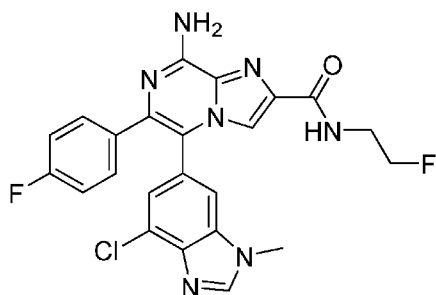
8-amino-6-(4-fluorophenyl)-N-(1-methoxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-methoxy-2-propylamine for ethylamine to lead to the title compound (28 mg, 42%) as yellow solid, hydrochloride salt. ESI-MS: 485.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.1 Hz, 1H), 8.47 (s, 1H), 8.28 (d, J = 8.8 Hz, 1H), 7.98 – 7.92 (m, 2H), 7.90 (d, J = 8.5 Hz, 1H), 7.83 (d, J = 5.2 Hz, 1H), 7.44 – 7.34 (m, 2H), 7.13 – 7.04 (m, 2H), 4.22 – 4.16 (m, 1H), 3.40 (dd, J = 9.6, 5.8 Hz, 1H), 3.33 (dd, J = 9.6, 5.2 Hz, 1H), 3.27 (s, 3H), 2.77 (s, 3H), 1.15 (d, J = 6.7 Hz, 3H).

Example 77:

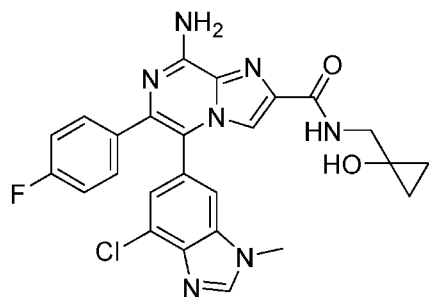
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2-fluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, **step a** performing this step at 100°C for 1 h and then following **Procedure C**, substituting 2-fluoroethylamine hydrochloride for ethylamine to the title compound (31 mg, 58%) as yellow solid, hydrochloride salt. ESI-MS: 482.20 [M+H]⁺. ¹H NMR (400 MHz, Methanol-*d*₄) δ 9.45 (s, 1H), 8.10 (s, 1H), 8.04 (s, 1H), 7.73 (d, J = 1.0 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.16 (t, J = 8.6 Hz, 2H), 4.65 (t, J = 4.9 Hz, 1H), 4.53 (t, J = 4.9 Hz, 1H), 4.11 (s, 3H), 3.77 (t, J = 5.0 Hz, 1H), 3.71 (t, J = 5.0 Hz, 1H).

Example 78:

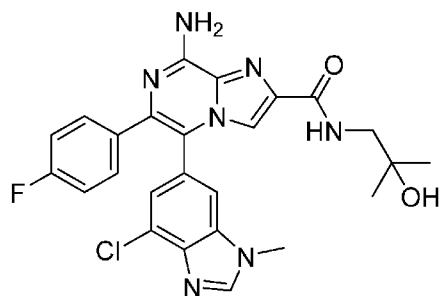
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-[(1-hydroxycyclopropyl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, **step a** and performing this step at 100°C for 1 h and performing **Procedure B**, **step b** at 80°C for 1 h and then following **Procedure C**, substituting 1-(aminoethyl)-cyclopropanol for ethylamine to lead to the title compound (16 mg, 31%) as off-white solid. ESI-MS: 506.20 [M+H]⁺. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.31 (s, 1H), 7.89 (s, 1H), 7.64 (d, J = 1.4 Hz, 1H), 7.46 – 7.31 (m, 3H), 6.96 (t, J = 8.8 Hz, 2H), 3.88 (s, 3H), 3.57 (s, 2H), 0.81 – 0.65 (m, 4H).

Example 79:

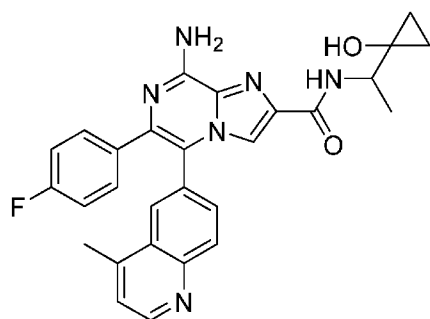
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, **step a** and performing this step at 100°C for 1 h and performing **Procedure B**, **step b** at 80°C for 1 h and then following **Procedure C**, substituting 1-amino-2-methylpropan-2-ol for ethylamine to lead to the title compound (5 mg, 38%) as yellow solid, hydrochloride salt. ESI-MS: 594.35 [M+H]⁺. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.31 (s, 1H), 7.88 (s, 1H), 7.64 (d, J = 1.4 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.35 (d, J = 1.4 Hz, 1H), 6.96 (t, J = 8.8 Hz, 2H), 3.88 (s, 3H), 3.43 (s, 2H), 1.26 (s, 6H).

Example 80:

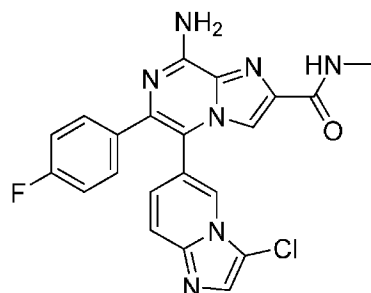
8-amino-6-(4-fluorophenyl)-N-[1-(1-hydroxycyclopropyl)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 1-(1-aminoethyl)cyclopropanol for ethylamine to lead to the title compound (41 mg, 66%) as yellow solid. ESI-MS: 497.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.98 (d, J = 4.8 Hz, 1H), 8.34 (d, J = 1.8 Hz, 1H), 8.15 (d, J = 8.7 Hz, 1H), 7.92 – 7.82 (m, 2H), 7.79 (s, 1H), 7.65 (d, J = 4.8 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.09 – 7.00 (m, 2H), 3.64 – 3.54 (m, 1H), 2.68 (s, 3H), 1.25 (d, J = 6.7 Hz, 3H), 0.65 – 0.46 (m, 4H).

Example 81:

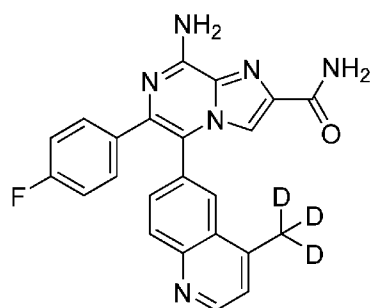
8-amino-5-{3-chloroimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure F** substituting {3-chloroimidazo[1,2-a]pyridin-6-yl}boronic acid [the approach outlined in **Procedure M**, substituting 6-bromo-3-chloroimidazo[1,2-a]pyridine for 6-bromo-4-ethylquinoline] for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline to lead to the title compound (18 mg, 29%) as yellow solid, hydrochloride salt. ESI-MS: 437.1 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.81 (s, 1H), 8.18 (s, 1H), 8.14 (q, J = 4.7 Hz, 2H), 8.10 (s, 1H), 7.86 (d, J = 9.3 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.15 (t, J = 8.8 Hz, 2H), 2.80 (d, J = 4.8 Hz, 3H).

Example 82:

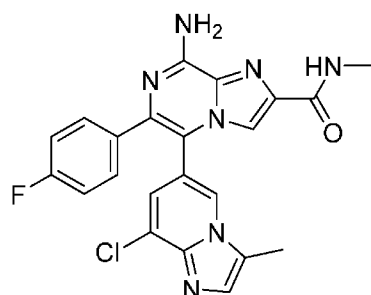
8-amino-6-(4-fluorophenyl)-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure K**, substituting (4-methylquinolin-6-yl)boronic acid for (8-chloroquinolin-6-yl)boronic acid in **Procedure K**, **step b** and then following **Procedure L**, substituting 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide hydrochloride for 8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide hydrochloride in this step to lead to the title compound (25 mg, 10%) as yellow solid, hydrochloride salt. ESI-MS: 416.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.1 Hz, 1H), 8.48 (d, J = 1.8 Hz, 1H), 8.27 (d, J = 8.7 Hz, 1H), 8.02 (s, 1H), 7.92 (dd, J = 8.7, 1.8 Hz, 1H), 7.83 (d, J = 5.1 Hz, 1H), 7.66 – 7.54 (m, 2H), 7.46 – 7.35 (m, 2H), 7.17 – 7.05 (m, 2H).

Example 83:

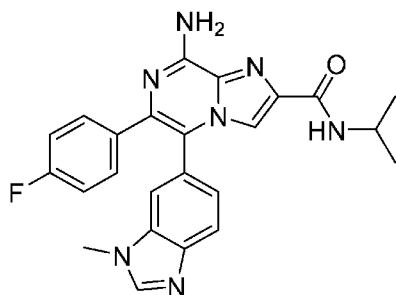
8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure F**, substituting {8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}boronic acid [the approach outlined in **Procedure M** substituting 6-bromo-8-chloro-3-methylimidazo[1,2-a]pyridine for 6-bromo-4-ethylquinoline and performing this step at 100°C for 4 h on oil bath] for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **Procedure F**, **step b** and performing this step at 100°C for 1.5 h on oil bath to lead to the title compound (15 mg, 67%) as yellowish solid, hydrochloride salt. ESI-MS: 450.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.94 (s, 1H), 8.13 (d, J = 12.5 Hz, 2H), 7.95 (d, J = 12.5 Hz, 2H), 7.81 (s, 2H), 7.51 – 7.44 (m, 2H), 7.18 – 7.09 (m, 2H), 2.81 (s, 3H), 2.80 (s, 3H).

Example 84:

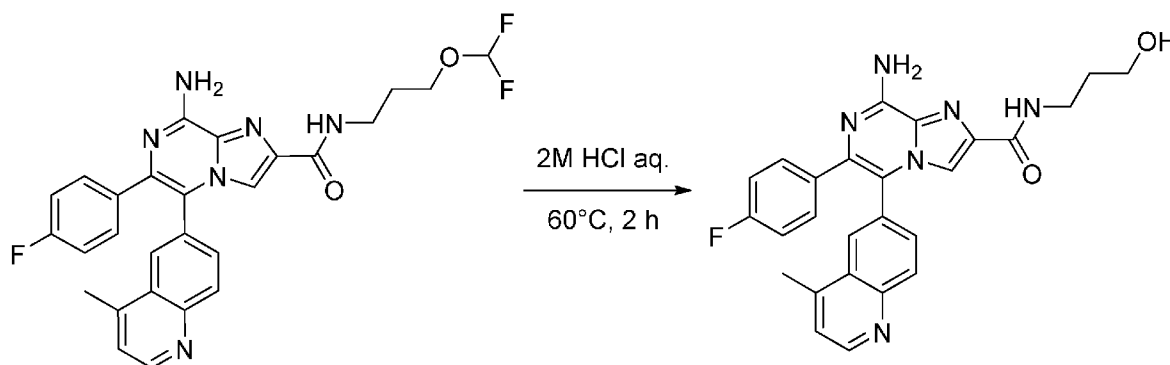
8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, step a and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, step a and performing this step for 2 h at 100°C and then following **Procedure C**, substituting isopropylamine for ethylamine to lead to the title compound (46 mg, 30%) as white solid, hydrochloride salt. ESI-MS: 444.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.45 (bs, 1H), 8.17 (s, 1H), 7.95 – 7.87 (m, 2H), 7.79 (s, 1H), 7.46 (dd, J = 8.5, 1.5 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.13 – 7.04 (m, 2H), 4.14 – 4.05 (m, 1H), 4.02 (s, 3H), 1.17 (d, J = 6.6 Hz, 6H).

Example 85:

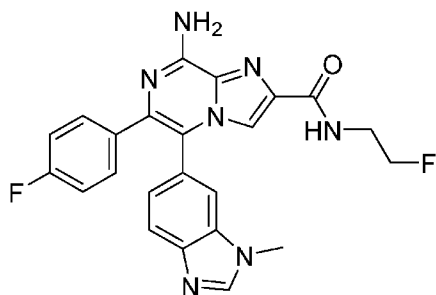
8-amino-6-(4-fluorophenyl)-N-(3-hydroxypropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized from the **Example 7**, by performing additional step. In a pressure tube 8-amino-N-[3-(difluoromethoxy)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide (**Example 7**, 32mg, 0.06mmol) in 2 ml of 2M HCl aq were stirred for 16 h at 60°C. Product was purified by flash reversed-phase chromatography to lead to the title compound (3 mg, 10%) as yellow solid, hydrochloride salt. ESI-MS: 471.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.10 (d, J = 5.2 Hz, 1H), 8.47 (s, 1H), 8.28 (d, J = 8.7 Hz, 1H), 8.22 (t, J = 5.9 Hz, 1H), 7.99 – 7.91 (m, 2H), 7.85 – 7.80 (m, 1H), 7.44 – 7.35 (m, 2H), 7.14 – 7.05 (m, 2H), 3.45 (t, J = 6.2 Hz, 2H), 3.33 (q, J = 6.6 Hz, 2H), 2.77 (s, 3H), 1.67 – 1.63 (m, 2H).

Example 86:

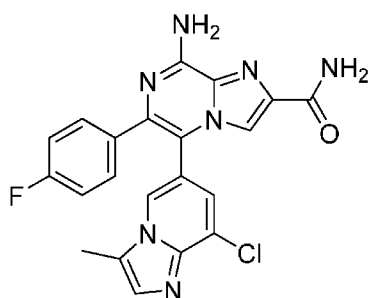
8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C to lead and then following **Procedure C**, substituting 2-fluoroethylamine hydrochloride for ethylamine to the title compound (13 mg, 10%) as white solid, hydrochloride salt. ESI-MS: 448.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.34 (s, 1H), 8.35 (t, J = 5.8 Hz, 1H), 8.14 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.78 (s, 1H), 7.44 (dd, J = 8.4, 1.5 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.07 (t, J = 8.9 Hz, 2H), 4.59 (t, J = 5.0 Hz, 1H), 4.47 (t, J = 5.0 Hz, 1H), 3.69 – 3.61 (m, 1H), 3.57 – 3.54 (m, 1H), 3.99 (s, 3H).

Example 87:

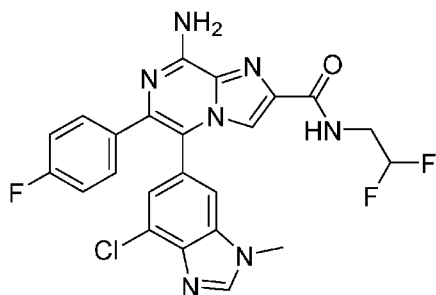
8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting {8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}boronic acid [the approach outlined in **Procedure M** substituting 6-bromo-8-chloro-3-methylimidazo[1,2-a]pyridine for 6-bromo-4-ethylquinoline and performing this step at 100°C for 4 h, without microwave irradiation] for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and instead of **step b** performing step according to **Procedure J** to lead to the title compound (43 mg, quant) as yellow solid, hydrochloride salt. ESI-MS: 436.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.89 (s, 1H), 8.14 (s, 1H), 7.90 (d, J = 12.3 Hz, 2H), 7.55 (s, 1H), 7.51 – 7.41 (m, 3H), 7.17 – 7.08 (m, 2H), 2.48 – 2.46 (m, 3H).

Example 88:

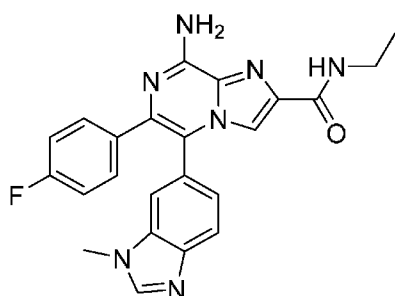
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, **step a** and performing this step at 100°C for 1 h and performing **step b** at 80°C for 1 h and then following **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine to lead to the title compound (13 mg, 39%) as white solid, hydrochloride salt. ESI-MS: 500.20 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.54 (t, J = 6.5 Hz, 2H), 7.96 (s, 1H), 7.80 (d, J = 1.4 Hz, 1H), 7.50 – 7.29 (m, 3H), 7.14 (dd, J = 10.1, 7.7 Hz, 2H), 6.12 (tt, J = 55.9, 3.8 Hz, 1H), 3.71 – 3.68 (m, 2H), 3.85 (s, 3H).

Example 89:

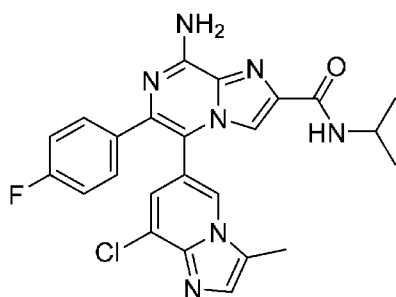
8-amino-N-ethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B**, **step a** and performing this step for 2 h at 100°C and then following **Procedure C** to lead to the title compound (9 mg, 10%) as white solid, hydrochloride salt. ESI-MS: 430.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.41 (s, 1H), 8.24 – 8.14 (m, 2H), 7.89 (d, J = 8.5 Hz, 1H), 7.77 (s, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.13 – 7.05 (m, 2H), 4.01 (s, 3H), 3.34 – 3.26 (m, 2H), 1.11 (t, J = 7.2 Hz, 3H).

Example 90:

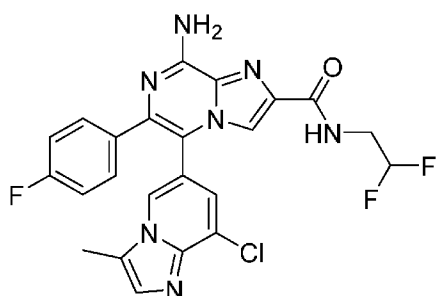
8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting {8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}boronic acid [the approach outlined in **Procedure M** substituting 6-bromo-8-chloro-3-methylimidazo[1,2-a]pyridine for 6-bromo-4-ethylquinoline and performing this step at 100°C for 4 h on oil bath] for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step at 100°C for 1.5 h and performing **step b** at 50°C for 16 h and then following **Procedure C**, substituting isopropylamine for ethylamine to lead to the title compound (31 mg, 83%) as yellowish solid, hydrochloride salt. ESI-MS: 478.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.91 (s, 1H), 8.13 (s, 1H), 7.94 (d, J = 12.1 Hz, 2H), 7.81 (d, J = 8.2 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.18 – 7.07 (m, 2H), 4.13 – 4.00 (m, 1H), 2.48 – 2.46 (m, 3H), 1.18 (d, J = 6.6 Hz, 6H).

Example 91:

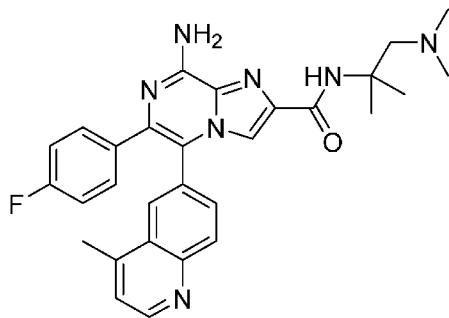
8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting {8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}boronic acid [the approach outlined in **Procedure M** substituting 6-bromo-8-chloro-3-methylimidazo[1,2-a]pyridine for 6-bromo-4-ethylquinoline and performing this step at 100°C for 4 h, without microwave irradiation] for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step at 100°C for 1.5 h and performing **step b** at 50°C for 16 h and then following **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine and substituting Et₃N for DIPEA in this procedure to lead to the title compound (20 mg, 30%) as yellowish solid, hydrochloride salt. ESI-MS: 500.20 [M+H]⁺. ¹H NMR (300 MHz, Deuterium Oxide) δ 8.74 (d, J = 1.3 Hz, 1H), 8.15 – 7.95 (m, 2H), 7.83 (s, 1H), 7.56 – 7.36 (m, 2H), 7.24 – 7.02 (m, 2H), 6.30 – 5.86 (m, 1H), 3.85 (td, J = 16.0, 3.4 Hz, 2H), 2.49 (s, 3H).

Example 92

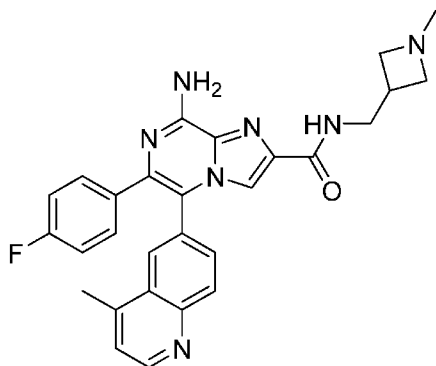
8-amino-N-[1-(dimethylamino)-2-methylpropan-2-yl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



5 The title compound was synthesized following the approach outlined in Procedure C, substituting 1-dimethylamino-2-methyl-2-aminopropane for ethylamine to lead to the title compound (21 mg, 29%) as yellow solid, hydrochloride salt. ESI-MS: 512.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.58 (s, 1H), 9.00 (d, J = 4.9 Hz, 1H), 8.34 (s, 1H), 8.20 (d, J = 8.8 Hz, 1H), 7.93 (s, 1H), 7.88 – 7.83 (m, 1H), 7.79 (s, 1H), 7.68 (d, J = 4.7 Hz, 1H), 7.37 (dd, J = 8.5, 5.5 Hz, 2H),
10 7.06 (t, J = 8.7 Hz, 2H), 3.63 (d, J = 4.0 Hz, 2H), 2.79 (d, J = 4.7 Hz, 6H), 2.69 (s, 3H), 1.48 (s, 6H).

Example 93

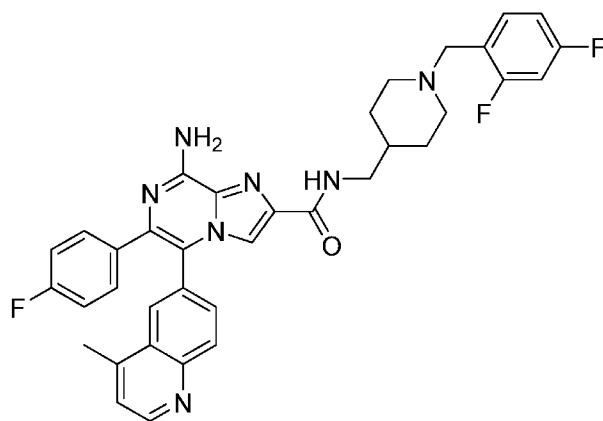
15 *8-amino-6-(4-fluorophenyl)-N-[(1-methylazetidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide*



The title compound was synthesized following the approach outlined in Procedure C, substituting 1-methyl-3-azetidinemethanamine for ethylamine to lead to the title compound (5 mg, 5%)
20 as yellow solid. ESI-MS: 496.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.65 (s, 1H), 8.90 (d, J = 4.6 Hz, 1H), 8.59 – 8.52 (m, 1H), 8.25 (dd, J = 3.7, 1.8 Hz, 1H), 8.14 – 8.09 (m, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.79 (dd, J = 8.7, 1.9 Hz, 1H), 7.54 (d, J = 4.6 Hz, 1H), 7.47 – 7.33 (m, 3H), 7.04 (t, J = 8.9 Hz, 2H), 4.17 – 4.16 (m, 1H), 4.04 – 4.02 (m, 1H), 3.94 – 3.92 (m, 1H), 3.79 – 3.74 (m, 1H), 3.56 – 3.50 (m, 1H), 3.49 – 3.45 (m, 1H), 3.03 – 2.92 (m, 1H), 2.79 (dd, J = 18.9,
25 5.2 Hz, 3H), 2.61 (s, 3H).

Example 94

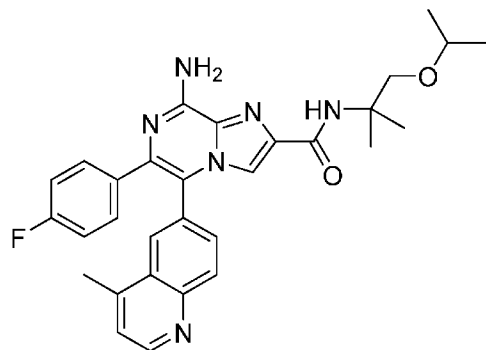
8-amino-N-[(1-[(2,4-difluorophenyl)methyl]piperidin-4-yl)methyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting {1-[(2,4-difluorophenyl)methyl]piperidin-4-yl}methanamine for ethylamine to lead to the title compound (22 mg, 26%) as yellow solid, hydrochloride salt. ESI-MS: 636.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.87 (s, 1H), 9.12 (d, J = 5.2 Hz, 1H), 8.50 (d, J = 1.8 Hz, 1H), 8.46 (t, J = 6.1 Hz, 1H), 8.37 (d, J = 8.7 Hz, 1H), 8.08 (s, 1H), 8.01 – 7.81 (m, 3H), 7.40 (td, J = 10.3, 9.4, 6.4 Hz, 3H), 7.22 (td, J = 8.4, 2.5 Hz, 1H), 7.17 – 7.04 (m, 2H), 4.26 (d, J = 4.8 Hz, 2H), 3.38 – 3.29 (m, 2H), 3.17 (t, J = 6.2 Hz, 2H), 2.93 (q, J = 11.3 Hz, 2H), 2.80 (s, 3H), 1.99 – 1.91 (m, 1H), 1.79 (d, J = 12.8 Hz, 2H), 1.57 (q, J = 13.5 Hz, 2H).

Example 95

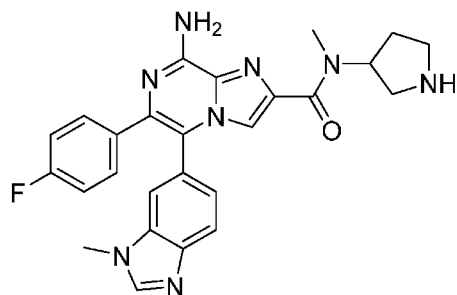
8-amino-6-(4-fluorophenyl)-N-[2-methyl-1-(propan-2-yloxy)propan-2-yl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-methyl-1-(propan-2-yloxy)propan-2-amine for ethylamine to lead to the title compound (40 mg, 42%) as yellow solid, hydrochloride salt. ESI-MS: 527.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.08 (d, J = 5.1 Hz, 1H), 8.24 (d, J = 8.7 Hz, 1H), 7.92 (dd, J = 8.8, 1.8 Hz, 1H), 7.79 (d, J = 5.6 Hz, 2H), 7.41 (s, 1H), 7.38 (dd, J = 8.7, 5.6 Hz, 2H), 7.11 – 7.03 (m, 2H), 3.59 – 3.53 (m, 1H), 3.52 (s, 2H), 2.74 (s, 3H), 1.34 (s, 6H), 1.09 (d, J = 6.1 Hz, 6H).

Example 96

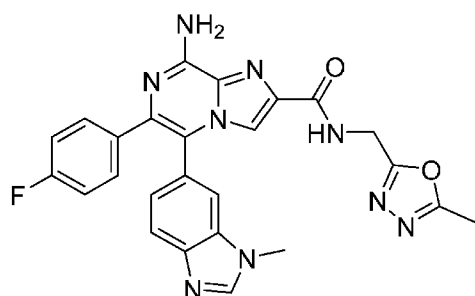
8-amino-6-(4-fluorophenyl)-N-methyl-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure C**, substituting 1-Boc-2-methylaminopyrrolidine for ethylamine to lead to the title compound (18 mg, 31%) as beige solid, hydrochloride salt. ESI-MS: 485.30 [M+H]⁺. ¹H NMR (400 MHz, Methanol-*d*₄) δ 9.20 (s, 1H), 8.06 (s, 1H), 7.90 (d, J = 7.0 Hz, 2H), 7.59 (d, J = 8.1 Hz, 1H), 7.49 – 7.40 (m, 2H), 7.09 – 6.99 (m, 2H), 4.81 – 4.62 (m, 1H), 4.08 (s, 3H), 3.75 – 3.64 (m, 1H), 3.58 (s, 3H), 3.47 – 3.35 (m, 2H), 3.13 – 2.99 (m, 1H), 2.54 – 2.39 (m, 1H), 2.37 – 2.24 (m, 1H).

Example 97

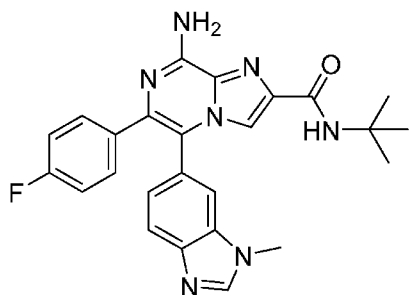
8-amino-6-(4-fluorophenyl)-N-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure C**, substituting (5-methyl-1,3,4-oxadiazol-2-yl)methylamine for ethylamine to lead to the title compound (2.2 mg, 4%) as beige solid. ESI-MS: 498.20 [M+H]⁺. ¹H NMR (300 MHz, Methanol-*d*₄) δ 8.24 (s, 1H), 7.88 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 1.2 Hz, 1H), 7.39 (dd, J = 8.7, 5.5 Hz, 2H), 7.30 (dd, J = 8.4, 1.6 Hz, 1H), 6.92 (t, J = 8.8 Hz, 2H), 4.81 (s, 2H), 3.87 (s, 3H), 2.53 (s, 3H).

Example 98

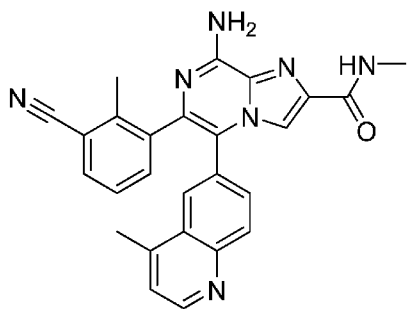
8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 **Procedure B, step a** and performing this step for 2 h at 100°C and then following **Procedure C**, substituting tert-butylamine for ethylamine to lead to the title compound (51 mg, 38%) as off-white solid, hydrochloride salt. ESI-MS: 458.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.49 (s, 1H), 8.24 – 8.10 (m, 1H), 7.89 (d, J = 8.5 Hz, 1H), 7.71 (s, 1H), 7.48 (s, 1H), 7.48 – 7.33 (m, 3H), 7.17 – 6.99 (m, 2H), 4.02 (s, 3H), 1.39 (s, 9H).

Example 99

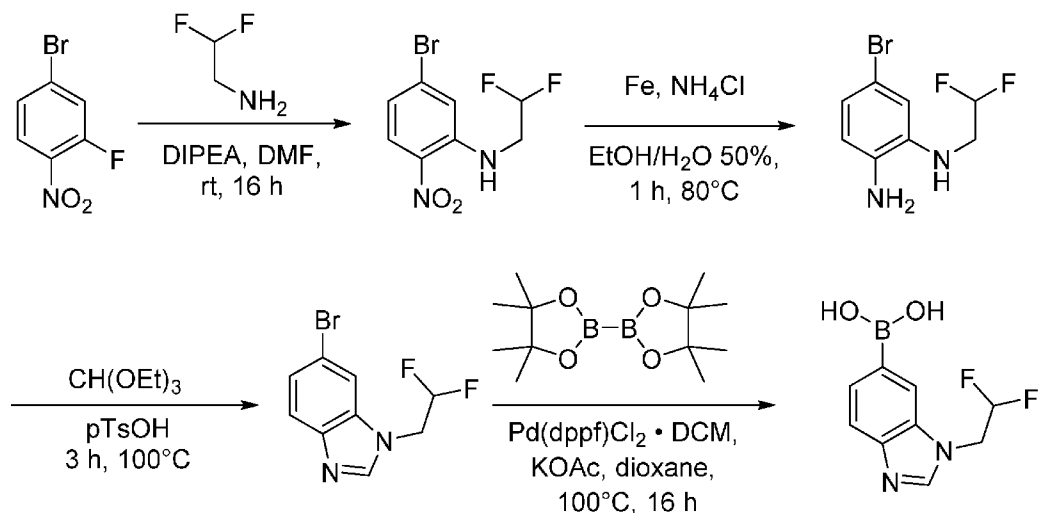
8-amino-6-(3-cyano-2-methylphenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



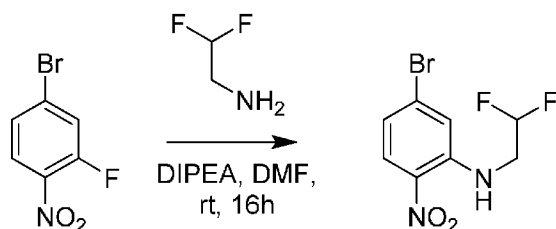
The title compound was synthesized following the approach outlined in **Procedure A, step a** substituting 3-cyano-2-methylphenylboronic acid for 4-fluorophenylboronic acid and then following **Procedure F**, substituting (4-methylquinolin-6-yl)boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **Procedure F, step b** and performing this step at 130°C for 1 h to lead to the title compound (20 mg, 17%) as yellow solid, hydrochloride salt. ESI-MS: 448.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (d, J = 5.1 Hz, 1H), 8.33 (s, 1H), 8.25 – 8.17 (m, 2H), 8.00 (s, 1H), 7.78 (d, J = 5.1 Hz, 1H), 7.70 (dd, J = 7.7, 1.3 Hz, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.27 (t, J = 7.7 Hz, 1H), 2.82 – 2.78 (m, 3H), 2.72 (s, 3H), 2.41 (s, 3H).

Procedure N

Preparation of [1-(2,2-difluoroethyl)-1H-1,3-benzodiazol-6-yl]boronic acid:

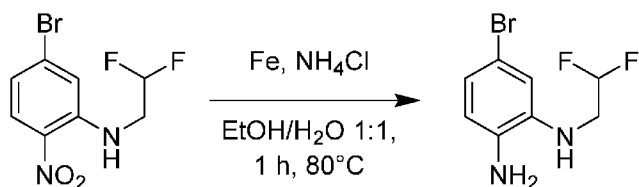


a. 5-bromo-N-(2,2-difluoroethyl)-2-nitroaniline



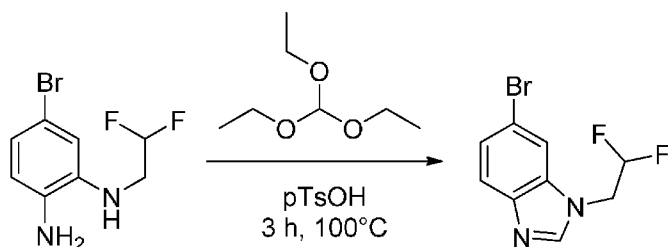
Into a stirred solution of 4-bromo-2-fluoro-1-nitrobenzene (2.20 g, 10 mmol), 2,2-difluoroethane-1-amine (0.811 g, 10 mmol) in DMF (10 ml), DIPEA (3.48 ml, 20 mmol) was added and stirred at room temperature for 16 h under argon atmosphere. After that time, the reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous MgSO_4 and concentrated under reduced pressure. Product was purified by flash chromatography (silica gel, hexane/EtOAc 0-10%) to afford the title compound of the yellow solid (2.44 g, 87%). ESI-MS: 448.30 $[\text{M}+\text{H}]^+$.

b. 5-bromo-N1-(2,2-difluoroethyl)benzene-1,2-diamine



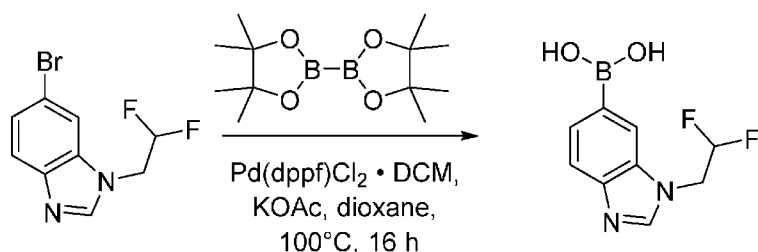
In a pressure tube a mixture of 5-bromo-N-(2,2-difluoroethyl)-2-nitroaniline (2.44 g, 8.68 mmol), iron powder (1.45 g, 26.04 mmol) and NH_4Cl (2.32 g, 43.41 mmol) in 50% aqueous ethanol (60 ml) was stirred at 80°C for 1 h. The resulting suspension was filtered through a Celite® pad, washed with DCM and water and the filtrate was extracted with DCM. The combined organic layers were washed with brine and dried over MgSO_4 . The solvent was evaporated and crude mixture was used for the next step without further purification. ESI-MS: 251.00 $[\text{M}+\text{H}]^+$.

c. 6-bromo-1-(2,2-difluoroethyl)-1H-1,3-benzodiazole



In a pressure tube to the solution of 5-bromo-N1-(2,2-difluoroethyl)benzene-1,2-diamine (1.98 g, 7.89 mmol) in triethyl orthoformate (5.56 ml, 39.43 mmol) was added p-toluenesulfonic acid monohydrate (136 mg, 0.789 mmol) and the reaction mixture was stirred at 60°C for 1.5 h. After cooling down, the reaction mixture was poured into water and extracted with ethyl acetate. The combined organic layers were washed with brine and dried over MgSO₄. The product was purified by flash chromatography (silica gel, hexane/EtOAc 0-10% EtOAc) to afford the title product as brown solid (1.71 g, 83%). ESI-MS: 263.10 [M+H]⁺.

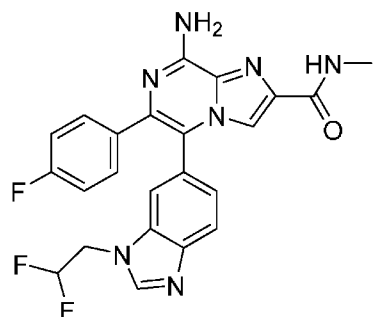
d. [1-(2,2-difluoroethyl)-1H-1,3-benzodiazol-6-yl]boronic acid



The pressure tube was charged with 6-bromo-1-(2,2-difluoroethyl)-1H-1,3-benzodiazole (1.71 g, 6.51 mmol), bis(pinacolato)diboron (2.15 g, 8.47 mmol) and potassium acetate (1.28 g, 13.02 mmol). To this mixture 1,4-dioxane (30 ml) was added. The resulting reaction mixture was purged with argon for 15 minutes. After that time, Pd(dppf)Cl₂ · DCM (106 mg, 0.13 mmol) was added and resulting mixture was heated in pre-heated oil bath at 100°C for 2 h. The mixture was filtered through Celite® pad and washed with ethyl acetate. The solvent was evaporated and the product was isolated by flash chromatography (silica gel, hexane/EtOAc) to afford the title compound (1.95 g, 97%) as brown oil. ESI-MS: 227.10 [M+H]⁺.

Example 100:

8-amino-5-[1-(2,2-difluoroethyl)-1H-1,3-benzodiazol-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide

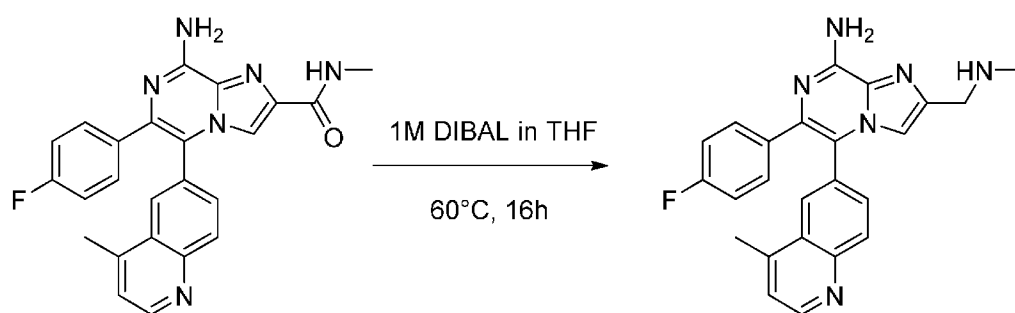


The title compound was synthesized following the approach outlined in **Procedure F**, substituting 1-(2,2-difluoroethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-1,3-benzodiazole (**Procedure N**) for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline to lead to the title compound (10 mg, 27%) as white solid, hydrochloride salt. ESI-MS: 466.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.99 (s, 1H), 8.30 (q, J = 4.8 Hz, 1H), 8.01 – 7.81 (m, 3H), 7.38 (dd, J = 8.5, 6.0 Hz, 3H), 7.13 (t, J = 8.7 Hz, 2H), 6.47 (t, J = 54.3 Hz, 1H), 4.94 (t, J = 16.4 Hz, 2H), 2.77 (d, J = 4.6 Hz, 3H).

Procedure O

Example 101

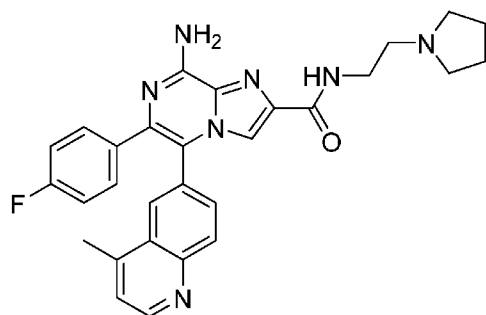
6-(4-fluorophenyl)-2-[(methylamino)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine



Into the pressure tube 8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide hydrochloride (synthesized following the approach outlined in **Procedure F**, substituting (4-methylquinolin-6-yl)boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **step b**) (212 mg, 0.5 mmol) and 3 ml of THF were added, into it diisobutylaluminium hydride (1M solution in THF, 3 ml) was added dropwise at room temperature, under argon atmosphere. The resulting reaction mixture was then heated to 60°C and stirred for 16 h. After that time reaction mixture was cooled down and carefully quenched by water and extracted with EtOAc/NaHCO₃ organic layer was washed with brine and dried over MgSO₄, filtered and concentrated. Product was purified by preparative HPLC and transformed into hydrochloride salt to afford the title product (17 mg, 7%) as yellow solid. ESI-MS: 413.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (s, 2H), 8.96 (s, 1H), 8.32 (s, 1H), 8.15 (d, J = 8.7 Hz, 1H), 7.84 – 7.73 (m, 2H), 7.63 (s, 1H), 7.39 (dd, J = 8.7, 5.5 Hz, 1H), 7.08 (t, J = 8.7 Hz, 1H), 4.22 (t, J = 5.6 Hz, 3H), 2.69 (s, 2H), 2.60 (t, J = 5.4 Hz, 3H).

Example 102

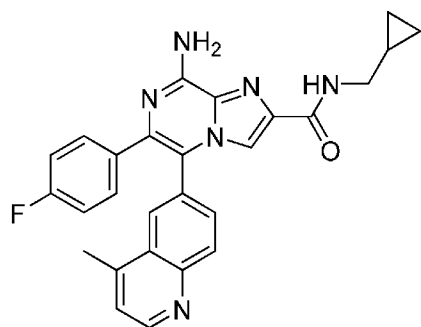
8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[2-(pyrrolidin-1-yl)ethyl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2-pyrrolidinoethylamine for ethylamine to lead to the title compound (20 mg, 100%) as yellow solid, hydrochloride salt. ESI-MS: 510.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.68 (s, 1H), 9.14 (d, J = 5.2 Hz, 1H), 8.76 (t, J = 5.9 Hz, 1H), 8.54 (s, 1H), 8.34 (d, J = 8.8 Hz, 1H), 8.29 (s, 1H), 7.95 – 7.86 (m, 2H), 7.41 (dd, J = 8.7, 5.5 Hz, 2H), 7.12 (t, J = 8.8 Hz, 2H), 3.67 – 3.60 (m, 2H), 3.59 – 3.52 (m, 2H), 3.32 – 3.26 (m, 2H), 3.04 – 2.94 (m, 2H), 2.85 (s, 3H), 2.04 – 1.92 (m, 2H), 1.90 – 1.79 (m, 2H).

Example 103

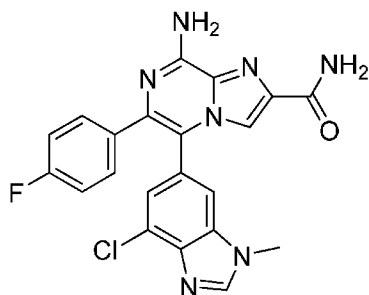
8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting (aminomethyl)cyclopropane for ethylamine to lead to the title compound (12 mg, 32%) as yellow solid, hydrochloride salt. ESI-MS: 467.40 [M+H]⁺. ¹H NMR (D₂O) δ 8.98 (d, J = 5.8 Hz, 1H), 8.48 (d, J = 1.7 Hz, 1H), 8.21 (d, J = 8.8 Hz, 1H), 8.06 (s, 1H), 8.03 (dd, J = 8.8; 1.7 Hz, 1H), 7.93 (dd, J = 5.8; 0.9 Hz, 1H), 7.42 - 7.34 (m, 2H), 7.10 - 6.96 (m, 2H), 1.81 (d, J = 7.0 Hz, 2H), 2.85 (s, 3H), 1.20 - 1.10 (m, 1H), 0.60 - 0.46 (m, 2H), 0.36 - 0.20 (m, 2H).

Example 104

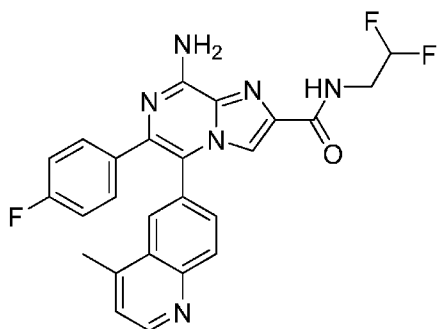
8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure K**, substituting (4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid (**Procedure H**) for (8-chloroquinolin-6-yl)boronic acid to lead to the title compound (32 mg, 34%) as white solid, hydrochloride salt. ESI-MS: 436.20 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.55 (s, 1H), 7.97 (s, 1H), 7.81 (d, J = 1.2 Hz, 1H), 7.62 (d, J = 18.3 Hz, 2H), 7.48 – 7.38 (m, 2H), 7.34 (d, J = 1.2 Hz, 1H), 7.22 – 7.12 (m, 2H), 3.86 (s, 3H).

10 Example 105

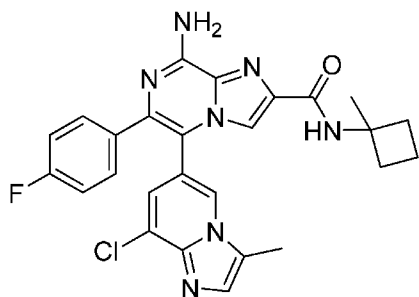
8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine to lead to the title compound (15 mg, 68%) as yellow solid, hydrochloride salt. ESI-MS: 477.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.14 (d, J = 5.0 Hz, 1H), 8.59 – 8.50 (m, 2H), 8.35 (d, J = 8.8 Hz, 1H), 8.09 (s, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 5.1 Hz, 1H), 7.41 (dd, J = 8.3, 5.6 Hz, 2H), 7.11 (t, J = 8.8 Hz, 2H), 6.13 (tt, J = 56.2, 3.6 Hz, 1H), 3.72 – 3.70 (m, 2H), 2.81 (s, 3H).

Example 107

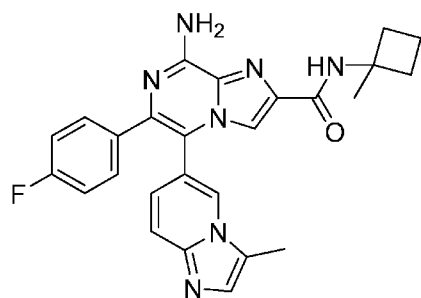
8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting {8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}boronic acid [the approach outlined in **Procedure M** substituting 6-bromo-8-chloro-3-methylimidazo[1,2-a]pyridine for 6-bromo-4-ethylquinoline and performing this step at 100°C for 4 h, without microwave irradiation] for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 in **Procedure B, step a** and performing this step at 100°C for 1.5 h and performing **step b** at 50°C for 16 h and then following **Procedure C**, substituting 1-methyl-cyclobutylamine for ethylamine and substituting Et₃N for DIPEA in this procedure to lead to the title compound (37 mg, 45%) as off-white solid, hydrochloride salt. ESI-MS: 504.40 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.89 (s, 1H), 8.09 (s, 1H), 7.98 – 7.86 (m, 3H), 7.52 – 7.43 (m, 2H), 7.13 (dd, *J* = 8.9 Hz, 2H), 2.48 (s, 3H), 2.41 – 2.33 (m, 2H), 2.06 – 1.96 (m, 2H), 1.88 – 1.77 (m, 2H), 1.49 (s, 3H).

Example 108

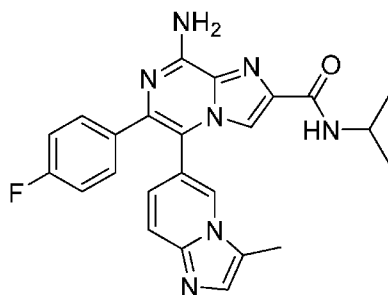
8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and substituting Pd(PPh₃)₄ for Sphos Pd G3 in **Procedure B, step a** and then following **Procedure C** substituting 1-methyl-cyclobutylamine for ethylamine and substituting Et₃N for DIPEA in this procedure to lead to the title compound (20 mg, 22%) as yellowish solid, hydrochloride salt. ESI-MS: 470.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (s, 1H), 8.16 (s, 1H), 8.07 (d, *J* = 1.3 Hz, 1H), 7.98 (dd, *J* = 9.2, 1.0 Hz, 1H), 7.93 (s, 1H), 7.74 (dd, *J* = 9.2, 1.5 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.10 (t, *J* = 8.9 Hz, 2H), 2.54 (d, *J* = 1.1 Hz, 3H), 2.41 – 2.34 (m, 2H), 2.05 – 1.96 (m, 2H), 1.88 – 1.78 (m, 2H), 1.49 (s, 3H).

Example 109

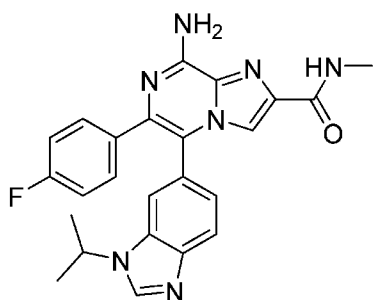
8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and performing this step at 110° C for 3 h and then following **Procedure C** substituting isopropylamine for ethylamine in this procedure to lead to the title compound (42 mg, 43%) as beige solid, hydrochloride salt. ESI-MS: 444.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.14 (t, J = 1.2 Hz, 1H), 8.31 (s, 1H), 8.08 (d, J = 1.3 Hz, 1H), 7.99 (dd, J = 9.3, 0.9 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.71 (dd, J = 9.3, 1.3 Hz, 1H), 7.52 – 7.37 (m, 2H), 7.20 – 7.02 (m, 2H), 4.20 – 3.97 (m, 1H), 2.55 (s, 3H), 1.18 (d, J = 6.5 Hz, 6H).

Example 110

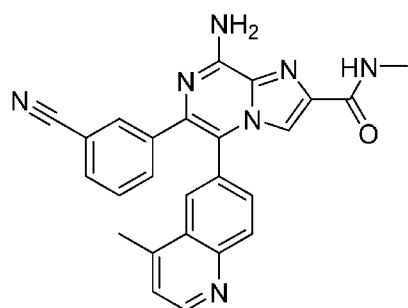
8-amino-6-(4-fluorophenyl)-N-methyl-5-[1-(propan-2-yl)-1H-1,3-benzodiazol-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B** substituting 1-(propan-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-1,3-benzodiazole [the approach outlined in **Procedure M**, substituting 6-bromo-1-(propan-2-yl)-1H-1,3-benzodiazole for 6-bromo-4-ethylquinoline and Pd₂(dba)₃ with tricyclohexylphosphine for Pd(dppf)Cl₂*DCM and performing this step at 85° C for 3 h, without MW irradiation] for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and performing this step at 110° C for 3 h to lead to the title compound (57 mg, 43%) as white solid, hydrochloride salt. ESI-MS: 444.20 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.65 (s, 1H), 8.25 (d, J = 4.9 Hz, 1H), 8.16 (d, J = 1.4 Hz, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.89 (s, 1H), 7.60 (dd, J = 8.5, 1.4 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.12 (t, J = 8.9 Hz, 2H), 4.92 (p, J = 6.7 Hz, 1H), 2.78 (d, J = 4.7 Hz, 3H), 1.52 (dd, J = 24.1, 6.7 Hz, 6H).

Example 111

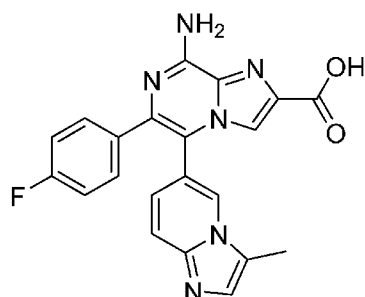
8-amino-6-(3-cyanophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 3-cyanophenylboronic acid for 4-fluorophenylboronic acid and then following **Procedure F**, substituting (4-methylquinolin-6-yl)boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **Procedure F, step b** and performing this step at 130° C for 1 h to lead to the title compound (6 mg, 21%) as yellow solid, hydrochloride salt. ESI-MS: 434.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.04 (d, J = 4.9 Hz, 1H), 8.42 (s, 1H), 8.22 (d, J = 8.7 Hz, 1H), 8.17 (d, J = 4.9 Hz, 1H), 7.96 – 7.90 (m, 1H), 7.89 – 7.84 (m, 2H), 7.73 (d, J = 4.4 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 2.79 (d, J = 4.7 Hz, 3H), 2.72 (s, 3H).

Example 112

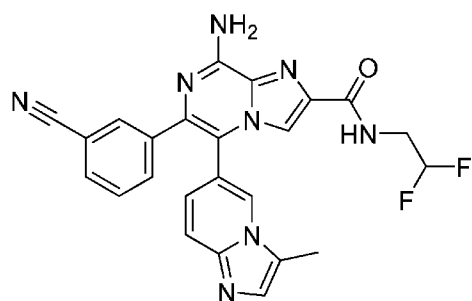
8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxylic acid



The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and performing this step at 110° C for 3 h to lead to the title compound (8 mg, 65%) as off-white solid, hydrochloride salt. ESI-MS: 403.20 [M+H]⁺. ¹H NMR (400 MHz, D₂O) δ 8.83 – 8.71 (m, 1H), 8.12 (s, 1H), 7.96 (dd, J = 9.4, 1.0 Hz, 1H), 7.89 (dd, J = 9.4, 1.5 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.52 – 7.38 (m, 2H), 7.20 – 7.07 (m, 2H), 2.48 (d, J = 1.1 Hz, 3H).

Example 113

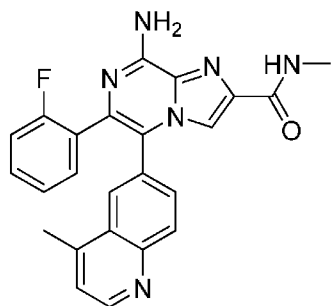
8-amino-6-(3-cyanophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 3-cyanophenylboronic acid for 4-fluorophenylboronic acid and then following **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **Procedure B**, **step a** and performing this step at 110° C for 3 h and then following **Procedure C** substituting 2,2-difluoroethan-1-amine for ethylamine in this procedure to lead to the title compound (20 mg, 14%) as yellowish solid, hydrochloride salt. ESI-MS: 473.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.15 (t, J = 1.2 Hz, 1H), 8.40 (t, J = 6.3 Hz, 1H), 8.27 (s, 1H), 8.08 (d, J = 1.3 Hz, 1H), 8.00 (dd, J = 9.2, 0.9 Hz, 1H), 7.94 (t, J = 1.8 Hz, 1H), 7.80 (dd, J = 9.2, 1.5 Hz, 1H), 7.74 (dt, J = 7.8, 1.4 Hz, 1H), 7.63 (dt, J = 8.0, 1.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 6.15 (t, J = 3.8 Hz, 1H), 3.74 (t, J = 16.5 Hz, 2H), 2.54 (d, J = 1.1 Hz, 3H).

Example 114

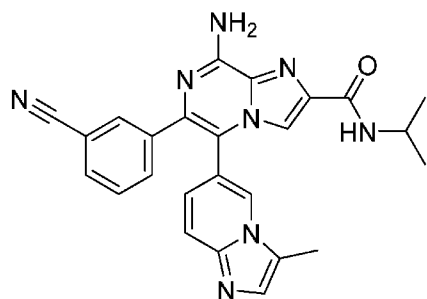
8-amino-6-(2-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 2-fluorophenylboronic acid for 4-fluorophenylboronic acid and then following **Procedure F**, substituting (4-methylquinolin-6-yl)boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline in **Procedure F**, **step b** and performing this step at 130° C for 1 h to lead to the title compound (6 mg, 21%) as yellow solid, hydrochloride salt. ESI-MS: 427.20 [M+H]⁺. ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.11 (d, J = 5.2 Hz, 1H), 8.36 (d, J = 1.7 Hz, 1H), 8.30 (d, J = 8.8 Hz, 1H), 8.27 – 8.19 (m, 1H), 8.06 – 8.00 (m, 2H), 7.84 (d, J = 5.3 Hz, 1H), 7.48 (td, J = 7.5, 1.8 Hz, 1H), 7.34 (tdd, J = 7.4, 5.3, 1.8 Hz, 1H), 7.19 – 7.03 (m, 2H), 2.79 (d, J = 4.6 Hz, 3H), 2.72 (s, 3H).

Example 115

8-amino-6-(3-cyanophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide

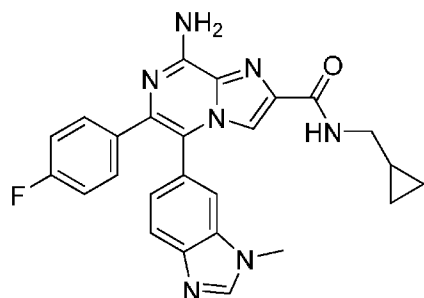


The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 3-cyanophenylboronic acid for 4-fluorophenylboronic acid and then following **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and performing this step at 110° C for 3 h and then following **Procedure C** substituting isopropylamine for ethylamine in this procedure to lead to the title compound (40 mg, 43%) as yellowish solid, hydrochloride salt.

ESI-MS: 451.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (t, J = 1.3 Hz, 1H), 8.18 (s, 1H), 8.07 (d, J = 1.2 Hz, 1H), 8.00 (dd, J = 9.3, 0.9 Hz, 1H), 7.94 (t, J = 1.7 Hz, 1H), 7.83 – 7.78 (m, 2H), 7.74 (dt, J = 7.7, 1.4 Hz, 1H), 7.62 (dt, J = 8.0, 1.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 4.09 (ddd, J = 12.9, 8.1, 6.4 Hz, 1H), 2.54 (d, J = 1.1 Hz, 3H), 1.19 (d, J = 6.6 Hz, 6H).

Example 116

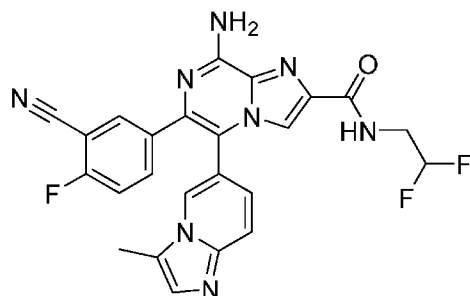
8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 and performing this step for 3 h at 130 °C and then following **Procedure C**, substituting cyclopropanemethylamine for ethylamine to lead to the title compound (68 mg, 46%) as white solid, hydrochloride salt. ESI-MS: 456.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.55 (s, 1H), 8.29 (t, J = 5.9 Hz, 1H), 8.22 – 8.18 (m, 1H), 7.94 – 7.86 (m, 2H), 7.47 (dd, J = 8.5, 1.5 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.16 – 7.09 (m, 2H), 4.05 (s, 3H), 3.18 – 3.12 (m, 2H), 1.07 – 0.96 (m, 1H), 0.47 – 0.41 (m, 2H), 0.26 – 0.20 (m, 2H).

Example 117

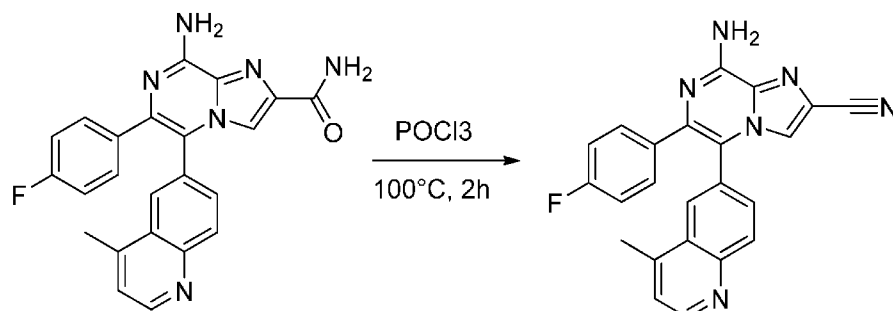
8-amino-6-(3-cyano-4-fluorophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 3-cyano-4-fluorophenylboronic acid for 4-fluorophenylboronic acid and performing this step at 80 °C for 16 h, in **step c** substituting ACN for DME and performing this step with addition of Sc(OTf)₃ (0.1 eq) at 100 °C for 24 h then following **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(PPh₃)₄ for Sphos Pd G3 and substituting cesium carbonate for sodium carbonate and performing this step at 120 °C for 1 h under microwave irradiation, and then following **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine and triethylamine for DIPEA to lead to the title compound (6 mg, 5%) as white solid, hydrochloride salt. ESI-MS: 491.30 [M+H]⁺. ¹H NMR (400 MHz, D₂O) δ 8.80 (s, 1H), 8.09 (s, 1H), 7.98 (d, J = 9.3, 1.0 Hz, 1H), 7.92 – 7.84 (m, 2H), 7.78 – 7.69 (m, 2H), 7.31 (t, J = 8.9 Hz, 1H), 6.09 (tt, J = 55.3, 3.4 Hz, 1H), 3.86 (td, J = 16.0, 3.4 Hz, 2H), 2.50 (s, 3H).

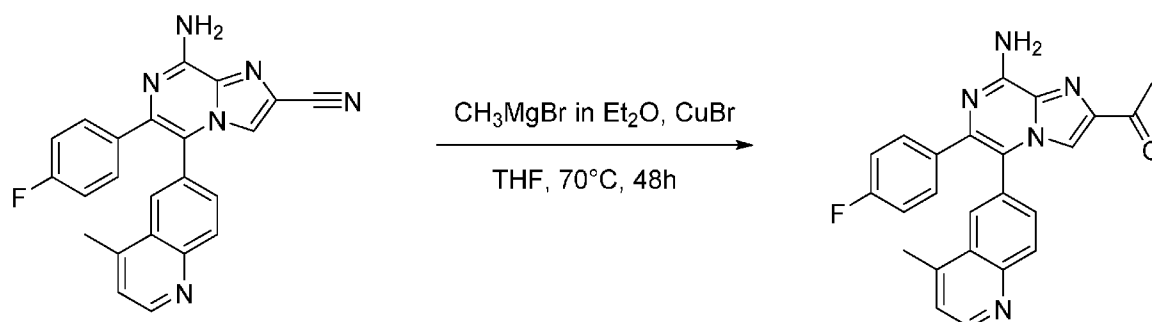
Procedure P

Example 118

*1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-2-yl]ethan-1-one*5 *a. 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonitrile*

8-Amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide was synthesized following the approach outlined in Procedure A, subsequently Procedure B, and then followed by Procedure J, substituting ethyl 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate for ethyl 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylate. Obtained 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide (300 mg, 0.73 mmol) was suspended in POCl_3 (1 ml) and it was heated for 2 h at 100°C . Then reaction mixture was cooled down in an ice bath and quenched by the dropwise addition of water followed by saturated aqueous solution of sodium bicarbonate. Product was extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous MgSO_4 , filtered off and the solvent was evaporated. The product was purified by flash chromatography (silica gel, eluted with DCM/MeOH from 0% MeOH to 5% MeOH) to lead to the 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonitrile (247 mg, 86%) as brown solid.

20 *b. 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-2-yl]ethan-1-one*



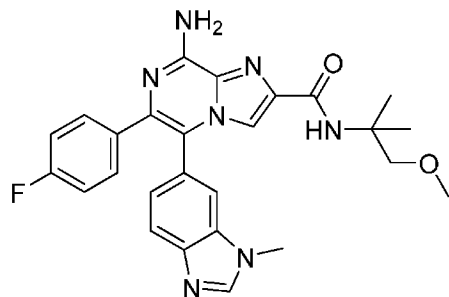
25 To the 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonitrile (125 mg, 0.32 mmol), dissolved in 3 ml of THF, methylmagnesium bromide solution in diethyl ether (3N, 0.32 ml) and CuBr (9.1 mg, 0.06 mmol) were added. Reaction mixture was stirred for 2 days at 70°C . Then reaction was quenched by water followed by saturated aqueous solution of sodium bicarbonate. Product was extracted three times with ethyl acetate. The combined organic layers were dried over anhydrous MgSO_4 , filtered off and the solvent was

30

evaporated in vacuo. The obtained crude material was purified by flash chromatography, then transformed into hydrochloride salt to give the title compound (3 mg, 2%) as yellow solid, hydrochloride salt. ESI-MS: 412.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.01 – 8.97 (m, 1H), 8.38 – 8.33 (m, 1H), 8.16 (d, J = 8.7 Hz, 1H), 8.01 (s, 1H), 7.87 – 7.82 (m, 1H), 7.69 – 7.64 (m, 1H), 7.39 – 7.33 (m, 2H), 7.08 – 7.01 (m, 2H), 2.69 (s, 3H), 2.58 (s, 3H).

Example 119

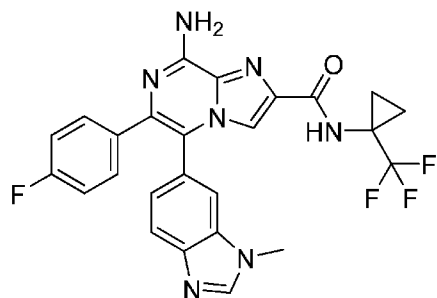
8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 and performing this step for 2 h at 100 °C and then following **Procedure C**, substituting 1-methoxy-2-methylpropan-2-amine for ethylamine and triethylamine for DIPEA to lead to the title compound (35 mg, 22%) as white solid, hydrochloride salt. ESI-MS: 488.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.47 (s, 1H), 8.17 (t, J = 1.0 Hz, 1H), 7.93 – 7.86 (m, 1H), 7.67 (s, 1H), 7.48 – 7.35 (m, 4H), 7.13 – 7.04 (m, 2H), 4.02 (s, 3H), 3.46 (s, 2H), 3.30 (s, 3H), 1.35 (s, 6H).

Example 120

8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-[1-(trifluoromethyl)cyclopropyl]imidazo[1,2-a]pyrazine-2-carboxamide

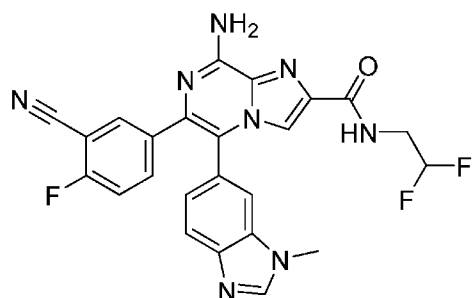


The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 and performing this step for 2 h at 100 °C and then following **Procedure C**, substituting 1-(trifluoromethyl)cyclopropanamine for ethylamine and triethylamine for DIPEA and performing this step for 5 days at room temperature to lead to the title compound (45 mg, 30%) as white solid, hydrochloride salt. ESI-MS: 510.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.50 (s, 1H), 9.02 (s, 1H), 8.17 (s, 1H), 7.98 (s, 1H),

7.92 (d, $J = 8.4$ Hz, 1H), 7.47 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.42 – 7.37 (m, 2H), 7.14 – 7.07 (m, 2H), 4.04 (s, 3H), 1.34 – 1.29 (m, 2H), 1.19 – 1.13 (m, 2H).

Example 121

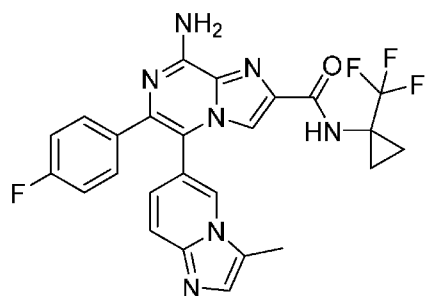
5 *8-amino-6-(3-cyano-4-fluorophenyl)-N-(2,2-difluoroethyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide*



The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 3-cyano-4-fluorophenylboronic acid for 4-fluorophenylboronic acid and performing this step at 80 °C for 16 h, in **step c** substituting ACN for DME and performing this step with addition of $\text{Sc}(\text{OTf})_3$ (0.1 eq) at 100 °C for 24 h then following **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting $\text{Pd}(\text{PPh}_3)_4$ for Sphos Pd G3 and substituting cesium carbonate for sodium carbonate and performing this step at 130 °C for 1 h under microwave irradiation, and then following **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine and triethylamine for DIPEA to lead to the title compound (6 mg, 9%) as white solid, hydrochloride salt. ESI-MS: 491.20 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, D_2O) δ 9.24 (s, 1H), 8.03 – 7.97 (m, 2H), 7.89 (dd, $J = 8.6, 0.8$ Hz, 1H), 7.76 (dd, $J = 6.0, 2.3$ Hz, 1H), 7.65 (ddd, $J = 8.8, 5.1, 2.4$ Hz, 1H), 7.59 (dd, $J = 8.6, 1.5$ Hz, 1H), 7.22 (d, $J = 8.9$ Hz, 1H), 6.24 – 5.93 (m, 1H), 4.06 – 4.01 (m, 3H), 3.85 (td, $J = 16.0, 3.4$ Hz, 2H).

Example 122

25 *8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-[1-(trifluoromethyl)cyclopropyl]imidazo[1,2-a]pyrazine-2-carboxamide*

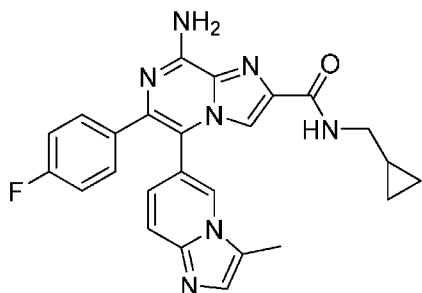


The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ for Sphos Pd G3 and substituting cesium carbonate for sodium carbonate and performing this step at 85 °C for 5 h, and then following **Procedure C**, substituting 1-trifluoromethyl-1-cyclopropylamine for ethylamine and triethylamine for DIPEA to lead to the title compound (82 mg, 27%) as off-white solid, hydrochloride salt. ESI-MS: 510.20 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, D_2O) δ 8.76 (t, $J = 1.3$ Hz, 1H),

8.11 (s, 1H), 7.97 (dd, J = 9.4, 1.0 Hz, 1H), 7.89 (dd, J = 9.4, 1.5 Hz, 1H), 7.75 (d, J = 1.1 Hz, 1H), 7.50 – 7.39 (m, 2H), 7.20 – 7.01 (m, 2H), 2.48 (d, J = 1.1 Hz, 3H), 1.51 – 1.41 (m, 2H), 1.27 (d, J = 7.0 Hz, 2H).

5 Example 123

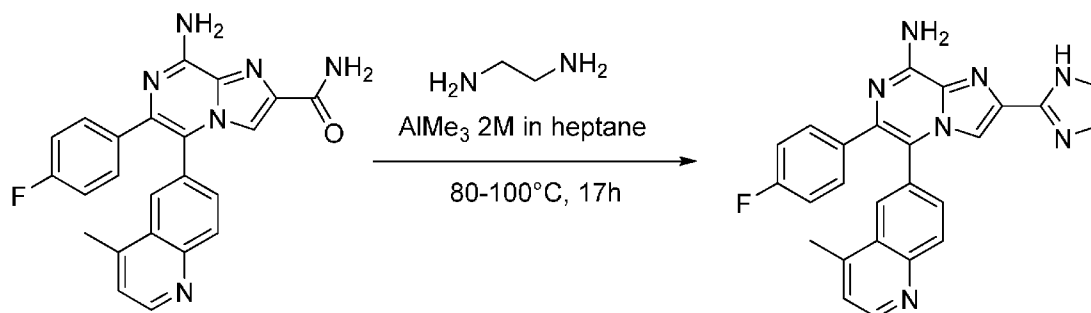
8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



10 The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(PPh₃)₂Cl₂ for Sphos Pd G3 and substituting cesium carbonate for sodium carbonate and performing this step at 85 °C for 5 h, and then following **Procedure C**, substituting 1-cyclopropylmethanamine for ethylamine and triethylamine for DIPEA and performing this step at room temperature for 4 h to lead to the title compound (72 mg, 43%) as off-white solid, hydrochloride salt. ESI-MS: 456.30 [M+H]⁺. 1H NMR (400 MHz, D₂O) δ 8.79 (t, J = 1.3 Hz, 1H), 8.08 (s, 1H), 7.98 (dd, J = 9.4, 1.0 Hz, 1H), 7.90 (dd, J = 9.4, 1.6 Hz, 1H), 7.76 (q, J = 1.0 Hz, 1H), 7.54 – 7.41 (m, 2H), 7.20 – 7.05 (m, 2H), 3.28 (d, J = 7.0 Hz, 2H), 2.49 (d, J = 1.1 Hz, 3H), 1.23 – 0.97 (m, 1H), 0.68 – 0.45 (m, 2H), 0.27 (dt, J = 6.0, 4.4 Hz, 2H).

Example 124

2-(4,5-dihydro-1H-imidazol-2-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine

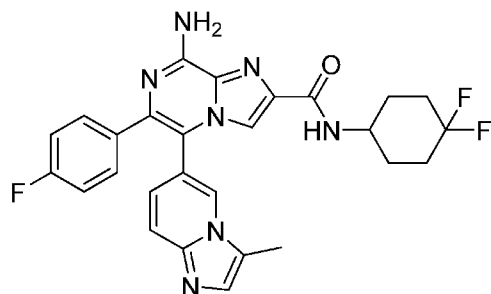


To the ethylene diamine (0.14 ml, 2.03 mmol) in dry toluene (3 ml), triethyl aluminium solution in heptane (2N, 0.63 ml) was added followed by the solution of 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonitrile (**Procedure P, step a**, 100 mg, 0.25 mmol) in toluene (3 ml). Reaction mixture was heated for 16 h at 80 °C. Then triethyl aluminium solution in heptane (2N, 0.30 ml) was added and reaction mixture was stirred for 1 h in 100 °C. Then the solvent was evaporated. The residue was diluted with ethyl acetate and washed with

water. Organic phase was dried over MgSO_4 , filtrated and concentrated. Crude product was purified by preparative HPLC and transformed into hydrochloride salt to afford the title product (53 mg, 48%) as yellow solid. ESI-MS: 438.30 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 10.65 (s, 2H), 9.08 (d, $J = 5.0$ Hz, 1H), 8.79 (s, 1H), 8.55 (s, 1H), 8.25 (d, $J = 8.8$ Hz, 1H), 7.86 – 7.78 (m, 2H), 7.41 – 7.34 (m, 2H), 7.10 – 7.03 (m, 2H), 3.97 (s, 3H), 2.83 (s, 2H).

Example 125

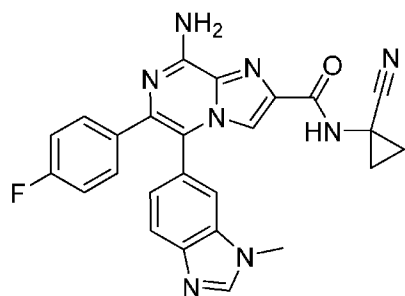
8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ for Sphos Pd G3 and substituting cesium carbonate for sodium carbonate and performing this step at 85 °C for 5 h, and then following **Procedure C**, substituting 4,4-difluorocyclohexan-1-amine for ethylamine and triethylamine for DIPEA and performing this step at room temperature for 4 h to lead to the title compound (135 mg, 71%) as beige solid, hydrochloride salt. ESI-MS: 520.30 $[\text{M}+\text{H}]^+$. ^1H NMR (400 MHz, DMSO-d_6) δ 9.14 (t, $J = 1.3$ Hz, 1H), 8.40 (s, 1H), 8.18 (d, $J = 8.2$ Hz, 1H), 8.07 (d, $J = 1.3$ Hz, 1H), 7.99 (dd, $J = 9.3, 0.9$ Hz, 1H), 7.70 (dd, $J = 9.3, 1.5$ Hz, 1H), 7.55 – 7.38 (m, 2H), 7.20 – 7.05 (m, 2H), 4.07 – 3.87 (m, 1H), 2.55 (d, $J = 1.1$ Hz, 3H), 2.13 – 1.78 (m, 6H), 1.77 – 1.56 (m, 2H).

Example 126

8-amino-N-(1-cyanocyclopropyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide



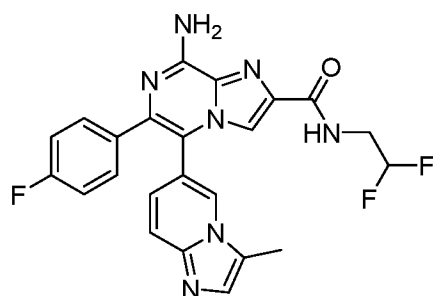
The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting $\text{Pd}(\text{amphos})\text{Cl}_2$ for Sphos Pd G3 and performing this step for 2 h at 100 °C and then following **Procedure C**, substituting 1-amino-1-cyclopropanecarbonitrile hydrochloride for ethylamine and triethylamine for DIPEA and performing this step at room temperature

for 7 h to lead to the title compound (24 mg, 14%) as white solid, hydrochloride salt. ESI-MS: 467.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.44 (s, 1H), 9.29 (s, 1H), 8.17 (s, 1H), 7.92 – 7.87 (m, 2H), 7.46 (dd, J = 8.5, 1.5 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.11 – 7.05 (m, 2H), 4.03 (s, 3H), 1.58 – 1.52 (m, 2H), 1.30 – 1.23 (m, 2H).

5

Example 127

8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide



10

The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(PPh₃)₂Cl₂ for Sphos Pd G3 and substituting cesium carbonate for sodium carbonate and performing this step at 85 °C for 5 h, and then following **Procedure C**, substituting 2,2-difluoroethylamine for ethylamine and triethylamine for DIPEA to lead to the title compound (238 mg, 73%) as off-white solid, hydrochloride salt. ESI-MS: 466.20 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.14 (t, J = 1.2 Hz, 1H), 8.46 (t, J = 6.3 Hz, 1H), 8.40 (s, 1H), 8.08 (d, J = 1.3 Hz, 1H), 8.00 (dd, J = 9.2, 0.9 Hz, 1H), 7.71 (dd, J = 9.2, 1.5 Hz, 1H), 7.56 – 7.41 (m, 2H), 7.23 – 7.06 (m, 2H), 6.15 (tt, J = 55.8, 3.8 Hz, 1H), 3.97 – 3.49 (m, 2H), 2.55 (d, J = 1.1 Hz, 3H).

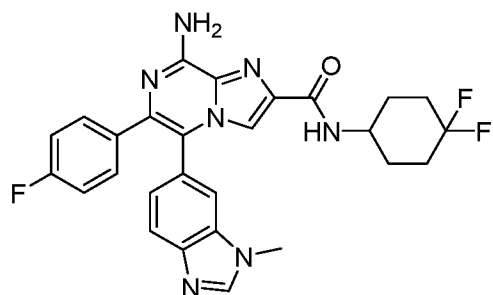
15

20

Example 128

8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide

25



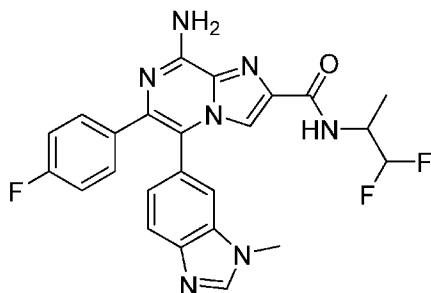
The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 and performing this step for 2 h at 100 °C and then following **Procedure C**, substituting 4,4-difluorocyclohexan-1-amine for ethylamine and triethylamine for DIPEA to lead to the title compound (23 mg, 13%) as white solid, hydrochloride salt. ESI-MS: 520.30 [M+H]⁺. ¹H NMR (400 MHz, DMSO-d₆) δ 9.42 (s, 1H), 8.20 – 8.14 (m, 2H), 7.90 (d, J = 8.5 Hz, 1H), 7.85 (s, 1H), 7.45 (dd, J = 8.5, 1.5 Hz, 1H), 7.42 – 7.36

30

(m, 2H), 7.12 – 7.06 (m, 2H), 4.02 (s, 3H), 4.00 – 3.93 (m, 1H), 2.07 – 1.83 (m, 6H), 1.70 – 1.57 (m, 2H).

Example 129

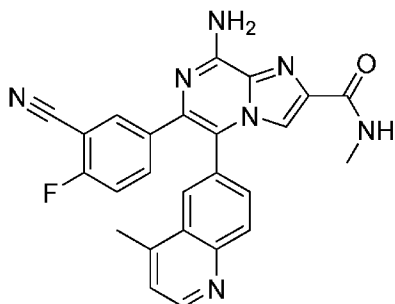
- 5 **8-amino-N-(1,1-difluoropropan-2-yl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide**



- The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **step a** and substituting Pd(amphos)Cl₂ for Sphos Pd G3 and performing this step for 2 h at 100 °C and then following **Procedure C**, substituting 1,1-difluoropropan-2-amine hydrochloride for ethylamine and triethylamine for DIPEA to lead to the title compound (55 mg, 29%) as white solid, hydrochloride salt. ESI-MS: 480.20 [M+H]⁺. 1H NMR (400 MHz, D₂O) δ 9.20 (s, 1H), 7.97 (s, 1H), 7.95 – 7.94 (m, 1H), 7.84 (dd, J = 8.6, 0.7 Hz, 1H), 7.58 (dd, J = 8.6, 1.5 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.03 – 6.96 (m, 2H), 5.91 (td, J = 55.5, 3.0 Hz, 2H), 4.49 – 4.37 (m, 1H), 3.97 (s, 3H), 1.28 (d, J = 7.1 Hz, 3H).

Example 130

- 20 **8-amino-6-(3-cyano-4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide**

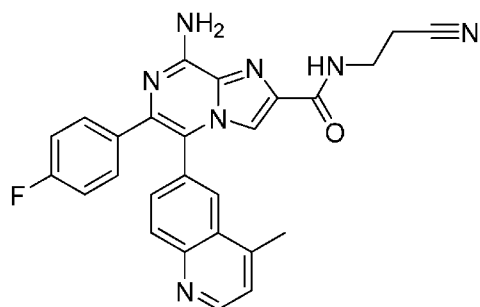


- The title compound was synthesized following the approach outlined in **Procedure A**, in **step a** substituting 3-cyano-4-fluorophenylboronic acid for 4-fluorophenylboronic acid and performing this step at 80 °C for 16 h, in **step c** substituting ACN for DME and performing this step with addition of Sc(OTf)₃ (0.1 eq) at 100 °C for 24 h then following **Procedure F**, performing **step a** at 110 °C for 8 h and in **step b** substituting (4-methylquinolin-6-yl)boronic acid for 4-(difluoromethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline and substituting Sphos Pd G3 for Pd(amphos)Cl₂ and performing this step at 130 °C for 1 h under microwave irradiation to lead to the title compound (36 mg, 40%) as yellow solid, hydrochloride salt. ESI-MS: 452.20 [M+H]⁺. 1H NMR (400 MHz, DMSO-d₆) δ 9.09 (d, J = 5.1 Hz, 1H), 8.48 (d, J = 1.8 Hz, 1H), 8.27 (d, J =

8.7 Hz, 1H), 8.15 (q, J = 4.6 Hz, 1H), 7.95 (ddd, J = 8.8, 7.5, 2.0 Hz, 2H), 7.86 (s, 1H), 7.81 (d, J = 5.1 Hz, 1H), 7.69 – 7.48 (m, 3H), 7.34 (t, J = 9.1 Hz, 1H), 2.80 – 2.75 (m, 6H).

Example 131

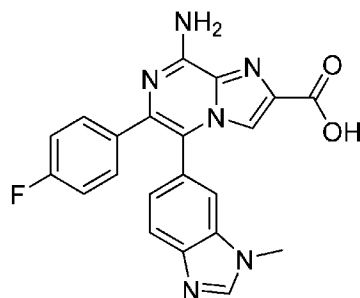
5 *8-amino-N-(2-cyanoethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide*



10 The title compound was synthesized following the approach outlined in **Procedure C**, substituting 3-aminopropionitrile for ethylamine and substituting HBTU for HATU to lead to the title compound (100 mg, 34%) as off-white solid, hydrochloride salt. ESI-MS: 466.2 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.14 (d, J = 5.2 Hz, 1H), 8.62 (t, J = 6.0 Hz, 1H), 8.53 (bs, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.05 (s, 1H), 7.97 (dd, J = 8.7, 1.8 Hz, 1H), 7.88 (d, J = 5.2 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.15 – 7.07 (m, 2H), 3.52 (q, J = 6.3 Hz, 2H), 2.84 – 2.74 (m, 5H).

Example 132

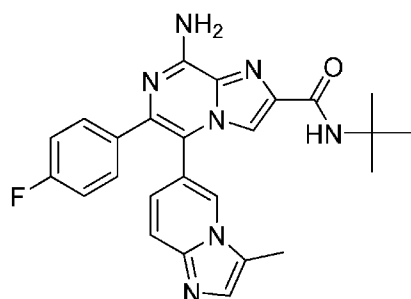
15 *8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid*



20 The title compound was synthesized following the approach outlined in **Procedure B**, substituting (1-methyl-1H-1,3-benzodiazol-6-yl)boronic acid for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and performing this step using Pd(PPh₃)₂Cl₂ instead Sphos Pd G3 and substituting Cs₂CO₃ for Na₂CO₃ at 100 °C for 3 h to lead to the title compound (196 mg, 75%) as off-white solid, hydrochloride salt. ESI-MS: 403.2 [M+H]⁺. ¹H NMR (400 MHz, D₂O) δ 9.28 (d, J = 0.7 Hz, 1H), 8.08 (s, 1H), 8.02 (dd, J = 1.5, 0.8 Hz, 1H), 7.91 (dd, J = 8.6, 0.8 Hz, 1H), 7.65 (dd, J = 8.6, 1.5 Hz, 1H), 7.48 – 7.31 (m, 2H), 7.06 (t, J = 8.8 Hz, 2H), 4.04 (s, 3H).

Example 133

30 *8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide*



The title compound was synthesized following the approach outlined in **Procedure B**, substituting 3-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-a]pyridine for (4-methylquinolin-6-yl)boronic acid in **Procedure B, step a** and performing this step using

- 5 Pd(PPh₃)₂Cl₂ instead Sphos Pd G3 and substituting Cs₂CO₃ for Na₂CO₃ at 85 °C for 5 h in **Procedure B, step a** and then following **Procedure C** substituting 2-methylpropan-2-amine for ethylamine and substituting Et₃N for DIPEA in this procedure to lead to the title compound (171 mg, 36%) as white solid, hydrochloride salt. ESI-MS: 458.3 [M+H]⁺. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.13 (s, 1H), 8.24 (s, 1H), 8.08 (d, J = 1.5 Hz, 1H), 7.99 (d, J = 9.2 Hz, 1H), 7.70 (dd, J = 9.2, 1.5 Hz, 1H), 7.53 – 7.40 (m, 3H), 7.13 (t, J = 8.9 Hz, 2H), 2.54 (s, 3H), 1.40 (s, 9H).
- 10

Part 2: Activity

A2A activity low adenosine

- 15 Examples 1 to 133 (see synthesis part above for the structures and names of these 133 compounds) were tested for their antagonistic activity at the rat A2A receptor (endogenously expressed in PC12 cells, which were used in the assay). The antagonistic activity was determined by measuring the effect of each compound on agonist-induced cAMP production using the assay based on time-resolved fluorescence resonance energy transfer (TR-FRET).

- 20 General reference as regards the cells and background can be made to Gao et al., “*Novel short-acting A2A adenosine receptor agonists for coronary vasodilation: inverse relationship between affinity and duration of action of A21A agonists*”, J. Pharmacol. Exp. Ther., 298, 209.

- More specifically, the assay to test each of examples 1 to 133 was performed as follows: The cells were suspended in HBSS buffer (Invitrogen) complemented with 20 mM HEPES (pH 7.4), with 0.1% BSA and 100 μM Rolipram (a phosphodiesterase-4 inhibitor to block the degradation of cAMP), then distributed in microplates at a density of 2.10³ cells/well (in a 384 well plate) in the presence of either (i) HBSS (basal control) with 0.2% DMSO, (ii) the test compound, i.e. each of examples 1 to 133, or (iii) the reference antagonist ZM 241385.
- 25

- Thereafter, the reference adenosine receptor agonist NECA (e.g. CAS 35920-39-9, Calbiochem) was added at a final concentration of 43 nM (concentration corresponding to EC₈₀). For basal control measurements, separate assay wells did not contain NECA.
- 30

Following 30 min incubation at room temperature, the cells were lysed and the detection mix was added (standard reagents used according to a standard protocol; LANCE™ cAMP 384 Kit, PerkinElmer).

- 35 After 60 min at room temperature, the fluorescence transfer was measured at λ_{ex}=340 nm and λ_{em}= 665 nm using a microplate reader according to a standard protocol (Envision, Perkin Elmer or Tecan Spark 20 M).

For test compounds % of normalized vehicle control was calculated for each data point and plotted against test compound concentration:

$$y = 100 - 100 * \frac{\text{Sample} - \text{Low control}}{\text{Vehicle control} - \text{Low control}}$$

- 5 Sample – mean fluorescence intensity of tested compound
Low control – mean fluorescence intensity of NECA 0.043 µM
Vehicle control – mean fluorescence intensity of DMSO 0.2%

10 EC₅₀, Hill slope and efficacy parameters were determined by fitting a variable-slope sigmoidal function.

For each of example 1 to 133, the apparent dissociation constant (K_B) was calculated using the modified Cheng Prusoff equation:

$$K_B = \frac{EC_{50}}{1 + \left(\frac{A}{EC_{50A}} \right)}$$

15 where A = concentration of reference agonist in the assay, and EC_{50A}= EC₅₀ value of the reference agonist.

The standard reference antagonist used was ZM 241385, which was tested in each experiment at several concentrations to generate a concentration-response curve from which its EC₅₀ value was calculated.

20 Each of examples 1 to 133 exhibited A_{2A} receptor antagonist activity (K_B < 1 µM). Thus, examples 1 to 133 as described herein are potent A_{2A} receptor antagonists.

A_{2A} activity high adenosine

25 Examples 1 to 133 (see synthesis part above for the structures and names of these 133 compounds) were tested for their antagonistic activity at the human A_{2A} receptor (endogenously expressed in PC12 cells, which were used in the assay) at high concentrations of adenosine. The antagonistic activity was determined by measuring the effect of each compound on agonist-induced cAMP production using the assay based on time-resolved fluorescence resonance energy transfer (TR-FRET).

30 General reference as regards the cells and background can be made to Gao et al., “*Novel short-acting A_{2A} adenosine receptor agonists for coronary vasodilation: inverse relationship between affinity and duration of action of A_{21A} agonists*”, J. Pharmacol. Exp. Ther., 298, 209.

35 More specifically, the assay to test each of examples 1 to 133 was performed as follows: The cells were suspended in HBSS buffer (Invitrogen) complemented with 20 mM HEPES (pH 7.4), with 0.1% BSA, 100 µM Rolipram (a phosphodiesterase-4 inhibitor to block the degradation of cAMP) and 10 µM EHNA - adenosine deaminase inhibitor, then distributed in microplates at a density of 2.0x10³ cells/well (in a 384 well plate) in the presence of either (i) HBSS (basal control) with 0.2% DMSO, (ii) the test compound, i.e. each of examples 1 to 133, or (iii) the reference antagonist ZM 241385.

40 After 2h incubation at room temperature, the nonselective adenosine receptor agonist – adenosine (e.g. CAS 58-61-7, Tocris) was added at a final concentration of 100 µM (corresponding

to high adenosine concentration in tumor). For basal control measurements, separate assay wells did not contain adenosine.

Following 30 min incubation at room temperature, the cells were lysed and the detection mix was added (standard reagents used according to a standard protocol; LANCE™ cAMP 384 Kit, PerkinElmer).

After 60 min at room temperature, the fluorescence transfer was measured at $\lambda_{ex}=340$ nm and $\lambda_{em}=665$ nm using a microplate reader according to a standard protocol (Tecan 20M Spark).

For test compounds % of normalized vehicle control was calculated for each data point and plotted against test compound concentration:

$$y = 100 - 100 * \frac{\text{Sample} - \text{Low control}}{\text{Vehicle control} - \text{Low control}}$$

Sample – mean fluorescence intensity of tested compound

Low control – mean fluorescence intensity of adenosine 100 μ M

Vehicle control – mean fluorescence intensity of DMSO 0.2%

EC50, Hill slope and efficacy parameters were determined by fitting a variable-slope sigmoidal function.

For each of example 1 to 133, the apparent dissociation constant (KB) was calculated using the modified Cheng Prusoff equation:

$$KB = \frac{EC50}{1 + \left(\frac{A}{EC50A}\right)}$$

where A = concentration of reference agonist in the assay, and EC50A= EC50 value of the reference agonist.

The standard reference antagonist used was ZM 241385, which was tested in each experiment at several concentrations to generate a concentration-response curve from which its EC50 value was calculated.

A2B activity low adenosine

Examples 1 to 133 (see synthesis part above for the structures and names of these 133 compounds) were tested for their antagonistic activity at the human A2B receptor (overexpressed in cAMPZen-A2BR-HEK293 cells, which were used in the assay). The antagonistic activity was determined by measuring the effect of each compound on agonist-induced cAMP production using the assay based on time-resolved fluorescence resonance energy transfer (TR-FRET).

General reference as regards the cells and background can be made to Cooper et al., “*An endogenous A2B adenosine receptor coupled to cyclic AMP generation in human embryonic kidney (HEK-293) cells*”, Brit. J. Pharmacol., 122: 546.

More specifically, the assay to test each of examples 1 to 133 was performed as follows: The cells were suspended in HBSS buffer (Invitrogen) complemented with 20 mM HEPES (pH 7.4), with 0.1% BSA and adenosine deaminase [0.02 U/ml], then distributed in microplates at a density of 2.5×10^3 cells/well (in a 384 well plate) in the presence of either (i) HBSS (basal control)

with 0.2% DMSO, (ii) the test compound, i.e. each of examples 1 to 133, or (iii) the reference antagonist XAC.

Thereafter, the reference adenosine receptor agonist NECA (e.g. CAS 35920-39-9, Calbiochem) was added at a final concentration of 100 nM (concentration corresponding to EC₈₀). For basal control measurements, separate assay wells did not contain NECA.

Following 30 min incubation at room temperature, the cells were lysed and the detection mix was added (standard reagents used according to a standard protocol; LANCE™ cAMP 384 Kit, PerkinElmer).

After 60 min at room temperature, the fluorescence transfer was measured at λ_{ex}=340 nm and λ_{em}= 665 nm using a microplate reader according to a standard protocol (Tecan Spark 20 M).

For test compounds % of normalized vehicle control was calculated for each data point and plotted against test compound concentration:

$$y = 100 - 100 * \frac{\text{Sample} - \text{Low control}}{\text{Vehicle control} - \text{Low control}}$$

Sample – mean fluorescence intensity of tested compound

Low control – mean fluorescence intensity of NECA 0.1 μM

Vehicle control – mean fluorescence intensity of DMSO 0.2%

EC₅₀, Hill slope and efficacy parameters were determined by fitting a variable-slope sigmoidal function.

For each of example 1 to 133, the apparent dissociation constant (KB) was calculated using the modified Cheng Prusoff equation:

$$KB = \frac{EC_{50}}{1 + \left(\frac{A}{EC_{50}A} \right)}$$

where A = concentration of reference agonist in the assay, and EC₅₀A= EC₅₀ value of the reference agonist.

The standard reference antagonist used was XAC, which was tested in each experiment at several concentrations to generate a concentration-response curve from which its EC₅₀ value was calculated.

A2B activity high adenosine

Examples 1 to 133 (see synthesis part above for the structures and names of these 133 compounds) were tested for their antagonistic activity at the human A2B receptor (overexpressed in cAMPZen-A2BR-HEK293 cells, which were used in the assay) at high concentrations of adenosine. The antagonistic activity was determined by measuring the effect of each compound on agonist-induced cAMP production using the assay based on time-resolved fluorescence resonance energy transfer (TR-FRET).

General reference as regards the cells and background can be made to Cooper et al., “An endogenous A2B adenosine receptor coupled to cyclic AMP generation in human embryonic kidney (HEK-293) cells”, Brit. J. Pharmacol., 122: 546.

More specifically, the assay to test each of examples 1 to 133 was performed as follows: The cells were suspended in HBSS buffer (Invitrogen) complemented with 20 mM HEPES (pH 7.4), with 0.1% BSA and EHNA - adenosine deaminase inhibitor [10 μ M], then distributed in microplates at a density of 2.5×10^3 cells/well (in a 384 well plate) in the presence of either (i) HBSS (basal control) with 0.2% DMSO, (ii) the test compound, i.e. each of examples 1 to 133, or (iii) the reference antagonist XAC.

After 2h incubation at room temperature, the nonselective adenosine receptor agonist – adenosine (e.g. CAS 58-61-7, Tocris) was added at a final concentration of 100 μ M (corresponding to high adenosine concentration in tumor). For basal control measurements, separate assay wells did not contain adenosine.

Following 30 min incubation at room temperature, the cells were lysed and the detection mix was added (standard reagents used according to a standard protocol; LANCE™ cAMP 384 Kit, PerkinElmer).

After 60 min at room temperature, the fluorescence transfer was measured at $\lambda_{ex}=340$ nm and $\lambda_{em}=665$ nm using a microplate reader according to a standard protocol (Tecan Spark 20M).

For test compounds % of normalized vehicle control was calculated for each data point and plotted against test compound concentration:

$$y = 100 - 100 * \frac{\text{Sample} - \text{Low control}}{\text{Vehicle control} - \text{Low control}}$$

Sample – mean fluorescence intensity of tested compound

Low control – mean fluorescence intensity of adenosine 100 μ M

Vehicle control – mean fluorescence intensity of DMSO 0.2%

EC₅₀, Hill slope and efficacy parameters were determined by fitting a variable-slope sigmoidal function.

For each of example 1 to 133, the apparent dissociation constant (K_B) was calculated using the modified Cheng Prusoff equation:

$$K_B = \frac{EC_{50}}{1 + \left(\frac{A}{EC_{50}A} \right)}$$

where A = concentration of reference agonist in the assay, and EC₅₀A= EC₅₀ value of the reference agonist.

The standard reference antagonist used was XAC, which was tested in each experiment at several concentrations to generate a concentration-response curve from which its EC₅₀ value was calculated.

Compounds of the present disclosure, as exemplified in the Examples, showed EC₅₀ values in the following ranges: + = EC₅₀ > 1 μ M; ++ = 0.1 μ M < EC₅₀ < 1 μ M; +++ = EC₅₀ < 0.1 μ M according to Table 2.

Table 2

Example	A2A Low Ado EC50 [uM]	A2A high Ado EC50 [uM]	A2B Low Ado EC50 [uM]	A2B high Ado EC50 [uM]
1	+++	+++	+++	+
2	+++	+++	+++	+
3	+++	++	++	+
4	+++	+++	+++	+
5	+++	+++	+++	++
6	+++	+++	+++	+
7	+++	+++	+++	+
8	+++	+++	+++	+
9	+++	+++	+++	+
10	+++	+++	+++	+
11	+++	++	+++	+
12	+++	+++	++	+
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81	+++	++	+++	+
82	+++	+++	+++	+

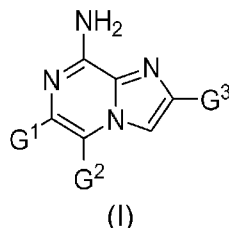
83	+++	+++	+++	+
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127	+++	+++	+++	++
128	+++	+++	+++	++
129	+++	+++	+++	+
130	+++	++	++	+
131	+++	+++	+++	++
132	+++	+++	+++	+
133	+++	+++	+++	++

Compounds 123 and 125 show particularly high activities in all four tests.

In particular, the present invention relates to the following further items.

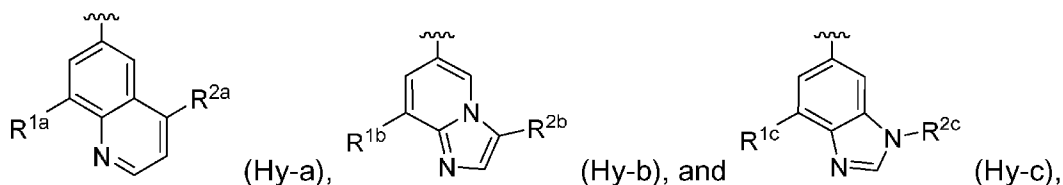
1. A compound of formula (I)



or a salt, stereoisomer, tautomer, isotopologue, or N-oxide thereof,
wherein

G^1 is selected from the group consisting of phenyl and a 5- to 6-membered fully unsaturated heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH_3 , F and CN.

G^2 is selected from the group consisting of



G^3 is selected from the group consisting of of

- (i) C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R^3 ;
- (ii) $C(=O)R^5$, $C(=O)OR^6$, $C(=O)SR^6$, $C(=O)N(R^{6a})(R^{6b})$, OR^6 , $S(=O)_nR^6$, $S(=O)_nN(R^{6a})(R^{6b})$, $S(=O)_mOR^6$, $N(R^{6a})(R^{6b})$, $N(R^6)C(=O)R^5$, $N(R^6)C(=O)OR^6$, $N(R^6)C(=O)N(R^{6a})(R^{6b})$, $N(R^6)S(=O)_n(R^6)$, $N(R^6)S(=O)_mN(R^{6a})(R^{6b})$, and $N(R^6)S(=O)_mOR^6$;

R^{1a} is selected from the group consisting of H and Cl;

R^{1b} is selected from the group consisting of H and Cl;

R^{1c} is selected from the group consisting of H and Cl;

- R^{2a} is selected from the group consisting of Cl and C_1 - C_3 -alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;
- R^{2b} is selected from the group consisting of Cl and C_1 - C_3 -alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;
- 5 R^{2c} is C_1 - C_3 -alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;
- R^3 is selected from the group consisting of
- 10 (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^4 ;
- 15 (ii) $C(=O)R^7$, $C(=O)OR^8$, $C(=O)SR^8$, $C(=O)N(R^{8a})(R^{8b})$, OR^8 , $S(=O)_nR^8$, $S(=O)_nN(R^{8a})(R^{8b})$, $S(=O)_mOR^8$, $N(R^{8a})(R^{8b})$, $N(R^8)C(=O)R^7$, $N(R^8)C(=O)OR^8$, $N(R^8)C(=O)N(R^{8a})(R^{8b})$, $N(R^8)S(=O)_n(R^8)$, $N(R^8)S(=O)_mN(R^{8a})(R^{8b})$, and $N(R^8)S(=O)_mOR^8$;
- 20 R^4 is selected from the group consisting of
- 25 (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^9 ;
- 30 (ii) $C(=O)R^{10}$, $C(=O)OR^{11}$, $C(=O)SR^{11}$, $C(=O)N(R^{11a})(R^{11b})$, OR^{11} , $S(=O)_nR^{11}$, $S(=O)_nN(R^{11a})(R^{11b})$, $S(=O)_mOR^{11}$, $N(R^{11a})(R^{11b})$, $N(R^{11})C(=O)R^{10}$, $N(R^{11})C(=O)OR^{11}$, $N(R^{11})C(=O)N(R^{11a})(R^{11b})$, $N(R^{11})S(=O)_n(R^{11})$, $N(R^{11})S(=O)_mN(R^{11a})(R^{11b})$, and $N(R^{11})S(=O)_mOR^{11}$;
- 35 R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;
- 40

R^7 , R^8 , R^{8a} , R^{8b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{13} ;

R^9 is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, $C(=O)R^{14}$, $C(=O)OR^{15}$, $C(=O)SR^{15}$, $C(=O)N(R^{15a})(R^{15b})$, OR^{15} , $S(=O)_nR^{15}$, $S(=O)_nN(R^{15a})(R^{15b})$, $S(=O)_mOR^{15}$, $N(R^{15a})(R^{15b})$, $N(R^{15})C(=O)R^{14}$, $N(R^{15})C(=O)OR^{15}$, $N(R^{15})C(=O)N(R^{15a})(R^{15b})$, $N(R^{15})S(=O)_n(R^{15})$, $N(R^{15})S(=O)_mN(R^{15a})(R^{15b})$, and $N(R^{15})S(=O)_mOR^{15}$;

R^{10} , R^{11} , R^{11a} , R^{11b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{17} ;

R^{12} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ;
- (ii) $C(=O)R^{19}$, $C(=O)OR^{20}$, $C(=O)SR^{20}$, $C(=O)N(R^{20a})(R^{20b})$, OR^{20} , $S(=O)_nR^{20}$, $S(=O)_nN(R^{20a})(R^{20b})$, $S(=O)_mOR^{20}$, $N(R^{20a})(R^{20b})$, $N(R^{20})C(=O)R^{19}$, $N(R^{20})C(=O)OR^{20}$, $N(R^{20})C(=O)N(R^{20a})(R^{20b})$, $N(R^{20})S(=O)_n(R^{20})$, $N(R^{20})S(=O)_mN(R^{20a})(R^{20b})$, and $N(R^{20})S(=O)_mOR^{20}$;

and/or two R^{12} present on one carbon atom together form $=O$;

R^{13} is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;
- (ii) C(=O)R²², C(=O)OR²³, C(=O)SR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, S(=O)_nR²³, S(=O)_nN(R^{23a})(R^{23b}), S(=O)_mOR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b}), N(R²³)S(=O)_n(R²³), N(R²³)S(=O)_mN(R^{23a})(R^{23b}), and N(R²³)S(=O)_mOR²³;
- R¹⁴, R¹⁵, R^{15a}, R^{15b} are independently selected from the group consisting of
- (i) H, C₁-C₆-alkyl, C₂-C₆-alkenyl, and C₂-C₆-alkynyl, wherein each substitutable carbon atom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R¹⁶;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R³²;
- R¹⁶ is selected from the group consisting of
- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, N(R^{33a})(R^{33b}), C(=O)NR^{33a}R^{33b}, S(=O)_nNR^{33a}R^{33b}, OR³³ and S(=O)_nR³³;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R³²;
- R¹⁷ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);
- R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;
- (ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)SR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, S(=O)_nR²⁶, S(=O)_nN(R^{26a})(R^{26b}), S(=O)_mOR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b}), N(R²⁶)S(=O)_n(R²⁶), N(R²⁶)S(=O)_mN(R^{26a})(R^{26b}), and N(R²⁶)S(=O)_mOR²⁶;
- R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;
- R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);
- R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;
- R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or

S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

R²⁸ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³¹;

R²⁹, R³⁰, R³¹ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

R³² is selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, C₂-C₄-haloalkynyl, C(=O)R³⁴, C(=O)OR³³, C(=O)SR³³, C(=O)N(R^{33a})(R^{33b}), OR³³, S(=O)_nR³³, S(=O)_nN(R^{33a})(R^{33b}), S(=O)_mOR³³, N(R^{33a})(R^{33b}), N(R³³)C(=O)R³⁴, N(R³³)C(=O)OR³³, N(R³³)C(=O)N(R^{33a})(R^{33b}), N(R³³)S(=O)_n(R³³), N(R³³)S(=O)_mN(R^{33a})(R^{33b}), and N(R³³)S(=O)_mOR³³;

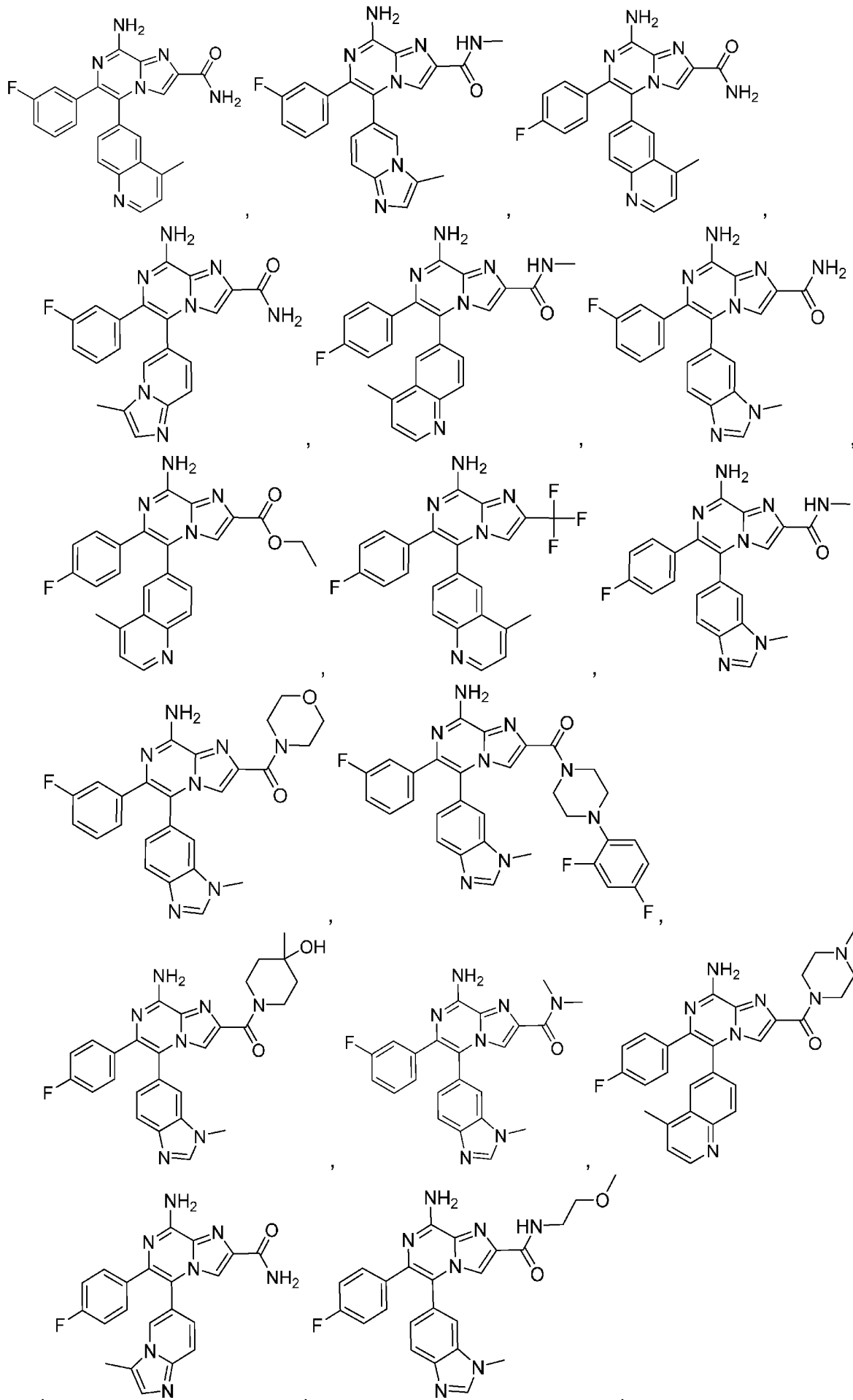
R³³, R^{33a}, R^{33b}, R³⁴ are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

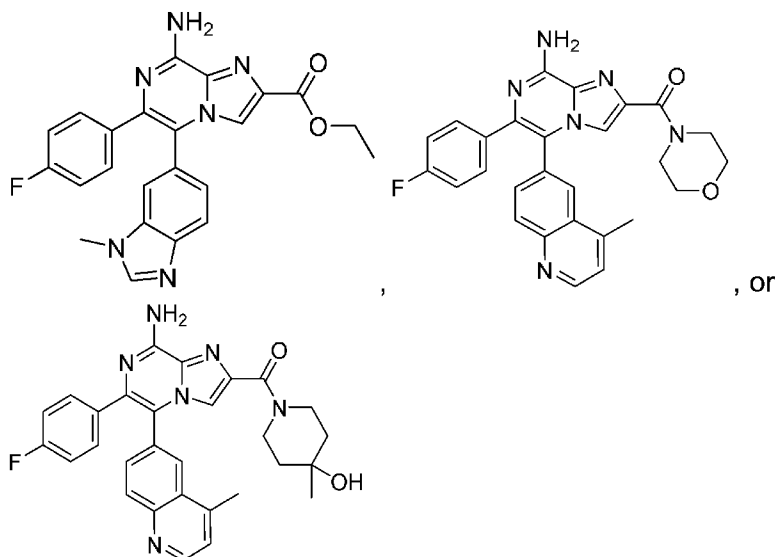
and wherein

n is 0, 1 or 2; and

m is 1 or 2;

and wherein the compound is not:





2. The compound according to item 1, wherein G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, furan-2-yl, furan-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, and pyrazol-5-yl, wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN, and wherein all other substituents have the meaning as defined in item 1.
3. The compound according to item 1, wherein G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-5-yl, furan-2-yl, and pyrazol-3-yl, wherein one or two of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN, and wherein all other substituents have the meaning as defined in item 1.
4. The compound according to any one of items 1, 2, or 3, wherein R^{1a} is selected from the group consisting of H and Cl; R^{1b} is selected from the group consisting of H and Cl; R^{1c} is selected from the group consisting of H and Cl; R^{2a} is CH₃; R^{2b} is CH₃; R^{2c} is CH₃; and wherein all other substituents have the meaning as defined in item 1.
5. The compound according to any one of items 1, 2, 3, or 4, wherein G³ is selected from the group consisting of
 - (i) C₁-C₆-alkyl, a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R³;
 - (ii) C(=O)R⁵, C(=O)OR⁶, and C(=O)N(R^{6a})(R^{6b});

wherein R³ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁴;
- (ii) C(=O)R⁷, C(=O)OR⁸, C(=O)N(R^{8a})(R^{8b}), OR⁸, N(R^{8a})(R^{8b}), N(R⁸)C(=O)R⁷, N(R⁸)C(=O)OR⁸, and N(R⁸)C(=O)N(R^{8a})(R^{8b});

wherein R⁴ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁹;
- (ii) C(=O)R¹⁰, C(=O)OR¹¹, C(=O)N(R^{11a})(R^{11b}), OR¹¹, N(R^{11a})(R^{11b}), N(R¹¹)C(=O)R¹⁰, N(R¹¹)C(=O)OR¹¹, N(R¹¹)C(=O)N(R^{11a})(R^{11b});

wherein R⁵, R⁶, R^{6a}, R^{6b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R⁷, R⁸, R^{8a}, R^{8b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹³;

wherein R⁹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁰, R¹¹, R^{11a}, R^{11b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁷;

wherein R¹² is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;

(ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹³ is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;

(ii) C(=O)R²², C(=O)OR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b});

wherein R¹⁷ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;

- (ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b});

wherein R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R^{25} , R^{26} , R^{26a} , R^{26b} are independently selected from the group consisting of H, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, and C_2 - C_4 -haloalkynyl;

wherein R^{27} is selected from the group consisting of halogen, CN, NO_2 , OH, $O(C_1-C_4$ -alkyl), NH_2 , $NH(C_1-C_4$ -alkyl), and $N(C_1-C_4$ -alkyl)(C_1-C_4 -alkyl), C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{30} ;

wherein R^{28} is selected from the group consisting of halogen, CN, NO_2 , OH, $O(C_1-C_4$ -alkyl), NH_2 , $NH(C_1-C_4$ -alkyl), and $N(C_1-C_4$ -alkyl)(C_1-C_4 -alkyl), C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{31} ;

wherein R^{29} , R^{30} , R^{31} are independently selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1-C_4$ -alkyl), NH_2 , $NH(C_1-C_4$ -alkyl), and $N(C_1-C_4$ -alkyl)(C_1-C_4 -alkyl), and

wherein all other substituents have the meaning as defined in item 1.

6. The compound according to any one of items 1, 2, 3, or 4, wherein G^3 is selected from the group consisting of $C(=O)R^5$, $C(=O)OR^6$, and $C(=O)N(R^{6a})(R^{6b})$;

wherein R^5 , R^6 , R^{6a} , R^{6b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{12} ;

wherein R^{12} is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;

(ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹⁸ is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;

(ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b});

wherein R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R^{25} , R^{26} , R^{26a} , R^{26b} are independently selected from the group consisting of H, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, and C_2 - C_4 -haloalkynyl;

wherein R^{27} is selected from the group consisting of halogen, CN, NO_2 , OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl), C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{30} ;

wherein R^{29} , R^{30} are independently selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl); and

wherein all other substituents have the meaning as defined in item 1.

7. The compound according to item 1, wherein said compound is selected from the group consisting of 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid; 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-{2,6-diazaspiro[3.4]octane-2-carbonyl}-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(pyridin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(4-fluoropyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[3-(difluoromethoxy)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(morpholin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[2-(methylamino)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1,1-dioxo-1 λ^6 -thiolan-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2-oxopyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-hydroxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(4,4-difluoropiperidine-1-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-

a]pyrazine-2-carboxamide; 8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-[4-(difluoromethyl)quinolin-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(²H₃)methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(3-ethylpyrrolidin-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(4-aminobutyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-[4-(2,4-difluorophenyl)piperazine-1-carbonyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 6-(4-fluorophenyl)-2-[4-(2-methoxyethyl)piperazine-1-carbonyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(piperidin-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-2-(piperazine-1-carbonyl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N,N-diethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(8-chloroquinolin-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-methylpyrrolidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[3-(dimethylamino)butyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-(dimethylamino)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(prop-2-yn-1-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)-5-(4-

- 5 methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylpiperidin-4-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[[6-(2-hydroxypropan-2-yl)pyridin-2-yl]methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(3,3,3-trifluoropropyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-ethylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-(dimethylamino)ethyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(3-hydroxybutan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(4-methylmorpholin-2-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-3-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[1-(methoxymethyl)cyclopropyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methyl-2-oxopyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-{2-[(oxolan-2-yl)methoxy]ethyl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(1,1,1-trifluoro-3-hydroxypropan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]-3-methylpyrrolidin-3-ol; 8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine; 8-amino-6-(4-fluorophenyl)-N-(1-methylpyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-hydroxycyclopentyl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-dimethylpropyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methoxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2-fluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-[(1-hydroxycyclopropyl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-

- 1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[1-(1-hydroxycyclopropyl)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{3-chloroimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(3-hydroxypropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[1-(dimethylamino)-2-methylpropan-2-yl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-methylazetidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-({1-[(2,4-difluorophenyl)methyl]piperidin-4-yl)methyl}-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[2-methyl-1-(propan-2-yloxy)propan-2-yl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-2-methylphenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-[1-(2,2-difluoroethyl)-1H-1,3-benzodiazol-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 6-(4-fluorophenyl)-2-[(methylamino)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[2-(pyrrolidin-1-yl)ethyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-{3-methylimidazo[1,2-a]pyridin-6-

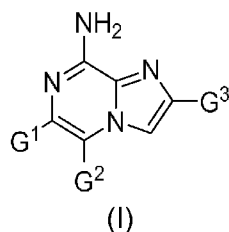
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- yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-[1-(propan-2-yl)-1H-1,3-benzodiazol-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyanophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxylic acid; 8-amino-6-(3-cyanophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(2-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; and 8-amino-6-(3-cyanophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide.
8. A pharmaceutical composition comprising a pharmaceutically effective amount of the compound according to any one of items 1 to 7 and optionally a pharmaceutically acceptable carrier, diluent or excipient.
9. A compound according to any one of items 1 to 7 and a pharmaceutical composition according to item 8 for use in medicine.
10. A compound for use according to item 9 or a pharmaceutical composition for use according to item 8 or 9, wherein said compound or pharmaceutical composition is for use in the treatment of a disease selected from the group consisting of cancer, Parkinson's disease, Huntington's disease, Alzheimer's disease, psychosis, stroke, extra pyramidal syndrome (in particular dystonia, akathisia, pseudoparkinsonism and tardive dyskinesia), attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), amyotrophic lateral sclerosis, cirrhosis, fibrosis, fatty liver, addictive behavior, dermal fibrosis (in particular dermal fibrosis in scleroderma), sleep disorders, AIDS, autoimmune diseases, infections, atherosclerosis and ischemia-reperfusion injury.
11. A compound for use according to item 9 or a pharmaceutical composition for use according to item 8 or 9, wherein said compound or pharmaceutical composition is for use in the treatment of cancer, and wherein at least one further anti-neoplastic agent is preferably coadministered with said compound and/or comprised in said pharmaceutical composition.
12. A compound for use according to item 11 or a pharmaceutical composition for use according to item 11, wherein said anti-neoplastic agent is selected from the group consisting of a chemotherapeutic agent, a topoisomerase II inhibitor, an antimetabolite, a topoisomerase I inhibitor, a hormone, a hormonal analogue, a signal transduction pathway inhibitor, a non-receptor tyrosine kinase inhibitor, an angiogenesis inhibitor, a proapoptotic agent, a cell cycle signaling inhibitor, a proteasome inhibitor, an inhibitors of cancer metabolism, and an immunotherapeutic agent, wherein said chemotherapeutic agent is preferably selected from the group consisting of an anti-microtubule

agent, an platinum coordination complex and an antibiotic agent; and wherein said immunotherapeutic agent is preferably selected from the group consisting of a STING pathway modulating compound, a TLR agonist and a checkpoint inhibitor.

- 5 13. A compound for use according to item 12 or a pharmaceutical composition for use according to item 12, wherein said checkpoint inhibitor targets PD-1, PD-L1, CTLA-4, IDO, KIR, TIM-3, LAG-3, CD39, CD73, ICOS, OX40, Tim-3, Vista, BTLA, TDO, or TIGIT.
- 10 14. A compound for use according to item 12 or 13 or a pharmaceutical composition for use according to item 12 or 13, wherein said checkpoint inhibitor is an antibody, a small molecule inhibitor or an antisense oligonucleotide selected from the group consisting of an anti-PD-1, anti-PD-L1, anti-CTLA-4, anti-IDO, anti-KIR, anti-TIM-3, anti-LAG-3, anti-CD39, anti-CD73, anti-ICOS, anti-OX40, anti-Tim-3, anti-Vista, anti-BTLA, anti-TDO, and anti-TIGIT-agent.
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Claims

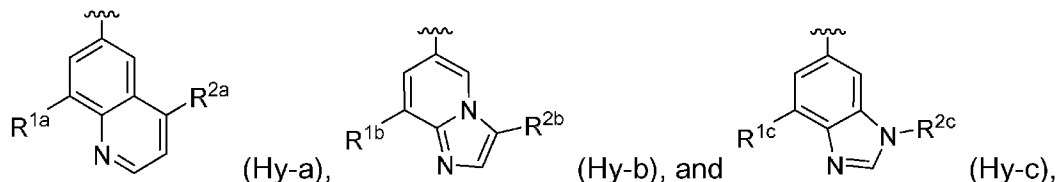
1. A compound of formula (I)



or a salt, stereoisomer, tautomer, isotopologue, or N-oxide thereof,
wherein

G^1 is selected from the group consisting of phenyl and a 5- to 6-membered fully unsaturated heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein one or more of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH_3 , F and CN.

G^2 is selected from the group consisting of



G^3 is selected from the group consisting of

- (i) C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R^3 ;
- (ii) $C(=O)R^5$, $C(=O)OR^6$, $C(=O)SR^6$, $C(=O)N(R^{6a})(R^{6b})$, OR^6 , $S(=O)_nR^6$, $S(=O)_nN(R^{6a})(R^{6b})$, $S(=O)_mOR^6$, $N(R^{6a})(R^{6b})$, $N(R^6)C(=O)R^5$, $N(R^6)C(=O)OR^6$, $N(R^6)C(=O)N(R^{6a})(R^{6b})$, $N(R^6)S(=O)_n(R^6)$, $N(R^6)S(=O)_mN(R^{6a})(R^{6b})$, and $N(R^6)S(=O)_mOR^6$;

R^{1a} is selected from the group consisting of H and Cl;

R^{1b} is selected from the group consisting of H and Cl;

R^{1c} is selected from the group consisting of H and Cl;

R^{2a} is selected from the group consisting of Cl and C₁-C₃-alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R^{2b} is selected from the group consisting of Cl and C₁-C₃-alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R^{2c} is C₁-C₃-alkyl, wherein each substitutable carbon atom is unsubstituted or substituted with one or more F;

R³ is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁴;

(ii) C(=O)R⁷, C(=O)OR⁸, C(=O)SR⁸, C(=O)N(R^{8a})(R^{8b}), OR⁸, S(=O)_nR⁸, S(=O)_nN(R^{8a})(R^{8b}), S(=O)_mOR⁸, N(R^{8a})(R^{8b}), N(R⁸)C(=O)R⁷, N(R⁸)C(=O)OR⁸, N(R⁸)C(=O)N(R^{8a})(R^{8b}), N(R⁸)S(=O)_n(R⁸), N(R⁸)S(=O)_mN(R^{8a})(R^{8b}), and N(R⁸)S(=O)_mOR⁸;

R⁴ is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁹;

(ii) C(=O)R¹⁰, C(=O)OR¹¹, C(=O)SR¹¹, C(=O)N(R^{11a})(R^{11b}), OR¹¹, S(=O)_nR¹¹, S(=O)_nN(R^{11a})(R^{11b}), S(=O)_mOR¹¹, N(R^{11a})(R^{11b}), N(R¹¹)C(=O)R¹⁰, N(R¹¹)C(=O)OR¹¹, N(R¹¹)C(=O)N(R^{11a})(R^{11b}), N(R¹¹)S(=O)_n(R¹¹), N(R¹¹)S(=O)_mN(R^{11a})(R^{11b}), and N(R¹¹)S(=O)_mOR¹¹;

R⁵, R⁶, R^{6a}, R^{6b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is

unsubstituted or substituted with one or more, same or different substituents R^{12} ;

R^7 , R^8 , R^{8a} , R^{8b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{13} ;

R^9 is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, $C(=O)R^{14}$, $C(=O)OR^{15}$, $C(=O)SR^{15}$, $C(=O)N(R^{15a})(R^{15b})$, OR^{15} , $S(=O)_nR^{15}$, $S(=O)_nN(R^{15a})(R^{15b})$, $S(=O)_mOR^{15}$, $N(R^{15a})(R^{15b})$, $N(R^{15})C(=O)R^{14}$, $N(R^{15})C(=O)OR^{15}$, $N(R^{15})C(=O)N(R^{15a})(R^{15b})$, $N(R^{15})S(=O)_n(R^{15})$, $N(R^{15})S(=O)_mN(R^{15a})(R^{15b})$, and $N(R^{15})S(=O)_mOR^{15}$;

R^{10} , R^{11} , R^{11a} , R^{11b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{17} ;

R^{12} is selected from the group consisting of

- (i) halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{18} ;
- (ii) $C(=O)R^{19}$, $C(=O)OR^{20}$, $C(=O)SR^{20}$, $C(=O)N(R^{20a})(R^{20b})$, OR^{20} , $S(=O)_nR^{20}$, $S(=O)_nN(R^{20a})(R^{20b})$, $S(=O)_mOR^{20}$, $N(R^{20a})(R^{20b})$, $N(R^{20})C(=O)R^{19}$, $N(R^{20})C(=O)OR^{20}$, $N(R^{20})C(=O)N(R^{20a})(R^{20b})$, $N(R^{20})S(=O)_n(R^{20})$, $N(R^{20})S(=O)_mN(R^{20a})(R^{20b})$, and $N(R^{20})S(=O)_mOR^{20}$;

and/or two R^{12} present on one carbon atom together form $=O$;

R^{13} is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;
- (ii) C(=O)R²², C(=O)OR²³, C(=O)SR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, S(=O)_nR²³, S(=O)_nN(R^{23a})(R^{23b}), S(=O)_mOR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b}), N(R²³)S(=O)_n(R²³), N(R²³)S(=O)_mN(R^{23a})(R^{23b}), and N(R²³)S(=O)_mOR²³;
- R¹⁴, R¹⁵, R^{15a}, R^{15b} are independently selected from the group consisting of
- (i) H, C₁-C₆-alkyl, C₂-C₆-alkenyl, and C₂-C₆-alkynyl, wherein each substitutable carbon atom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R¹⁶;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R³²;
- R¹⁶ is selected from the group consisting of
- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, N(R^{33a})(R^{33b}), C(=O)NR^{33a}R^{33b}, S(=O)_nNR^{33a}R^{33b}, OR³³ and S(=O)_nR³³;
- (ii) a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned cyclic or bicyclic moieties is independently unsubstituted or substituted with one or more, same or different substituents R³²;
- R¹⁷ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);
- R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;
- (ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)SR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, S(=O)_nR²⁶, S(=O)_nN(R^{26a})(R^{26b}), S(=O)_mOR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b}), N(R²⁶)S(=O)_n(R²⁶), N(R²⁶)S(=O)_mN(R^{26a})(R^{26b}), and N(R²⁶)S(=O)_mOR²⁶;
- R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;
- R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);
- R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;
- R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or

S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

R²⁸ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³¹;

R²⁹, R³⁰, R³¹ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

R³² is selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, C₂-C₄-haloalkynyl, C(=O)R³⁴, C(=O)OR³³, C(=O)SR³³, C(=O)N(R^{33a})(R^{33b}), OR³³, S(=O)_nR³³, S(=O)_nN(R^{33a})(R^{33b}), S(=O)_mOR³³, N(R^{33a})(R^{33b}), N(R³³)C(=O)R³⁴, N(R³³)C(=O)OR³³, N(R³³)C(=O)N(R^{33a})(R^{33b}), N(R³³)S(=O)_n(R³³), N(R³³)S(=O)_mN(R^{33a})(R^{33b}), and N(R³³)S(=O)_mOR³³;

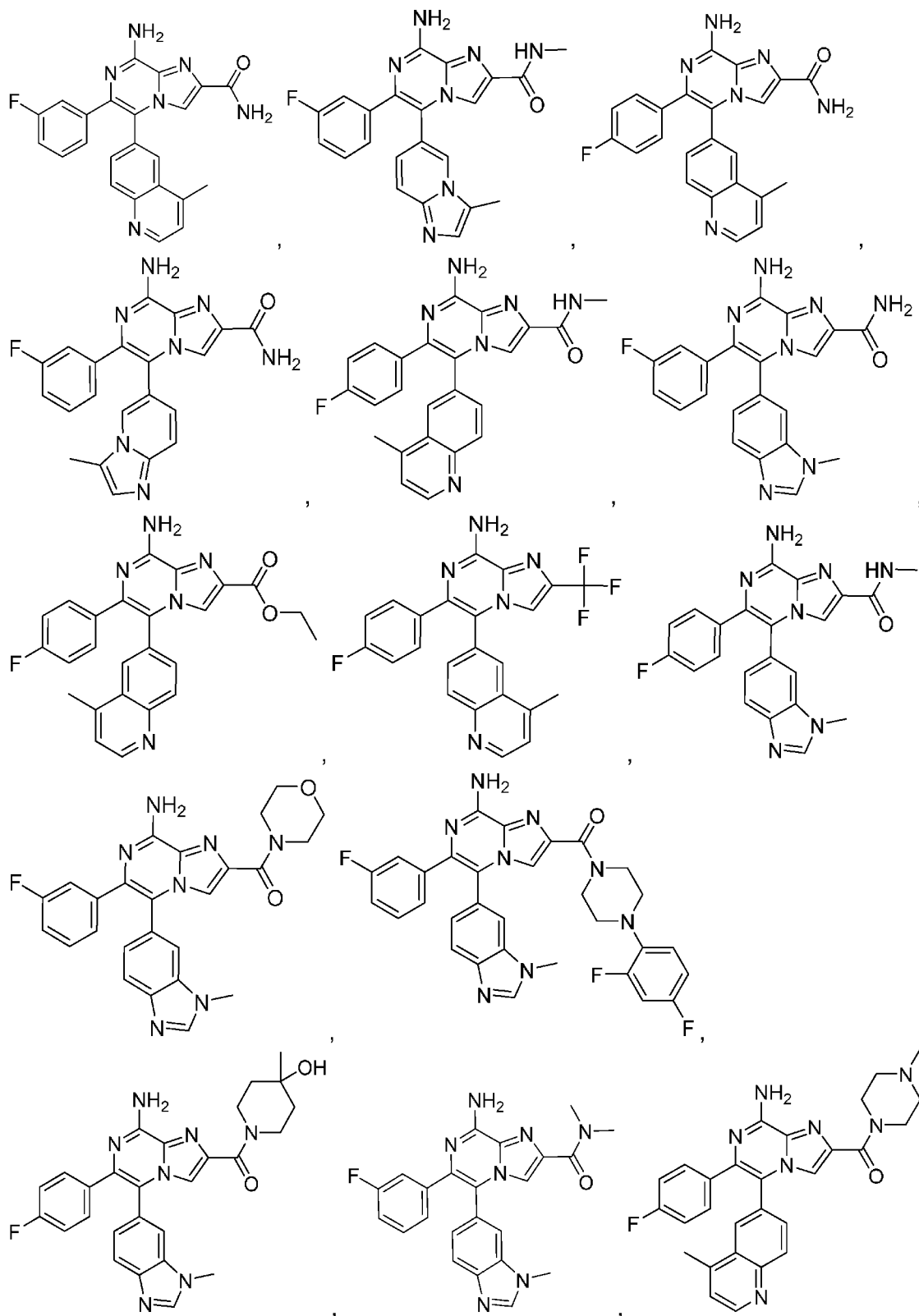
R³³, R^{33a}, R^{33b}, R³⁴ are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

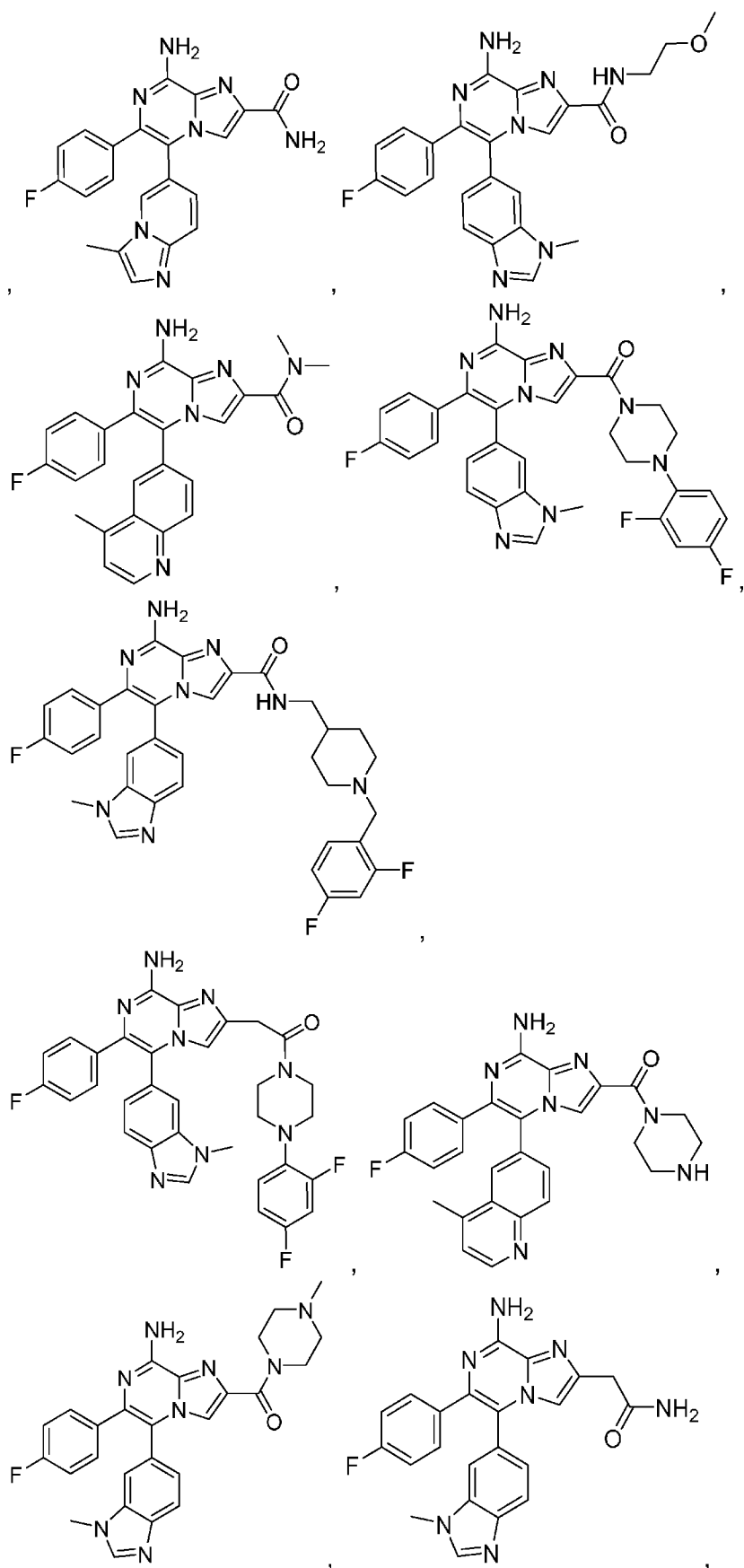
and wherein

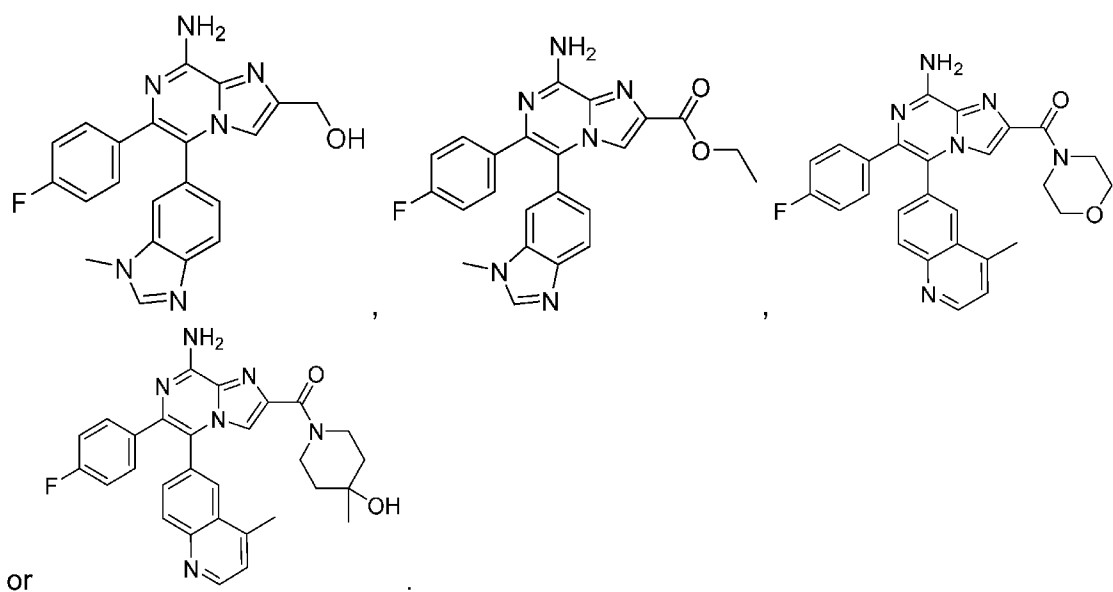
n is 0, 1 or 2; and

m is 1 or 2;

2. The compound according to claim 1, wherein the compound is not:

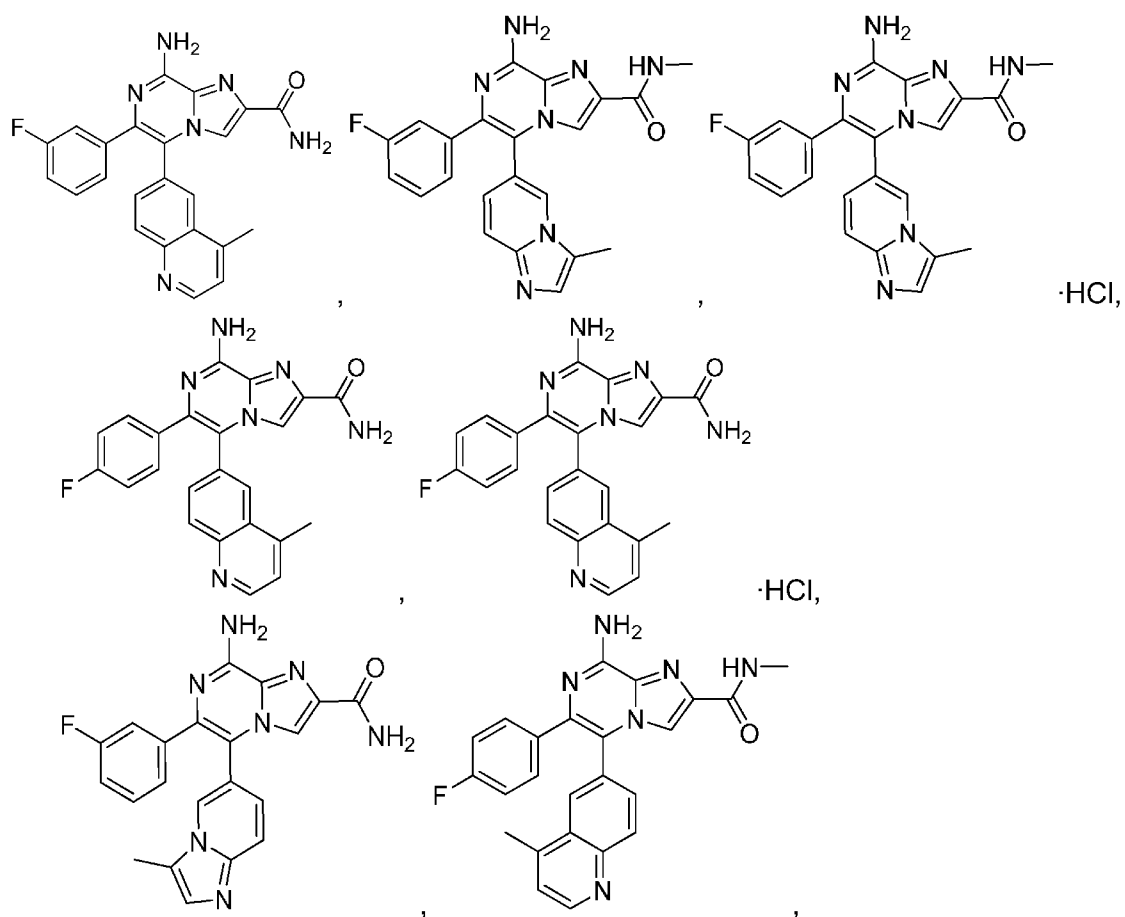


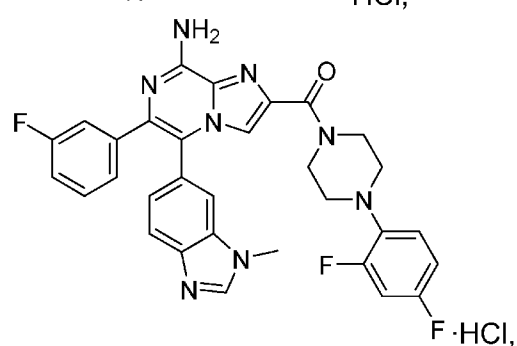
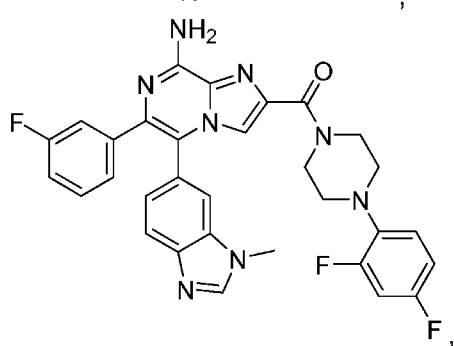
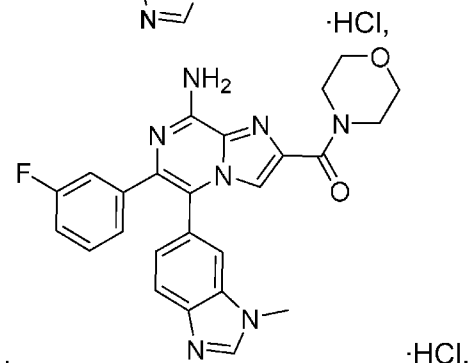
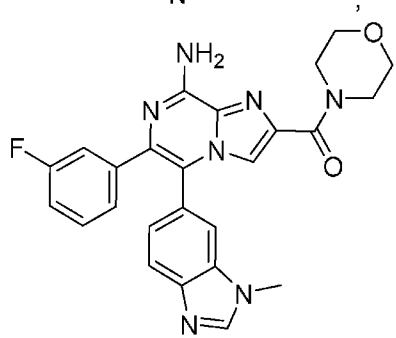
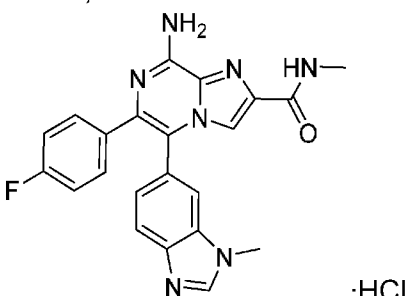
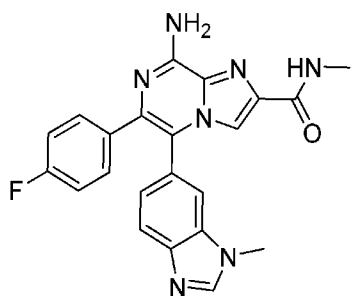
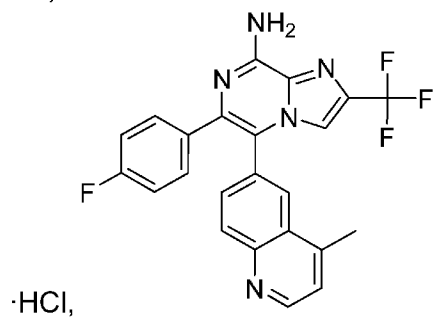
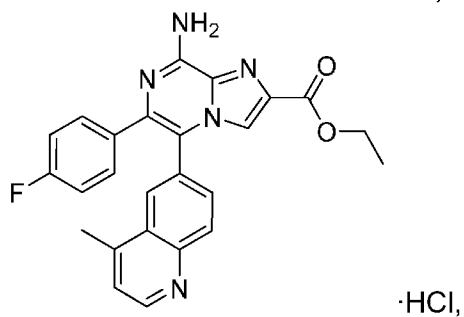
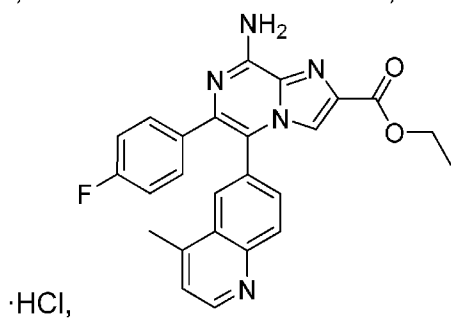
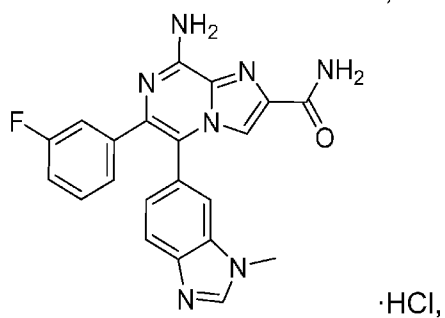
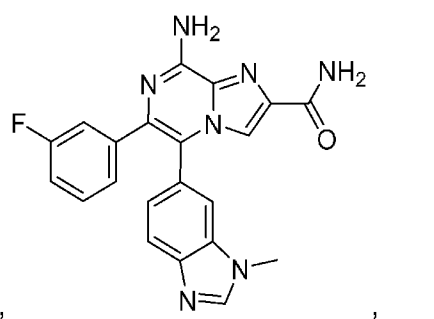
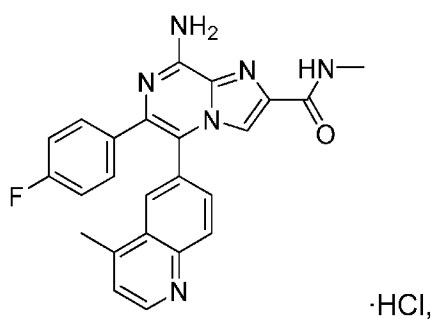


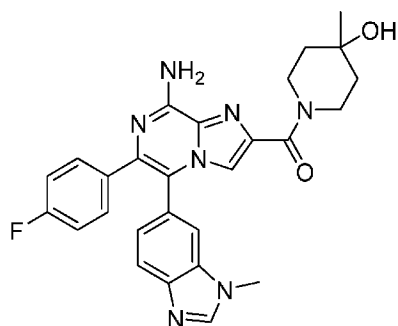
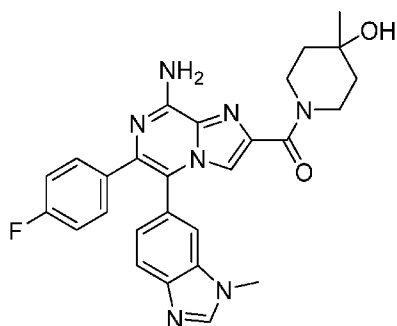


3. The compound according to claim 1, wherein the compound is not:

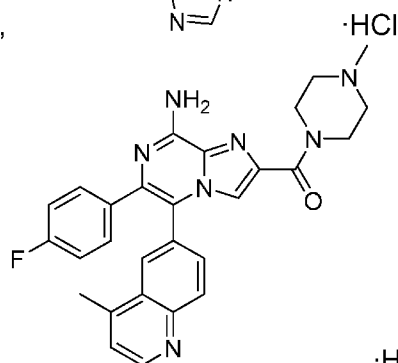
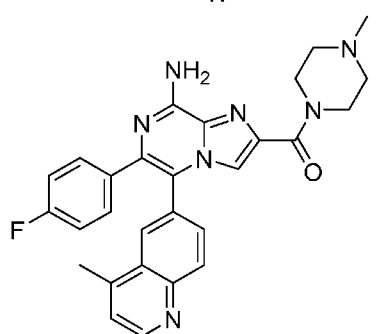
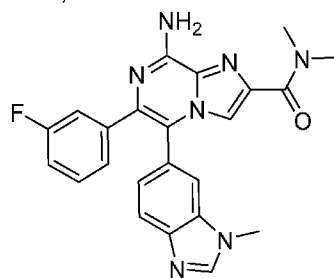
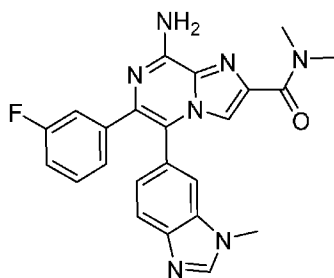
5



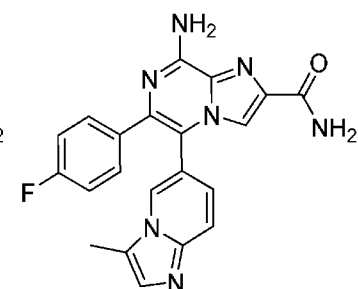
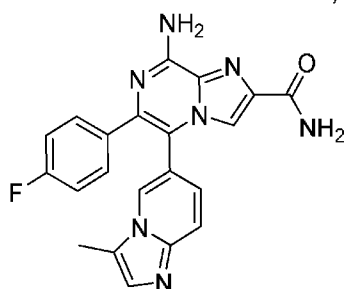




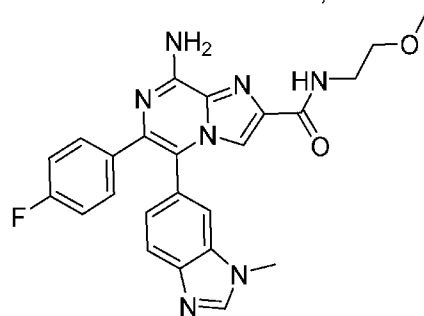
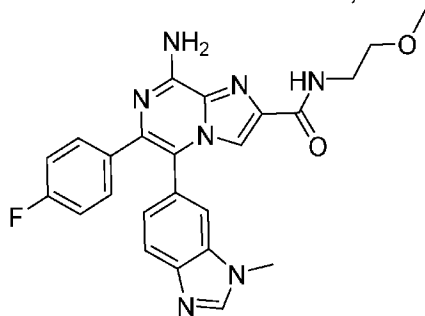
·HCl,



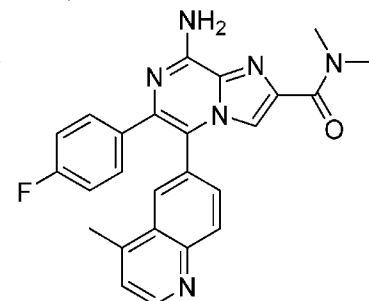
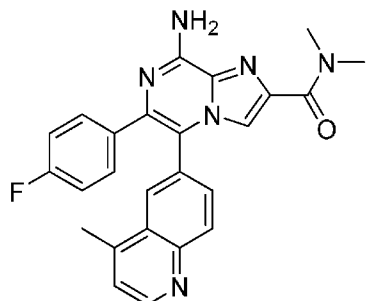
·HCl,



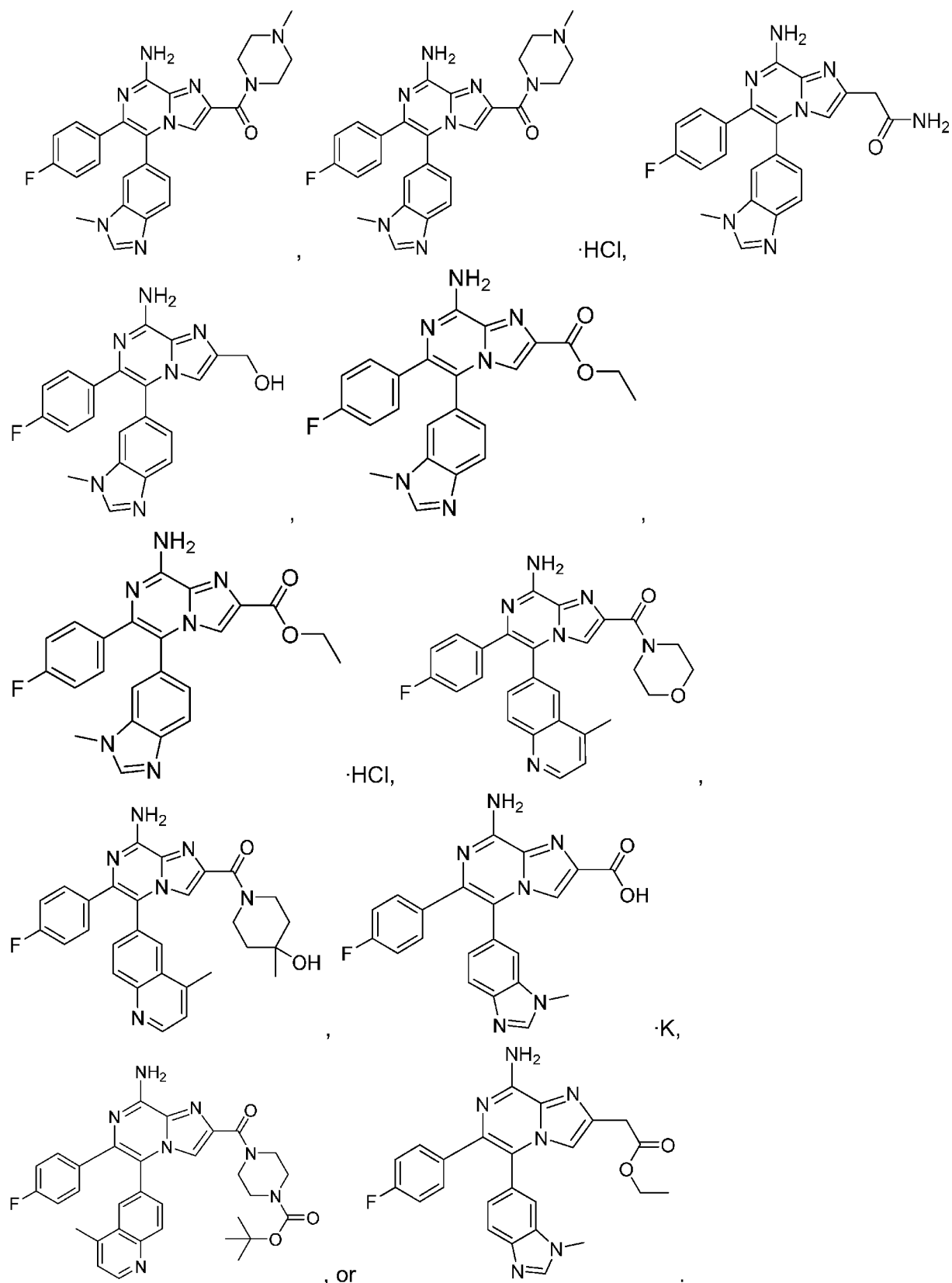
·HCl,



·HCl,



·HCl,



4. The compound according to any one of claims 1 to 3, wherein G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, furan-2-yl, furan-3-yl, pyrazol-1-yl, pyrazol-3-yl, pyrazol-4-yl, and pyrazol-5-yl, wherein one or more of the substitutable carbon or heteroatoms in

the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN, and wherein all other substituents have the meaning as defined in claim 1.

5. The compound according to any one of claims 1 to 3, wherein G¹ is selected from the group consisting of phenyl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyrimidin-5-yl, furan-2-yl, and pyrazol-3-yl, wherein one or two of the substitutable carbon or heteroatoms in the aforementioned cyclic moieties is substituted with same or different substituents selected from the group consisting of CH₃, F and CN, and wherein all other substituents have the meaning as defined in claim 1.

6. The compound according to any one of claims 1 to 5, wherein R^{1a} is selected from the group consisting of H and Cl; R^{1b} is selected from the group consisting of H and Cl; R^{1c} is selected from the group consisting of H and Cl; R^{2a} is CH₃; R^{2b} is CH₃; R^{2c} is CH₃; and wherein all other substituents have the meaning as defined in claim 1.

7. The compound according to any one of claims 1 to 6, wherein G³ is selected from the group consisting of

(i) C₁-C₆-alkyl, a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or heteroatom in the aforementioned moieties is independently unsubstituted or substituted with one or more, same or different substituents R³;

(ii) C(=O)R⁵, C(=O)OR⁶, and C(=O)N(R^{6a})(R^{6b});

wherein R³ is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁴;

(ii) C(=O)R⁷, C(=O)OR⁸, C(=O)N(R^{8a})(R^{8b}), OR⁸, N(R^{8a})(R^{8b}), N(R⁸)C(=O)R⁷, N(R⁸)C(=O)OR⁸, and N(R⁸)C(=O)N(R^{8a})(R^{8b});

wherein R⁴ is selected from the group consisting of

(i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic

clic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R⁹;

- (ii) C(=O)R¹⁰, C(=O)OR¹¹, C(=O)N(R^{11a})(R^{11b}), OR¹¹, N(R^{11a})(R^{11b}), N(R¹¹)C(=O)R¹⁰, N(R¹¹)C(=O)OR¹¹, N(R¹¹)C(=O)N(R^{11a})(R^{11b});

wherein R⁵, R⁶, R^{6a}, R^{6b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R⁷, R⁸, R^{8a}, R^{8b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹³;

wherein R⁹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁰, R¹¹, R^{11a}, R^{11b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁷;

wherein R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or

fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;

- (ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹³ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²¹;

- (ii) C(=O)R²², C(=O)OR²³, C(=O)N(R^{23a})(R^{23b}), OR²³, N(R^{23a})(R^{23b}), N(R²³)C(=O)R²², N(R²³)C(=O)OR²³, N(R²³)C(=O)N(R^{23a})(R^{23b});

wherein R¹⁷ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;

- (ii) C(=O)R²⁵, C(=O)OR²⁶, C(=O)N(R^{26a})(R^{26b}), OR²⁶, N(R^{26a})(R^{26b}), N(R²⁶)C(=O)R²⁵, N(R²⁶)C(=O)OR²⁶, N(R²⁶)C(=O)N(R^{26a})(R^{26b});

wherein R¹⁹, R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and

wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²¹ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

wherein R²², R²³, R^{23a}, R^{23b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁸;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R²⁵, R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₂-C₄-alkenyl, C₂-C₄-haloalkenyl, C₂-C₄-alkynyl, and C₂-C₄-haloalkynyl;

wherein R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

wherein R²⁸ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more,

same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³¹;

wherein R²⁹, R³⁰, R³¹ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), and

wherein all other substituents have the meaning as defined in claim 1.

8. The compound according to any one of claims 1 to 6, wherein G³ is selected from the group consisting of C(=O)R⁵, C(=O)OR⁶, and C(=O)N(R^{6a})(R^{6b});

wherein R⁵, R⁶, R^{6a}, R^{6b} are independently selected from the group consisting of H, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;
- (ii) C(=O)R¹⁹, C(=O)OR²⁰, C(=O)N(R^{20a})(R^{20b}), OR²⁰, N(R^{20a})(R^{20b}), N(R²⁰)C(=O)R¹⁹, N(R²⁰)C(=O)OR²⁰, N(R²⁰)C(=O)N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon

or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{24} ;

- (ii) $C(=O)R^{25}$, $C(=O)OR^{26}$, $C(=O)N(R^{26a})(R^{26b})$, OR^{26} , $N(R^{26a})(R^{26b})$, $N(R^{26})C(=O)R^{25}$, $N(R^{26})C(=O)OR^{26}$, $N(R^{26})C(=O)N(R^{26a})(R^{26b})$;

wherein R^{19} , R^{20} , R^{20a} , R^{20b} are independently selected from the group consisting of H, C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{27} ;

wherein R^{24} is selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{29} ;

wherein R^{25} , R^{26} , R^{26a} , R^{26b} are independently selected from the group consisting of H, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, C_2 - C_4 -alkenyl, C_2 - C_4 -haloalkenyl, C_2 - C_4 -alkynyl, and C_2 - C_4 -haloalkynyl;

wherein R^{27} is selected from the group consisting of halogen, CN, NO_2 , OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl), C_1 - C_6 -alkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkynyl, a 3- to 9-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring and a 6- to 14-membered saturated, partially unsaturated or fully unsaturated carbobicyclic or heterobicyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R^{30} ;

wherein R^{29} , R^{30} are independently selected from the group consisting of halogen, CN, NO_2 , C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, OH, $O(C_1$ - C_4 -alkyl), NH_2 , $NH(C_1$ - C_4 -alkyl), and $N(C_1$ - C_4 -alkyl)(C_1 - C_4 -alkyl); and

wherein all other substituents have the meaning as defined in claim 1.

9. The compound according to any one of claims 1 to 6, wherein G^3 is selected from the group consisting of $C(=O)N(R^{6a})(R^{6b})$;

wherein R^{6a} is H,

wherein R^{6b} is selected from the group consisting of C₁-C₆-alkyl, C₂-C₆-alkynyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹²;

wherein R¹² is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R¹⁸;

- (ii) OR²⁰, N(R^{20a})(R^{20b});

and/or two R¹² present on one carbon atom together form =O;

wherein R¹⁸ is selected from the group consisting of

- (i) halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁴;

- (ii) OR²⁶, N(R^{26a})(R^{26b});

wherein R²⁰, R^{20a}, R^{20b} are independently selected from the group consisting of H, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁷;

wherein R²⁴ is selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R²⁹;

wherein R²⁶, R^{26a}, R^{26b} are independently selected from the group consisting of H, C₁-C₄-alkyl, and C₁-C₄-haloalkyl;

wherein R²⁷ is selected from the group consisting of halogen, CN, NO₂, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl), C₁-C₄-alkyl, and a 3- to 6-membered saturated, partially unsaturated or fully unsaturated carbocyclic or heterocyclic ring, wherein said heterocyclic or heterobicyclic ring comprises one or more, same or different heteroatoms selected from O, N or S, wherein said N- and/or S-atoms are independently oxidized or non-oxidized, and wherein each substitutable carbon or hetero-atom in the aforementioned moieties is unsubstituted or substituted with one or more, same or different substituents R³⁰;

wherein R²⁹, R³⁰ are independently selected from the group consisting of halogen, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-haloalkyl, OH, O(C₁-C₄-alkyl), NH₂, NH(C₁-C₄-alkyl), and N(C₁-C₄-alkyl)(C₁-C₄-alkyl);

10. The compound according to claim 1, wherein said compound is selected from the group consisting of 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid; 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-{2,6-diazaspiro[3.4]octane-2-carbonyl}-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-8-amine; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(pyridin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(4-fluoropyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[3-(difluoromethoxy)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(morpholin-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[2-(methylamino)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1,1-dioxo-1λ⁶-thiolan-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(2-oxopyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-hydroxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(4,4-difluoropiperidine-1-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-8-amine; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-[4-(difluoromethyl)quinolin-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(²H₃)methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide;

8-amino-N-(3-ethylpyrrolidin-3-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-(2,6-dimethylmorpholine-4-carbonyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(4-aminobutyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]ethyl}-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 2-[4-(2,4-difluorophenyl)piperazine-1-carbonyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 6-(4-fluorophenyl)-2-[4-(2-methoxyethyl)piperazine-1-carbonyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-6-(4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(oxan-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(piperidin-4-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-2-(piperazine-1-carbonyl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N,N-diethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxyethyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-methylpyrrolidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[3-(dimethylamino)butyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-(dimethylamino)propyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(prop-2-yn-1-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylpiperidin-4-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-2-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-{[6-(2-hydroxypropan-2-yl)pyridin-2-yl]methyl}-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2,2-trifluoroethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(3,3,3-trifluoropropyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-

amino-6-(4-fluorophenyl)-N-methyl-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-ethylquinolin-6-yl)-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[2-(dimethylamino)ethyl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(3-hydroxybutan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(4-methylmorpholin-2-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[(oxetan-3-yl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxolan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[1-(methoxymethyl)cyclopropyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methyl-2-oxopyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-{2-[(oxolan-2-yl)methoxy]ethyl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(2-methoxy-2-methylpropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(1,1,1-trifluoro-3-hydroxypropan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]-3-methylpyrrolidin-3-ol; 8-amino-5-(8-chloro-4-methylquinolin-6-yl)-6-(4-fluorophenyl)-N-(2-methoxyethyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carbonyl]pyrrolidin-3-amine; 8-amino-6-(4-fluorophenyl)-N-(1-methylpyrrolidin-3-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-hydroxycyclopentyl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-dimethylpropyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methoxypropan-2-yl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2-fluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-[(1-hydroxycyclopropyl)methyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)-N-(2-hydroxy-2-methylpropyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[1-(1-hydroxycyclopropyl)ethyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{3-chloroimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-[4-(²H₃)methylquinolin-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-

- fluorophenyl)-N-(3-hydroxypropyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-fluoroethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-ethyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-[1-(dimethylamino)-2-methylpropan-2-yl]-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(1-methylazetidin-3-yl)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-({1-[(2,4-difluorophenyl)methyl]piperidin-4-yl}methyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[2-methyl-1-(propan-2-yloxy)propan-2-yl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-(pyrrolidin-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-[(5-methyl-1,3,4-oxadiazol-2-yl)methyl]-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-2-methylphenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-[1-(2,2-difluoroethyl)-1H-1,3-benzodiazol-6-yl]-6-(4-fluorophenyl)-N-methylimidazo[1,2-a]pyrazine-2-carboxamide; 6-(4-fluorophenyl)-2-[(methylamino)methyl]-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-8-amine; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-[2-(pyrrolidin-1-yl)ethyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-(4-chloro-1-methyl-1H-1,3-benzodiazol-6-yl)-6-(4-fluorophenyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)-N-(oxetan-3-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-5-{8-chloro-3-methylimidazo[1,2-a]pyridin-6-yl}-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-(1-methylcyclobutyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-N-methyl-5-[1-(propan-2-yl)-1H-1,3-benzodiazol-6-yl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyanophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxylic acid; 8-amino-6-(3-cyanophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(2-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-

- amino-6-(3-cyanophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-(propan-2-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-4-fluorophenyl)-N-(2,2-difluoroethyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 1-[8-amino-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-2-yl]ethan-1-one; 8-amino-6-(4-fluorophenyl)-N-(1-methoxy-2-methylpropan-2-yl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)-N-[1-(trifluoromethyl)cyclopropyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-4-fluorophenyl)-N-(2,2-difluoroethyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}-N-[1-(trifluoromethyl)cyclopropyl]imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(cyclopropylmethyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 2-(4,5-dihydro-1H-imidazol-2-yl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazin-8-amine; 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1-cyanocyclopropyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2,2-difluoroethyl)-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(4,4-difluorocyclohexyl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(1,1-difluoropropan-2-yl)-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(3-cyano-4-fluorophenyl)-N-methyl-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-N-(2-cyanoethyl)-6-(4-fluorophenyl)-5-(4-methylquinolin-6-yl)imidazo[1,2-a]pyrazine-2-carboxamide; 8-amino-6-(4-fluorophenyl)-5-(1-methyl-1H-1,3-benzodiazol-6-yl)imidazo[1,2-a]pyrazine-2-carboxylic acid; and 8-amino-N-tert-butyl-6-(4-fluorophenyl)-5-{3-methylimidazo[1,2-a]pyridin-6-yl}imidazo[1,2-a]pyrazine-2-carboxamide.
11. A pharmaceutical composition comprising a pharmaceutically effective amount of the compound according to any one of claims 1 to 10 and optionally a pharmaceutically acceptable carrier, diluent or excipient.
12. A compound according to any one of claims 1 to 10 and a pharmaceutical composition according to claim 11 for use in medicine.
13. A compound for use according to claim 12 or a pharmaceutical composition for use according to claim 11 or 12, wherein said compound or pharmaceutical composition is for use in the treatment of a disease selected from the group consisting of cancer, Parkinson's disease, Huntington's disease, Alzheimer's disease, psychosis, stroke, extra pyramidal syndrome (in particular dystonia, akathisia, pseudoparkinsonism and tardive dyskinesia), attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), amyotrophic lateral sclerosis, cirrhosis, fibrosis, fatty liver, addictive behavior,

dermal fibrosis (in particular dermal fibrosis in scleroderma), sleep disorders, AIDS, autoimmune diseases, infections, atherosclerosis, ischemia-reperfusion injury, idiopathic pulmonary fibrosis, systemic sclerosis, irritable bowel disease and as analgesic.

- 5 14. A compound for use according to claim 12 or a pharmaceutical composition for use according to claim 11 or 12, wherein said compound or pharmaceutical composition is for use in the treatment of cancer, and wherein at least one further anti-neoplastic agent is preferably coadministered with said compound and/or comprised in said pharmaceutical composition.
- 10 15. A compound for use according to claim 14 or a pharmaceutical composition for use according to claim 14, wherein said anti-neoplastic agent is selected from the group consisting of a chemotherapeutic agent, a topoisomerase II inhibitor, an antimetabolite, a topoisomerase I inhibitor, a hormone, a hormonal analogue, a signal transduction pathway inhibitor, a tyrosine kinase inhibitor, an angiogenesis inhibitor, a proapoptotic agent, a cell cycle signaling inhibitor, a proteasome inhibitor, an inhibitors of cancer metabolism, and an immunotherapeutic agent, wherein said chemotherapeutic agent is preferably selected from the group consisting of an anti-microtubule agent, an platinum coordination complex and an antibiotic agent; and wherein said immunotherapeutic agent is preferably selected from the group consisting of a STING pathway modulating compound, a TLR agonist and a checkpoint inhibitor.
- 15 16. A compound for use according to claim 15 or a pharmaceutical composition for use according to claim 15, wherein said checkpoint inhibitor targets PD-1, PD-L1, CTLA-4, IDO, KIR, TIM-3, LAG-3, CD39, CD73, ICOS, OX40, Tim-3, Vista, BTLA, TDO, or TIGIT.
- 20 17. A compound for use according to claim 15 or 16 or a pharmaceutical composition for use according to claim 15 or 16, wherein said checkpoint inhibitor is an antibody, a small molecule inhibitor or an antisense oligonucleotide selected from the group consisting of an anti-PD-1, anti-PD-L1, anti-CTLA-4, anti-IDO, anti-KIR, anti-TIM-3, anti-LAG-3, anti-CD39, anti-CD73, anti-ICOS, anti-OX40, anti-Tim-3, anti-Vista, anti-BTLA, anti-TDO, and anti-TIGIT-agent.
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2019/086786

A. CLASSIFICATION OF SUBJECT MATTER		
INV.	C07D487/04	A61K31/4985
	A61P9/00	A61P35/00
		A61P31/00
		A61P1/00
		A61P25/00
ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols) C07D		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
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☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 31 January 2020		Date of mailing of the international search report 12/02/2020
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Bérillon, Laurent

INTERNATIONAL SEARCH REPORT

International application No
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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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