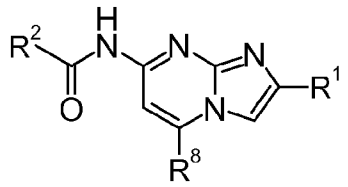
N-(IMIDAZOPYRIMIDIN-7-YL)-HETEROARYLAMIDE DERIVATIVES AND THEIR USE AS PDE10A INHIBITORS

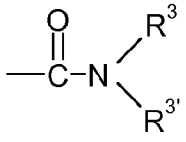
The invention is concerned with novel imidazopyrimidine derivatives of formula (I)



(I)

wherein

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of hydroxyl, halogen, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkoxy lower alkyl, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy and phenyl;

R^2 is 5- or 6-membered monocyclic heteroaryl having 1 to 3 heteroatoms independently selected from N and O, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of , halogen, hydroxyl, nitro, lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy-C(O)-, lower hydroxyalkyl, lower haloalkyl, lower alkoxy lower alkyl, lower alkyl-C(O)-, cycloalkyl, heterocyclyl, aryl, heteroaryl and amino optionally substituted by heteroaryl, wherein two substituents of R^2, together with said heteroaryl to which they are attached, may form a 9- or 10-membered bicyclic ring;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl, cyanocycloalkyl, heterocyclyl or aryl, wherein said lower alkyl is optionally substituted by lower haloalkoxy, cycloalkyl,

aryl or heteroaryl, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, lower alkyl, lower haloalkyl, lower alkoxy and cycloalkyl, and wherein said heterocyclyl is optionally substituted by lower alkyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl, 2,5-dihydro-1H-pyrrole, 2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole or 2-oxa-6-azaspiro[3.3]heptane, wherein said heterocyclyl is optionally substituted by 1 to 3 halogen, hydroxyl, oxo, lower alkyl or heteroaryl;

R^8 is hydrogen, lower alkyl, lower alkoxy or lower alkoxy lower alkyl;

or pharmaceutically acceptable salts thereof.

Further, the invention is concerned with a process for the manufacture of the above compounds, pharmaceutical preparations which contain such compounds as well as the use of these compounds for the production of pharmaceutical preparations.

Schizophrenia is a progressive and devastating neurological disease characterized by episodic positive symptoms such as delusions, hallucinations, thought disorders and psychosis and persistent negative symptoms such as flattened affect, impaired attention and social withdrawal, and cognitive impairments (Lewis DA and Lieberman JA, *Neuron, , 28:325-33, 2000*). For decades research has focused on the "dopaminergic hyperactivity" hypothesis which has led to therapeutic interventions involving blockade of the dopaminergic system (Vandenberg RJ and Aubrey KR., *Exp. Opin. Ther. Targets, 5(4): 507-518, 2001*; Nakazato A and Okuyama S, et al., *Exp. Opin. Ther. Patents, 10(1): 75-98, 2000*). This pharmacological approach, besides ameliorating positive symptoms in schizophrenic patients, poorly addresses negative and cognitive symptoms which are the best predictors of functional outcome (Sharma T., *Br.J. Psychiatry, 174(suppl. 28): 44-51, 1999*). In addition, current antipsychotic treatment is associated with adverse effects like weight gain, extrapyramidal symptoms or effects on glucose and lipid metabolism, related to their unspecific pharmacology.

In conclusion there is still a need for developing new antipsychotics with improved efficacy and safety profile. A complementary model of schizophrenia was proposed in the mid-

1960' based upon the psychotomimetic action caused by the blockade of the glutamate system by compounds like phencyclidine (PCP) and related agents (ketamine) which are non-competitive NMDA receptor antagonists. Interestingly, in healthy volunteers PCP-induced psychotomimetic action incorporates positive and negative symptoms as well as cognitive dysfunction, thus closely resembling schizophrenia in patients (Javitt DC et al., *Biol. Psychiatry, 45: 668-679,* 1999).

Cyclic nucleotides cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) are ubiquitous second messengers responsible for mediating the biological response of a variety of extracellular signals, including neurotransmitters, light and hormones. cAMP and cGMP regulate a variety of intracellular processes particularly in neurons of the central nervous system by activating cAMP- and cGMP-dependent kinases which then phosphorylate proteins involved in the regulation of synaptic transmission, neuronal differentiation and survival.

A crucial mechanism for controlling intracellular cyclic nucleotide levels and therefore cyclic nucleotide signaling is via hydrolysis of the 3',5'-phosphodiester bond by phosphodiesterases. Phosphodiesterases (PDEs) are a family of widely expressed enzymes encoded by 21 different genes in humans, with each gene encoding several splice variants (Beavo, J., *Physiol. Rev.* **1995**, 75, 725–748; Conti, M., Jin, S.L., *Prog. Nucleic Acid Res. Mol. Biol.* **1999**, 63, 1–38; Soderling, S.H., Beavo, J.A., *Curr. Opin. Cell Biol.* **2000**,12, 174–179, Manallack, D.T. et al. *J. Med.Chem.* **2005**, *48* (10), 3449-3462).

The PDE families differ in their substrate specificy for the cyclic nucleotides, their mechanism of regulation and their sensitivity to inhibitors. Moreover, they are differentially localized in the organism, among the cells of an organ and even within the cells. These differences lead to a differentiated involvement of the PDE families in the various physiological functions.

PDE10A is a dual substrate PDE encoded by a single gene as reported in 1999 by three separate research groups (Fujishige K., et al., *Eur J Biochem* (1999) **266**(3):1118-1127, Soderling S.H., et al., *ProcNatl Acad Sci USA* (1999) **96**(12):7071-7076, Loughney K., et al., *Gene* (1999) **234**(1):109-117). PDE10A is unique from other members of the multigene family

with respect to amino acid sequence (779 aa), tissue-specific pattern of expression, affinity for cAMP and cGMP and the effect on PDE activity by specific and general inhibitors.

PDE10A has one of the most restricted distribution of any PDE family being primarily expressed in the brain particularly in the nucleus accumbens and the caudate putamen. Additionally thalamus, olfactory bulb, hippocampus and frontal cortex show moderate levels of PDE10A expression. All these brain areas have been suggested to be involved in the pathophysiology of schizophrenia and psychosis, suggesting a central role of PDE10A in this devastating mental illness. Outside the central nervous system PDE10A transcript expression is also observed in peripheral tissues like thyroid gland, pituitary gland, insulin secreting pancreatic cells and testes (Fujishige, K. et al., *J. Biol. Chem.* **1999**, 274, 18438–18445, Sweet, L. (2005) WO 2005/012485). On the other hand expression of PDE10A protein has been observed only in enteric ganglia, in testis and epididymal sperm (Coskran T.M, et al., *J. Histochem. Cytochem.* **2006**, 54 (11), 1205-1213).

In the striatum both mRNA and protein are expressed only in the GABA (□-aminobutyric acid)-containing medium spiny projection neurons making it an intriguing target for the treatment of diseases of the central nervous system (Fujishige, K. et al., *Eur. J. Biochem.* **1999**, *266*, 1118-1127; Seeger, T.F. et al., *Brain Res.* **2003**, *985*, 113-126). The striatal medium spiny neurons are the principal input site and first site for information integration in the basal ganglia circuit of the mammalian brain. The basal ganglia are a series of interconnected subcortical nuclei that integrate widespread cortical input with dopaminergic signaling to plan and execute relevant motor and cognitive patterns while suppressing unwanted or irrelevant patterns (Graybiel, A.M. *Curr. Biol.* **2000**, *10,* R509–R511 (2000).

Papaverine, a relatively specific PDE10A inhibitor, and PDE10A-knockout mice have been used to explore the physiology of this enzyme and the possible therapeutic utility of PDE10A inhibition. Inhibition of this enzyme pharmacologically or through gene disruption causes a reduction in activity and a reduced response to psychomotor stimulants. Inhibition also reduces the conditioned avoidance response, a behavioural response that is predictive of clinical antipsychotic activity (Siuciak, J.A.; et al., *Neuropharmacology* **2006**, *51* (2), 386-396; Siuciak, J.A.; et al., *Neuropharmacology* **2006**, *51* (2), 374-385).

In addition PDE10A inhibition bears the potential to improve the negative and cognitive symptoms associated to schizophrenia. Indeed papaverine have been shown to attenuate the deficits in the extra-dimensional shift learning induced in rats by sub-chronic treatment with PCP, an animal paradigm of NMDA receptor hypofunction (Rodefer, J,S., et al., *Eur. J. Neuroscience* **2005**, *2,*: 1070-1076).In addition increased social interaction in PDE10A2-deficient mice have been observed (Sano, H. *J. Neurochem.* **2008**, *105*, 546-556).

Diseases that can be treated with PDE10A inhibitors include, but are not limited to, diseases thought to be mediated in part by dysfunction of the basal ganglia, of other parts of the central nervous system and of other PDE10A expressing tissues. In particular, diseases can be treated, where inhibition of PDE10A can have therapeutic effects.

These diseases include, but are not limited to, certain psychotic disorders such as schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder or substance-induced psychotic disorder, anxiety disorders such as panic disorder, obsessive-compulsive disorder, acute stress disorder or generalized anxiety disorder, obsessive/compulsive disorders, drug addictions, movement disorders such as Parkinson's disease or restless leg syndrome, cognition deficiency disorders such as Alzheimer's disease or multi-infarct dementia, mood disorders such as depression or bipolar disorders, or neuropsychiatric conditions such as psychosis, attention-deficit/hyperactivity disorder (ADHD) or related attentional disorders.

The compounds of the present invention are also suitable for the treatment of diabetes and related disorders such as obesity by regulating the cAMP signaling system.

PDE10A inhibitors might also be useful in preventing neurons from undergoing apoptosis by raising cAMP and cGMP levels and, thus, might possess anti-inflammatory properties. Neurodegenerative disorders treatable with PDE10A inhibitors include, but are not limited to, as Alzheimer's disease, Huntington's disease, Parkinson's disease, multiple sclerosis, stroke or spinal cord injury.

The growth of cancer cells is inhibited by cAMP and cGMP. Thus by raising cAMP and cGMP, PDE10A inhibitors can also be used for the treatment of different solid tumors and hematological malignancies such as renal cell carcinoma or breast cancer.

Unless otherwise indicated, the following definitions are set forth to illustrate and define the meaning and scope of the various terms used to describe the invention herein.

It must be noted that, as used in the specification and the appended claims, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise.

When indicating the number of subsituents, the term "one or more" means from one substituent to the highest possible number of substitution, i.e. replacement of one hydrogen up to replacement of all hydrogens by substituents.

In this specification the term “lower” is used to mean a group consisting of one to seven, more specifically of one to four carbon atom(s).

The term “halogen” refers to fluorine, chlorine, bromine and iodine, more speficially fluorine, chlorine and bromine.

The term “alkyl”, alone or in combination with other groups, refers to a branched or straight-chain monovalent saturated aliphatic hydrocarbon radical of one to twenty carbon atoms, more specifically one to sixteen carbon atoms, yet more specifically one to ten carbon atoms.

The term “lower alkyl”, alone or in combination with other groups, refers to a branched or straight-chain monovalent alkyl radical of one to seven carbon atoms, more specifically one to four carbon atoms. This term is further exemplified by such radicals as methyl, ethyl, n-propyl, isopropyl, n-butyl, s-butyl, t-butyl and the like.

The term "alkenyl", alone or in combination with other groups, refers to a straight-chain or branched hydrocarbon residue comprising an olefinic bond and up to 20, preferably up to 16 carbon atoms. The term "lower alkenyl" refers to a straight-chain or branched hydrocarbon

residue comprising an olefinic bond and up to 7, preferably up to 4 carbon atoms, such as e.g. ethenyl or 2-propenyl.

The term "cycloalkyl", alone or in combination with other groups, refers to a monovalent carbocyclic radical of 3 to 10 carbon atoms, more specifically 3 to 6 carbon atoms, such as cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

The term "cyanocycloalkyl" refers to cycloalkyl which is mon- or multiply substituted with cyano. Examples of cyanoalkyl is e.g. 1-cyanocyclopropyl.

The term "lower haloalkyl", alone or in combination with other groups, refers to lower alkyl groups which are mono- or multiply substituted with halogen, particularly fluoro. Examples of lower haloalkyl groups are e.g. $-CFH_2$, $-CF_2H$, $-CF_3$, CF_3CH_2-, $CF_3(CH_2)_2-$, $(CF_3)_2CH-$ and CF_2H-CH_2-.

The term "alkoxy" refers to the group R'-O-, wherein R' is an alkyl. The term "lower alkoxy", alone or in combination with other groups, refers to the group R'-O-, wherein R' is a lower alkyl.

The term "lower alkoxy lower alkyl" refers to lower alkyl groups which are mono- or multiply substituted with lower alkoxy. Examples of lower alkoxy lower alkyl groups are e.g. $-CH_2-O-CH_3$, $-CH_2-CH_2-O-CH_3$, and $-CH_2-O-CH_2-CH_3$.

The term "lower hydroxyalkyl" refers to a lower alkyl group as defined above, which is substituted by 1 to 3 hydroxy groups. Examples of lower hydroxyalkyl groups are e.g. hydroxy-methyl, 2-hydroxy-ethyl, hydroxy propyl, 3-hydroxy-propyl, 2-hydroxy-propyl, 3-hydroxy-prop-2-yl, 2,3-dihydroxy-propyl and 1,3-dihydroxy-prop-2-yl.

The term "lower haloalkoxy" refers to a group of the formula lower haloalkyl-O-.

The term "lower cyanoalkyl" refers to a lower alkyl group as defined above, which is substituted by 1 to 3 cyano groups. Examples of lower cyanoalkyl groups are e.g. cyanomethyl and cyanoethyl.

The term “amino” refers to a monovalent group that has a nitrogen atom with two hydrogen atoms (represented by $-NH_2$).

The term "oxo" when referring to substituents on heterocyclyl means that an oxygen atom is attached to the heterocyclyl ring. Thereby, the "oxo" may either replace two hydrogen atoms on a carbon atom, or it may simply be attached to sulfur, so that the sulfur exists in oxidized form, i.e. bearing one or two oxygens.

The term “heterocyclyl” refers to a monovalent saturated 4- to 6-membered monocyclic ring containing one, two or three ring heteroatoms independently selected from N, O and S, the remaining ring atoms being carbon atoms, wherein the point of attachment can be through either a carbon atom or a heteroatom. Examples of heterocyclyl are e.g. morpholinyl, tetrahydropyranyl and piperidinyl.

The term “aryl” refers to a monovalent aromatic hydrocarbon ring. The aryl group more specifically includes 6 to 10 carbon atoms. Examples of aryl groups are e.g. phenyl and naphthyl.

The term “heteroaryl” refers to an aromatic 5- or 6-membered monocyclic ring or 9- or 10-membered bicyclic ring which comprises 1 to 4 atoms independently selected from nitrogen, oxygen and/or sulphur, such as furyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, thienyl, isoxazolyl, oxazolyl, oxadiazolyl, imidazolyl, pyrrolyl, pyrazolyl, triazolyl, tetrazolyl, thiazolyl, isothiazolyl, thiadiazolyl, benzoimidazolyl, indolyl, indazolyl, benzothiazolyl, benzoisothiazolyl, benzoxazolyl, benzoisoxazolyl, quinolinyl and isoquinolinyl. Examples of heteroaryl groups are pyridinyl, pyrimidinyl, pyrazinyl, quinolinyl or imidazolyl.

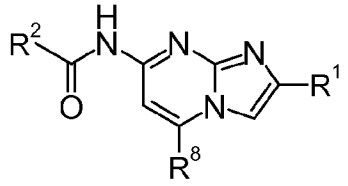
The term "bicyclic ring" refers to two rings, wherein the two rings are fused. Each ring is independently aromatic or non-aromatic. In certain embodiments, both rings are aromatic. In certain embodiments, both rings are non-aromatic. In certain embodiments, one ring is aromatic and one ring is non-aromatic.

Compounds of formula (I) can form pharmaceutically acceptable salts. Examples of such pharmaceutically acceptable salts are salts of compounds of formula (I) with physiologically

compatible mineral acids, such as hydrochloric acid, sulphuric acid, sulphurous acid or phosphoric acid; or with organic acids, such as methanesulphonic acid, p-toluenesulphonic acid, acetic acid, lactic acid, trifluoroacetic acid, citric acid, fumaric acid, maleic acid, tartaric acid, succinic acid or salicylic acid. The term "pharmaceutically acceptable salts" refers to such salts. Compounds of formula (I) which comprise an acidic group, such as e.g. a COOH group, can further form salts with bases. Examples of such salts are alkaline, earth-alkaline and ammonium salts such as e.g. Na-, K-, Ca- and trimethylammonium salt. The term "pharmaceutically acceptable salts" also refers to such salts. Particular salts are those obtained by the addition of an acid.

The term "pharmaceutically acceptable esters" embraces derivatives of the compounds of formula (I), in which a carboxy group has been converted to an ester. Lower-alkyl, hydroxy-lower-alkyl, lower-alkoxy-lower-alkyl, amino-lower-alkyl, mono- or di-lower-alkyl-amino-lower-alkyl, morpholino-lower-alkyl, pyrrolidino-lower-alkyl, piperidino-lower-alkyl, piperazino-lower-alkyl, lower-alkyl-piperazino-lower-alkyl and aralkyl esters are examples of suitable esters. Particular esters are methyl, ethyl, propyl, butyl and benzyl esters. The term "pharmaceutically acceptable esters" furthermore embraces compounds of formula (I) in which hydroxy groups have been converted to the corresponding esters with inorganic or organic acids such as, nitric acid, sulphuric acid, phosphoric acid, citric acid, formic acid, maleic acid, acetic acid, succinic acid, tartaric acid, methanesulphonic acid, p-toluenesulphonic acid and the like, which are non toxic to living organisms.

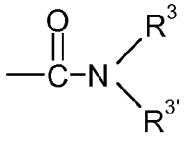
In detail, the present invention relates to compounds of formula (I)



(I)

wherein

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of hydroxyl, halogen, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkoxy lower alkyl, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy and phenyl;

R^2 is 5- or 6-membered monocyclic heteroaryl having 1 to 3 heteroatoms independently selected from N and O, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of , halogen, hydroxyl, nitro, lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy-C(O)-, lower hydroxyalkyl, lower haloalkyl, lower alkoxy lower alkyl, lower alkyl-C(O)-, cycloalkyl, heterocyclyl, aryl, heteroaryl and amino optionally substituted by heteroaryl, wherein two substituents of R^2, together with said heteroaryl to which they are attached, may form a 9- or 10-membered bicyclic ring;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl, cyanocycloalkyl, heterocyclyl or aryl, wherein said lower alkyl is optionally substituted by lower haloalkoxy, cycloalkyl, aryl or heteroaryl, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, lower alkyl, lower haloalkyl, lower alkoxy and cycloalkyl, and wherein said heterocyclyl is optionally substituted by lower alkyl, or

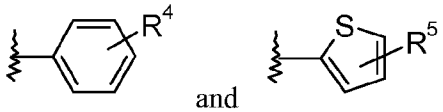
R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl, 2,5-dihydro-1H-pyrrole, 2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole or 2-oxa-6-azaspiro[3.3]heptane, wherein said heterocyclyl is optionally substituted by 1 to 3 halogen, hydroxyl, oxo, lower alkyl or heteroaryl;

R^8 is hydrogen, lower alkyl, lower alkoxy or lower alkoxy lower alkyl;

or pharmaceutically acceptable salts thereof.

The compounds of formula (I) can have one or more asymmetric C atoms and can therefore exist as an enantiomeric mixture, mixture of stereoisomers or as optically pure compounds.

A particular embodiment of the present invention relates to compounds of formula (I) as described above, wherein R^1 is selected from the group consisting of:



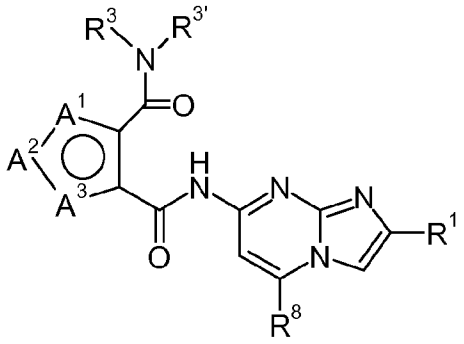
and

wherein R^4 is hydrogen, hydroxyl, halogen, lower alkoxy, lower haloalkoxy, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy or phenyl, and R^5 is halogen. More specifically, R^4 is hydrogen, hydroxyl, chloro, fluoro, bromo, methoxy, fluoromethoxy, trifluoromethoxy, 2-fluoroethoxy, -$OC(O)CH_3$, -$OCH_2C(O)OCH_3$ or phenyl, and R^5 is chloro. Further more specifically, R^1 is phenyl, 3-chloro-phenyl, 3-fluorophenyl, 3-bromophenyl, 4-fluoro-phenyl, 3-methoxy-phenyl, 3-trifluoromethoxy-phenyl, 5-chloro-thiophen-2-yl, 3-(fluoromethoxy)phenyl, 3-hydroxy-phenyl, 3-(2-fluoroethoxy)phenyl, 3-acetoxyphenyl, 3-acetoxymethoxyphenyl, biphenyl-3-yl.

Particular compounds of formula (I) are described in the examples as individual compounds as well as pharmaceutically acceptable salts as well as pharmaceutically acceptable esters thereof. Furthermore, the substituents as found in the specific examples described below, individually constitute particular embodiments of the present invention.

Another embodiment of the present invention relates to compounds of formula (I) as described above, wherein R^8 is hydrogen or lower alkoxy lower alkyl, more specifically hydrogen or methoxymethyl, yet more specifically hydrogen.

Another embodiment of the present invention relates to compounds of formula (Ia) or pharmaceutically acceptable salts thereof



(Ia)

wherein

A^1 is -NH-, -N=, -NR^6- or -CH=;

A^2 is -N= or -$NR^{6'}$-;

A^3 is -N=, -$NR^{6''}$- or -CH=;

R^6 is lower alkyl;

$R^{6'}$ is lower alkyl;

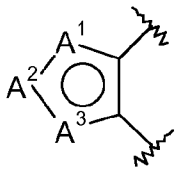
$R^{6''}$ is lower alkyl or lower alkenyl;

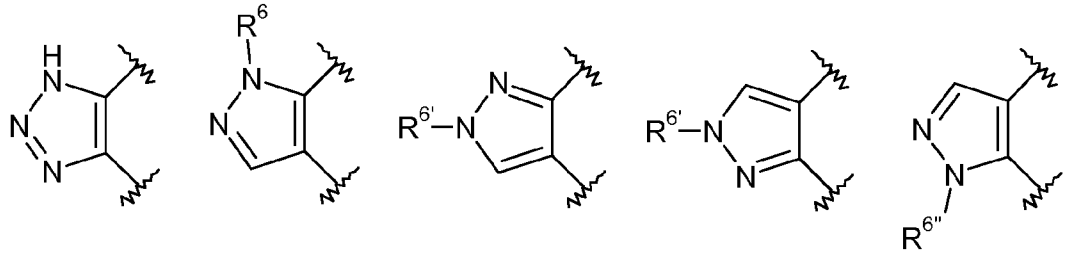
R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of hydroxyl, halogen, lower alkoxy, lower haloalkoxy, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy and phenyl;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl, cyanocycloalkyl, heterocyclyl or aryl, wherein said lower alkyl is optionally substituted by lower haloalkoxy, cycloalkyl, aryl or heteroaryl, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, lower alkyl, lower haloalkyl, lower alkoxy and cycloalkyl, and wherein said heterocyclyl is optionally substituted by lower alkyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl, 2,5-dihydro-1H-pyrrole, 2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole or 2-oxa-6-azaspiro[3.3]heptane, wherein said heterocyclyl is optionally substituted by 1 to 3 halogen, hydroxyl, oxo, lower alkyl or heteroaryl;

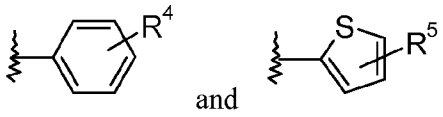
R^8 is hydrogen, lower alkyl, lower alkoxy or lower alkoxy lower alkyl.

More specifically,  of formula (Ia) is selected from the group consisting of:



wherein R^6 is lower alkyl, more specifically methyl; $R^{6'}$ is lower alkyl, more specifically methyl; $R^{6''}$ is lower alkyl or lower alkenyl, more specifically methyl, ethyl or allyl.

A particular embodiment of the present invention relates to compounds of formula (Ia) as described above, wherein R^1 is selected from the group consisting of:



wherein R^4 is hydrogen, hydroxyl, halogen, lower alkoxy, lower haloalkoxy, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy or phenyl, and R^5 is halogen. More specifically, R^4 is hydrogen, hydroxyl, chloro, fluoro, bromo, methoxy, fluoromethoxy, trifluoromethoxy, 2-fluoroethoxy, -$OC(O)CH_3$, -$OCH_2C(O)OCH_3$ or phenyl, and R^5 is chloro. Further more specifically, R^1 is phenyl, 3-chloro-phenyl, 3-fluorophenyl, 3-bromophenyl, 4-fluoro-phenyl, 3-methoxy-phenyl, 3-trifluoromethoxy-phenyl, 5-chloro-thiophen-2-yl, 3-(fluoromethoxy)phenyl, 3-hydroxy-phenyl, 3-(2-fluoroethoxy)phenyl, 3-acetoxyphenyl, 3-acetoxymethoxyphenyl, biphenyl-3-yl.

Another embodiment of the present invention relates to compounds of formula (Ia) as described above, wherein R^3 and $R^{3'}$ are independently hydrogen, methyl, cyclopropylmethyl, cyanomethyl, oxazol-2-ylmethyl, oxazol-4-ylmethyl, isoxazol-5-ylmethyl, 3-methylisoxazol-5-ylmethyl, 5-methylisoxazol-3-ylmethyl, 3-ethylisoxazol-5-ylmethyl, 2-cyclopropyl-5-methyloxazol-4-ylmethyl, 3-isopropyl-1,2,4-oxadiazol-5-ylmethyl, 5-cyclopropyl-1,2,4-oxadiazol-3-ylmethyl, 3-cyclopropyl-1,2,4-oxadiazol-5-ylmethyl, 5-methyl-1,2,4-oxadiazol-3-ylmethyl, 1H-pyrazol-5-ylmethyl, 1,3-dimethyl-4-nitro-1H-pyrazol-5-ylmethyl, 5-methyl-1H-pyrazol-3-ylmethyl, 1-methyl-1H-pyrazol-3-ylmethyl, 4-chloro-1-methyl-1H-pyrazol-3-ylmethyl, 1-propyl-1H-pyrazol-3-ylmethyl, 5-cyclopropyl-1H-pyrazol-3-ylmethyl, 2-methylthiazol-4-ylmethyl, 5-methylthiazol-2-ylmethyl, 4-cyanothiazol-2-ylmethyl, 1H-tetrazol-5-ylmethyl, pyridin-2-ylmethyl, pyridin-4-ylmethyl, 5-bromopyridin-2-ylmethyl, 6-chloropyridin-3-ylmethyl, 5-methylpyridin-2-ylmethyl, 6-(trifluoromethyl)pyridin-3-ylmethyl, 2-methoxypyridin-3-ylmethyl, 6-cyanopyridin-3-ylmethyl, imidazo[1,2-a]pyridin-2-ylmethyl, imidazo[2,1-b]thiazol-6-ylmethyl, benzo[d]oxazol-2-ylmethyl, ethyl, 2-hydroxy-ethyl, 2-cyano-ethyl, 2-hydroxy-1-methyl-ethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoro-ethyl, 2-methoxy-ethyl, 2-(2-fluoroethoxy)ethyl, 1-(pyridin-3-yl)ethyl, propyl, isopropyl, 3-hydroxy-propyl, 2-hydroxy-propyl, 3,3,3-trifluoropropyl, 2-hydroxy-2-methyl-propyl, isobutyl, tert-butyl, 3-methoxy-propyl, cyclopropyl, 1-cyanocyclopropyl, cyclobutyl, oxetan-3-yl, 3-methyloxetan-3-yl, tetrahydro-furan-3-yl, phenyl or benzyl, or R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form azetidine ring, 3-fluoroazetidine ring, 3,3-difluoro-azetidine ring, 3-hydroxy-azetidine ring, pyrrolidine ring, 2-methylpyrrolidine ring, 2,5-dihydro-1H-pyrrole ring,

piperidine ring, morpholine ring, 1,1-dioxo-1λ6-thiomorpholine ring, 3-(pyridin-3-yl)morpholine ring, 2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole ring, 2-oxa-6-azaspiro[3.3]heptane ring.

Particular compounds of formula (Ia) are those selected from the group consisting of:

5-(Azetidine-1-carbonyl)-1H-[1,2,3]triazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-4-(morpholine-4-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(4-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide,

4-(3,3-Difluoro-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(3-Hydroxy-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

4-(1,1-Dioxo-1λ6-thiomorpholine-4-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-methoxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-[(tetrahydro-furan-3-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-1-methyl-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-diethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-4-(piperidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isopropyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(methyl-propyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-propylamide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylmethyl-amide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclobutylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-isopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-trifluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-methylamide 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

3-(Azetidine-1-carbonyl)-1-methyl-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 3-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-cyano-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isobutyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-2-methyl-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(azetidine-1-carbonyl)-N-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-hydroxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

N5-(2-(3-hydroxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,N4,1-trimethyl-1H-pyrazole-4,5-dicarboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide},

N4-ethyl-N5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-ethyl-N5-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,N4,1-trimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-ethyl-N5-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

4-(3-fluoroazetidine-1-carbonyl)-N-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

4-(azetidine-1-carbonyl)-N-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

4-(3-fluoroazetidine-1-carbonyl)-N-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

3-(7-(4-(dimethylcarbamoyl)-1-methyl-1H-pyrazole-5-carboxamido)imidazo[1,2-a]pyrimidin-2-yl)phenyl acetate,

N5-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,N4,1-trimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-fluoroethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide) 4-[(2-methoxy-ethyl)-methyl-amide],

N4-ethyl-N5-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

4-(3-fluoroazetidine-1-carbonyl)-N-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-fluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-[(2-methoxy-ethyl)-methyl-amide],

methyl 2-(3-(7-(4-(ethyl(methyl)carbamoyl)-1-methyl-1H-pyrazole-5-carboxamido)imidazo[1,2-a]pyrimidin-2-yl)phenoxy)acetate,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide},

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide),

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid {2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide,

N4-(2-fluoroethyl)-N5-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

3-(7-(4-(azetidine-1-carbonyl)-1-methyl-1H-pyrazole-5-carboxamido)imidazo[1,2-a]pyrimidin-2-yl)phenyl acetate,

N4-(2-(2-fluoroethoxy)ethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-[(2-methoxy-ethyl)-methyl-amide],

N4-(2-fluoroethyl)-N5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-(2-fluoroethoxy)ethyl)-N5-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-(2-fluoroethoxy)ethyl)-N5-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-fluoroethyl)-N5-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-(oxazol-4-ylmethyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-((1H-pyrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

4-(2,5-dihydro-1H-pyrrole-1-carbonyl)-1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
4-(3-fluoroazetidine-1-carbonyl)-1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
1-methyl-4-(2-methylpyrrolidine-1-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
4-(azetidine-1-carbonyl)-N-(2-(3-bromophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-2-ylmethyl)-1H-pyrazole-4,5-dicarboxamide,
N4-(cyanomethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-allyl-4-(azetidine-1-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
1-methyl-N4-((5-methyl-1H-pyrazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-(oxazol-2-ylmethyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-(2-fluoroethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((5-methylthiazol-2-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-(cyanomethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(3,3,3-trifluoropropyl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((3-methylisoxazol-5-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
4-(azetidine-1-carbonyl)-N-(2-(biphenyl-3-yl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,
N4-(2,2-difluoroethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(2,2,2-trifluoroethyl)-1H-pyrazole-4,5-dicarboxamide,

N4-(isoxazol-5-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-4-(2-oxa-6-azaspiro[3.3]heptane-6-carbonyl)-1H-pyrazole-5-carboxamide,

1-methyl-N4-phenyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-(3-methyloxetan-3-yl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-2-ylmethyl)-1H-pyrazole-4,5-dicarboxamide,

N4-((5-bromopyridin-2-yl)methyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-4-(3-(pyridin-3-yl)morpholine-4-carbonyl)-1H-pyrazole-5-carboxamide,

N4-tert-butyl-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(1-(pyridin-3-yl)ethyl)-1H-pyrazole-4,5-dicarboxamide,

N4-((1,3-dimethyl-4-nitro-1H-pyrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N5-(oxetan-3-yl)-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide,

N4-((6-cyanopyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-((5-methylisoxazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-pyrazole-4,5-dicarboxamide,

N4-(1-cyanocyclopropyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N5-(5-(methoxymethyl)-2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-((1H-tetrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-4-ylmethyl)-1H-pyrazole-4,5-dicarboxamide,

N4-(imidazo[1,2-a]pyridin-2-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N5-(2-methoxyethyl)-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide,

N4-((4-cyanothiazol-2-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-((5-cyclopropyl-1H-pyrazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-(imidazo[2,1-b]thiazol-6-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-((6-chloropyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-((5-methylpyridin-2-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N5-propyl-1H-1,2,3-triazole-4,5-dicarboxamide,

1-methyl-N4-((1-methyl-1H-pyrazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-((4-chloro-1-methyl-1H-pyrazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N5-cyclopropyl-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide,

N4-((3-ethylisoxazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-((2-methoxypyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

N4-benzyl-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-((2-methylthiazol-4-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-((1-propyl-1H-pyrazol-3-yl)methyl)-1H-pyrazole-4,5-dicarboxamide,
N4-((2-cyclopropyl-5-methyloxazol-4-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((5-cyclopropyl-1,2,4-oxadiazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((3-cyclopropyl-1,2,4-oxadiazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((5-methyl-1,2,4-oxadiazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-4-(2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole-5-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
N4-(benzo[d]oxazol-2-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((3-isopropyl-1,2,4-oxadiazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

or pharmaceutically acceptable salts thereof.

Another embodiment of the present invention relates to compounds of formula (Ia) as described above, wherein R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by halogen or lower alkoxy; R^3 and $R^{3'}$ are independently lower alkyl or lower alkoxy lower alkyl, or R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form an azetidine ring, pyrrolidine ring or piperidine ring, wherein said azetizine ring is optionally substituted by 1 or 2 substituents independently selected from the group consisting of hydroxyl and halogen.

Particular compounds of formula (Ia) are those selected from the group consisting of:
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-4-(morpholine-4-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

4-(3,3-Difluoro-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

4-(3-Hydroxy-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-4-(piperidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

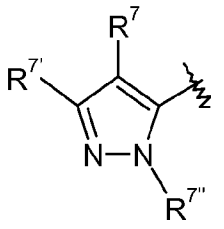
4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

or pharmaceutically acceptable salts thereof.

Another embodiment of the present invention relates to compounds of formula (I) or pharmaceutically acceptable salts thereof as described above, wherein R^2 is , wherein

R^7 is hydrogen, halogen, lower alkoxy-C(O)- or heteroaryl, more specifically hydrogen, bromo, chloro, ethoxycarbonyl or isoxazol-5-yl;

$R^{7'}$ is hydrogen, lower alkyl or nitro, more specifically hydrogen, methyl or nitro;

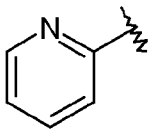
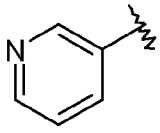
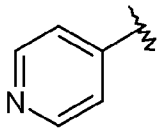
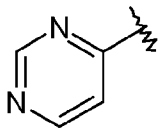
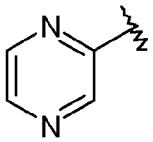
$R^{7''}$ is lower alkyl, cycloalkyl or aryl, more specifically methyl, ethyl, propyl, isopropyl, butyl, sec-butyl, isobutyl, cyclopentyl or phenyl.

Particular compounds of formula (I) are those selected from the group consisting of:
4-Chloro-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Phenyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-propyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-isopropyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

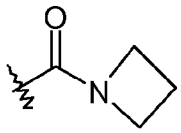
2-sec-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-isobutyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Isobutyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Cyclopentyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Ethyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Isopropyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Isoxazol-5-yl-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
1-Ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester,
or pharmaceutically acceptable salts thereof.

Yet particular compounds of formula (I) are those selected from the group consisting of:
Isoxazole-5-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4,5,6,7-Tetrahydro-benzo[d]isoxazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
5-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid methyl ester,
1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
or pharmaceutically acceptable salts thereof.

Another embodiment of the present invention relates to compounds of formula (I) or pharmaceutically acceptable salts thereof as described above, wherein R^2 is 6-membered heteroaryl selected from the group consisting of:

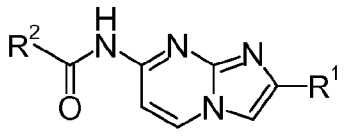
wherein said heteroaryl is substituted by 1 to 3 substituents independently selected from the group consisting of bromo, chloro, methyl, methoxy, cyclopropyl, -C(O)NHCH$_2$CF$_3$,



and pyrimidin-5-ylamino.

Particular compounds of formula (I) are those selected from the group consisting of:
3,6-Dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Chloro-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-isonicotinamide,
6-Chloro-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
6-Methoxy-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
5-Bromo-3-methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-3,6-dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
6-Methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
Pyrazine-2,3-dicarboxylic acid 2-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 3-[(2,2,2-trifluoro-ethyl)-amide],
2-(Azetidine-1-carbonyl)-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-nicotinamide,
6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-methoxy-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)nicotinamide,
5-chloro-2-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)pyrimidine-4-carboxamide,
2-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)isonicotinamide,
2-chloro-6-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)isonicotinamide,
or pharmaceutically acceptable salts thereof.

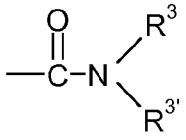
Another embodiment of the present invention relates to compounds of formula (I')



(I')

wherein

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy and lower alkoxy lower alkyl;

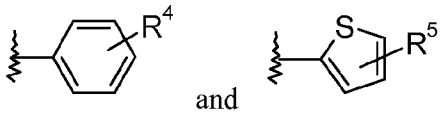
R^2 is 5- or 6-membered monocyclic heteroaryl having 1 to 3 heteroatoms independently selected from N and O, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of , halogen, hydroxyl, nitro, lower alkyl, lower alkoxy, lower alkoxy-C(O)-, lower hydroxyalkyl, lower haloalkyl, lower alkoxy lower alkyl, lower alkyl-C(O)-, cycloalkyl, heterocyclyl, aryl, heteroaryl and amino optionally substituted by heteroaryl, wherein two substituents of R^2, together with said heteroaryl to which they are attached, may form a 9- or 10-membered bicyclic ring;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl optionally substituted by cycloalkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl or heterocyclyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl optionally substituted by 1 to 3 halogen, hydroxyl or oxo;

or pharmaceutically acceptable salts thereof.

A particular embodiment of the present invention relates to compounds of formula (I') as described above, wherein R^1 is selected from the group consisting of:



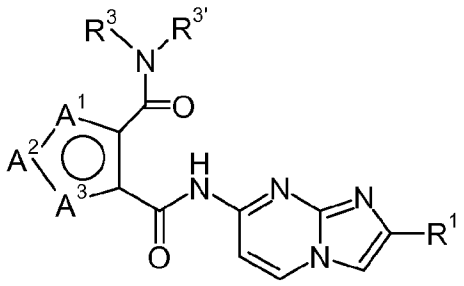
and

wherein

R^4 is hydrogen, halogen, lower alkoxy or lower haloalkoxy;

R^5 is halogen.

Another embodiment of the present invention relates to compounds of formula (Ia')



(Ia')

wherein

A^1 is -NH-, -N=, -NR^6- or -CH=;

A^2 is -N= or -$NR^{6'}$-;

A^3 is -N=, -$NR^{6''}$- or -CH=;

R^6 is lower alkyl;

$R^{6'}$ is lower alkyl;

$R^{6''}$ is lower alkyl;

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, lower alkoxy and lower haloalkoxy;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl optionally substituted by cycloalkyl, lower hydroxyalkyl, lower cyanoalkyl, lower alkoxy lower alkyl, cycloalkyl or heterocyclyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl optionally substituted by 1 or 2 halogen, hydroxyl or oxo.

Particular compounds of formula (Ia') are those selected from the group consisting of:
5-(Azetidine-1-carbonyl)-1H-[1,2,3]triazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-4-(morpholine-4-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(4-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide,
4-(3,3-Difluoro-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(3-Hydroxy-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

4-(1,1-Dioxo-1λ6-thiomorpholine-4-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-methoxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-[(tetrahydro-furan-3-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-1-methyl-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-diethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-4-(piperidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isopropyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(methyl-propyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-propylamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylmethyl-amide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclobutylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-isopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-trifluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-methylamide 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

3-(Azetidine-1-carbonyl)-1-methyl-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 3-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-cyano-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isobutyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-2-methyl-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
or pharmaceutically acceptable salts thereof.

Another embodiment of the present invention relates to compounds of formula (Ia') as described above,

wherein

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by halogen or lower alkoxy;

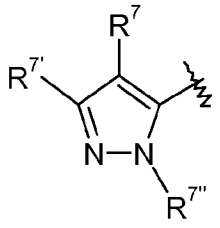
R^3 and $R^{3'}$ are independently lower alkyl or lower alkoxy lower alkyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form an azetidine ring or pyrrolidine ring.

Particular compounds of formula (Ia') are those selected from the group consisting of:
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
or pharmaceutically acceptable salts thereof.

Yet particular compounds of formula (Ia') are those selected from the group consisting of:
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
or pharmaceutically acceptable salts thereof.

Another embodiment of the present invention relates to compounds of formula (I') as described above, wherein R^2 is ,

wherein

R^7 is hydrogen, halogen, lower alkoxy-C(O)- or heteroaryl;

$R^{7'}$ is hydrogen, lower alkyl or nitro;

$R^{7''}$ is lower alkyl, cycloalkyl or aryl.

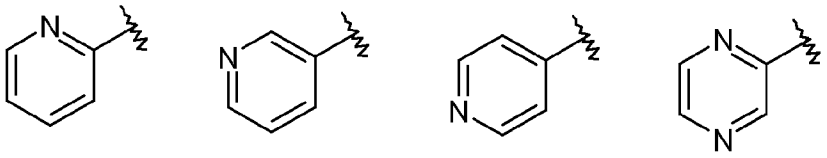
Particular compounds of formula (I') are those selected from the group consisting of:

4-Chloro-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Phenyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-propyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-isopropyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-sec-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-isobutyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Isobutyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Cyclopentyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Ethyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Isopropyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Isoxazol-5-yl-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
1-Ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester,
or pharmaceutically acceptable salts thereof.

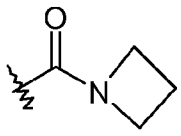
Yet particular compounds of formula (I') are those selected from the group consisting of:

Isoxazole-5-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4,5,6,7-Tetrahydro-benzo[d]isoxazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
5-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid methyl ester,
1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
or pharmaceutically acceptable salts thereof.

Another embodiment of the present invention relates to compounds of formula (I') as described above, wherein R^2 is 6-membered heteroaryl selected from the group consisting of:



wherein said heteroaryl is substituted by 1 to 3 substituents independently selected from the group consisting of bromo, chloro, methyl, methoxy, cyclopropyl, $-C(O)NHCH_2CF_3$,



and pyrimidin-5-ylamino.

Particular compounds of formula (I') are those selected from the group consisting of:
3,6-Dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Chloro-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-isonicotinamide,
6-Chloro-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
6-Methoxy-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
5-Bromo-3-methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-3,6-dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
6-Methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
Pyrazine-2,3-dicarboxylic acid 2-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 3-[(2,2,2-trifluoro-ethyl)-amide],

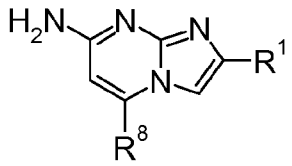
2-(Azetidine-1-carbonyl)-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-nicotinamide,
6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
or pharmaceutically acceptable salts thereof.

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It will be appreciated that the compounds of general formula (I) in this invention may be derivatised at functional groups to provide derivatives which are capable of conversion back to the parent compound in vivo.

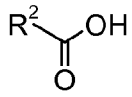
The invention further relates to a process for the manufacture of compounds of formula (I) as defined above, which process comprises:

reacting a compound of formula 3



3

with a compound of formula 2



2

wherein R^1, R^2 and R^8 are as defined above, and if desired, converting the compounds into pharmaceutically acceptable salts thereof.

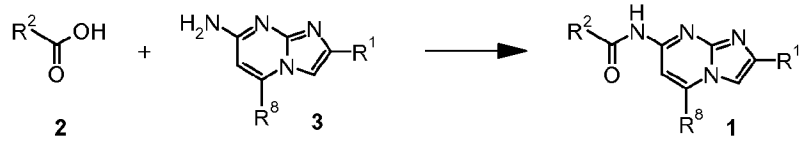
The reaction described above can be carried out under conditions as described in the description and examples or under conditions well known to the person skilled in the art.

The compounds of formula 2 and 3 can be prepared by methods known in the art or as described below or in analogy thereto.

The present invention also relates to compounds of formula (I) as defined above, when prepared by a process as described above.

Compounds of formula 1 can be prepared from building blocks 2 and 3 according to Scheme 1. The conversion, commonly known as amide coupling, can be achieved in several ways. In one method, the acid 2 is activated with a coupling reagent, such as 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), or propylphosphonic anhydride, and converted by addition of amine 3 to the desired product, 1. In another method, the acid 2 is activated by transformation into an acid chloride, e.g. by reaction with thionyl chloride. The acid chloride is then converted by addition of the amine 3 to the desired product, 1. A base, e.g. diisopropylethylamine (DIPEA), is usually added to bind liberated HCl.

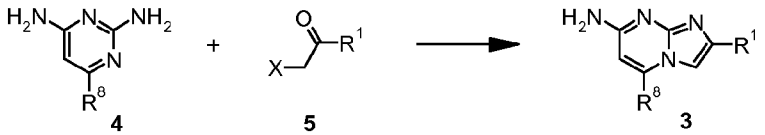
Scheme 1



2 3 1

Compounds of formula 3 can be prepared according to Scheme 2: 2,4-diaminopyrimidine (4) is reacted with a compound 5, such as a (substituted) 2-bromoacetophenone, or such as a (substituted) 2-bromo-1-thiophen-2-yl-ethanone, with a suitable base, such as $NaHCO_3$, to give 3. 2,4-Diaminopyrimidine 4 is commercially available; compounds 5 are either commercially available, or can be prepared by methods well known in the art.

Scheme 2

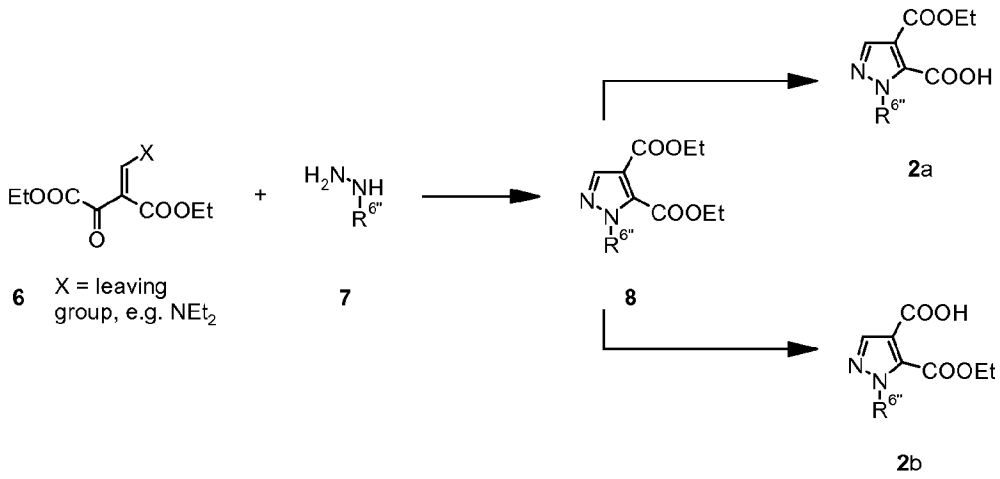


4 5 3

X = leaving group, e.g. Br

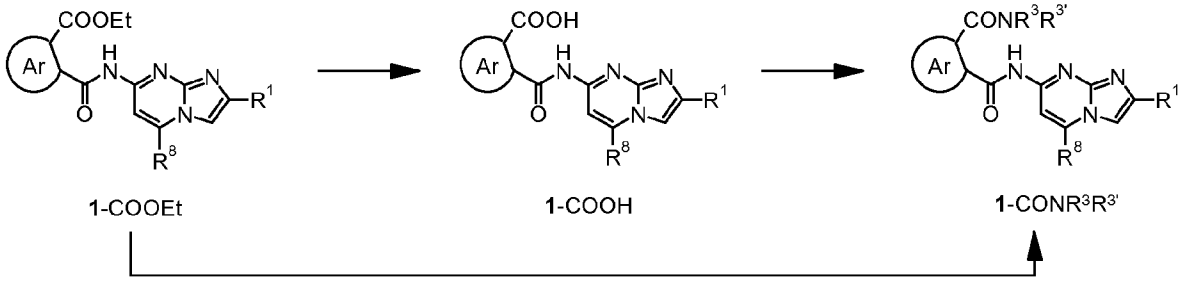
Compounds of formula 2, with R^2 being a pyrazolyl carboxylic acid derivative, can be prepared according to Scheme 3, wherein $R^{6''}$ is as defined above: Compound 6 is reacted with a hydrazine 7, or a salt thereof, to give a pyrazole 8 (similar to the method of A. Hanzlowsky, B. Jelencic, S. Recnik, J. Svete, A. Golobic, B. Stanovnik *J. Heterocyclic Chem.* 2003, *40*(3), 487-498). Selective mono-saponification of the diester 8 yields, depending on the reaction conditions, compound 2a or its isomer, compound 2b.

Scheme 3



Compounds of formula 1, with R^2 being a lower alkoxycarbonyl-substituted heteroaromatic ring, can be further transformed according to Scheme 4, wherein R^3 and $R^{3'}$ are as defined above. For instance, compounds of the general formula 1-COOEt can be saponified by suitable methods, e.g. by reaction with KOH, to give 1-COOH. Upon activation with a suitable reagent such as TBTU, 1-COOH can be converted with a primary or secondary amine to 1-CONR^{3}R$^{3'}$. Alternatively, 1-COOEt can be directly converted into 1-CO NR^{3}R$^{3'}$, e.g. by reaction with an amine such as methylamine.

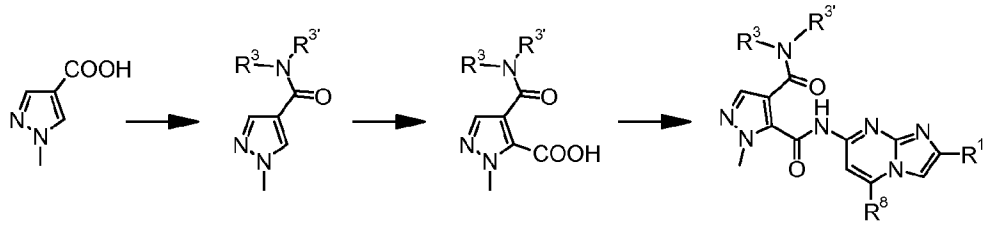
Scheme 4



Alternatively, compounds of formula 1, with R^2 being an amide-substituted pyrazole ring, can be obtained according to Scheme 5: Upon activation with a suitable reagent such as TBTU, 1-methyl-1H-pyrazole-4-carboxylic acid (9) can be converted with a primary or secondary amine to 10. A suitable base, such as triethylamine, may be added. Metallation with a suitable agent such as tBuLi, and subsequent reaction with CO_2 yields carboxylic acid 11. A complexing agent,

such as pentamethyldiethylenetriamine, may be added in the metallation step. Coupling of 11 with 3, in close analogy to Scheme 1, delivers 1-pyrazolylamide.

Scheme 5



9 10 11 1-pyrazolylamide

All reactions are typically performed in a suitable solvent and under an atmosphere of argon or nitrogen.

The corresponding salts with acids can be obtained by standard methods known to the person skilled in the art, e.g. by dissolving the compound of formula (I) in a suitable solvent such as e.g. dioxane or THF and adding an appropriate amount of the corresponding acid. The products can usually be isolated by filtration or by chromatography. The conversion of a compound of formula (I) into a pharmaceutically acceptable salt with a base can be carried out by treatment of such a compound with such a base. One possible method to form such a salt is e.g. by addition of 1/n equivalents of a basic salt such as e.g. $M(OH)_n$, wherein M is metal or ammonium cation and n is number of hydroxide anions, to a solution of the compound in a suitable solvent (e.g. ethanol, ethanol-water mixture, tetrahydrofuran-water mixture) and to remove the solvent by evaporation or lyophilisation.

The conversion of compounds of formula (I) into pharmaceutically acceptable esters can be carried out e.g. by treatment of a suitable carboxy group present in the molecule with a suitable alcohol using e.g. a condensating reagent such as benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP), N,N-dicylohexylcarbodiimide (DCC), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDCI) or O-(1,2-dihydro-2-oxo-1-pyridyl)-N,N,N,N-tetra-methyluronium-tetrafluoroborate (TPTU), or by direct reaction with a suitable alcohol under acidic conditions, as for example in the presence of a strong mineral acid like hydrochloric acid, sulfuric acid and the

like. Compounds having a hydroxyl group can be converted to esters with suitable acids by analogous methods.

Insofar as their preparation is not described in the examples, the compounds of formula (I) as well as all intermediate products can be prepared according to analogous methods or according to the methods set forth above. Starting materials are commercially available, known in the art or can be prepared by methods known in the art or in analogy thereto.

As described above, the novel compounds of the present invention have been found to inhibit PDE10A activity. The compounds of the present invention can therefore be used, either alone or in combination with other drugs, for the treatment and/or prophylaxis of diseases which are modulated by PDE10A inhibitors. These diseases include, but are not limited to, certain psychotic disorders such as schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder or substance-induced psychotic disorder, anxiety disorders such as panic disorder, obsessive/compulsive disorders, acute stress disorder or generalized anxiety disorder, drug addictions, movement disorders such as Parkinson's disease or restless leg syndrome, cognition deficiency disorders such as Alzheimer's disease or multi-infarct dementia, mood disorders such as depression or bipolar disorders, or neuropsychiatric conditions such as psychosis, attention-deficit/hyperactivity disorder (ADHD) or related attentional disorders. Other disorders are diabetes and related disorders, such as type 2 diabetes mellitus, neurodegenerative disorders such as Alzheimer's disease, Huntington's disease, Parkinson's disease, multiple sclerosis, stroke or spinal cord injury, solid tumors and hematological malignancies such as renal cell carcinoma or breast cancer.

The invention therefore also relates to pharmaceutical compositions comprising a compound as defined above and a pharmaceutically acceptable carrier and/or adjuvant.

The invention likewise embraces compounds as described above for use as therapeutically active substances, especially as therapeutically active substances for the treatment and/or prophylaxis of diseases which are modulated by PDE10A inhibitors, particularly as therapeutically active substances for the treatment and/or prophylaxis of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma and breast cancer.

In another embodiment, the invention relates to a method for the therapeutic and/or prophylactic treatment of diseases which are modulated by PDE10A inhibitors, particularly for the therapeutic and/or prophylactic treatment of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma and breast cancer, which method comprises administering a compound as defined above to a human being or animal.

The invention also embraces the use of compounds as defined above for the therapeutic and/or prophylactic treatment of diseases which are modulated by PDE10A inhibitors, particularly for the therapeutic and/or prophylactic treatment of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma and breast cancer.

The invention also relates to the use of compounds as described above for the preparation of medicaments for the therapeutic and/or prophylactic treatment of diseases which are modulated by PDE10A inhibitors, particularly for the therapeutic and/or prophylactic treatment of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety

disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma and breast cancer. Such medicaments comprise a compound as described above.

In another embodiment, the invention relates to a compound or a pharmaceutically acceptable salt thereof as defined above for the treatment or prophylaxis of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma or breast cancer.

Prevention and/or treatment of schizophrenia is a particular indication. Yet particular indication is prevention and/or treatment of positive, negative and/or cognitive symptoms associated with schizophrenia.

The following test was carried out in order to determine the activity of the compounds of the present invention. PDE10 activity of the compounds of the present invention was determined using a Scintillation Proximity Assay (SPA)-based method similar to the one previously described (Fawcett, L. et al., ProcNatl Acad Sci USA (2000) 97(7):3702-3707).

The human PDE10A full length assay was performed in 96-well micro titer plates. The reaction mixture of 50 µl contained 20 mM HEPES pH=7.5 /10 mM $MgCl_2$/0.05 mg/ml BSA (Sigma cat. # A-7906), 50 nM cGMP (Sigma, cat. # G6129) and 50 nM [^{3}H]-cGMP (GE Healthcare, cat. # TRK392 S.A. 13.2Ci/mmol), 3.75 ng/well PDE10A enzyme (Enzo Life Science, Lausen, Switzerland cat # SE-534) with or without a specific test compound. A range of concentrations of the potential inhibitor was used to generate data for calculating the concentration of inhibitor resulting in 50% of the effect (e.g. IC_{50}, the concentration of the competitor inhibiting PDE10A activity by 50%). Non-specific activity was tested without the enzyme. The reaction was initiated by the addition of the substrate solution (cGMP and [^{3}H]-cGMP) and allowed to progress for 20 minutes at room temperature. The reaction was terminated by adding 25 µl of YSi-SPA scintillation beads (GE Healthcare, cat. # RPNQ0150) in 18 mM zinc sulphate solution (stop reagent). After 1 h under shaking, the plate was centrifuged one minute at 170 g to allow beads to settle. Afterwards, radioactive counts were measured on a Perkin Elmer TopCount Scintillation plate reader.

The compounds according to formula (I) have an IC_{50} value below 10 µM, more specifically below 5 µM, yet more specifically below 1 µM. The following table shows data for some examples.

Example	PDE10A inhibition IC_{50} [µmol/l]
2	0.9513
3	0.097
4	0.6709
5	0.0268
6	0.3841

Example	PDE10A inhibition IC_{50} [µmol/l]
7	0.1404
8	0.0647
9	0.0446
10	0.105
11	0.1053
12	0.0188
13	0.0479
14	0.1252
15	0.7485
16	0.0821
17	0.0283
18	0.1475
19	0.5529
20	0.6431
21	0.3136
22	0.042
23	0.0643
24	0.3207
25	0.324
26	0.024
27	0.1627
28	0.2509
29	0.0033
30	0.0331

Example	PDE10A inhibition IC_{50} [µmol/l]
32	0.0228
34	0.035
36	0.032
38	0.0229
39	0.0864
43	0.8996
44	0.8128
45	0.0083
46	0.7848
47	0.0152
48	0.0035
49	0.0019
50	0.0244
51	0.0148
52	0.0029
53	0.0236
54	0.0343
55	0.0085
56	0.0173
57	0.023
58	0.0273
59	0.0211
60	0.0806
61	0.0235

Example	PDE10A inhibition IC_{50} [µmol/l]
62	0.0129
63	0.0048
64	0.0065
65	0.0348
66	0.0115
67	0.0257
68	0.0377
69	0.0044
70	0.0332
71	0.0176
72	0.4634
73	0.0028
74	0.004
75	0.0049
77	0.0063
78	0.1246
79	0.2467
80	0.4963
81	0.7034
82	0.0034
83	0.0034
84	0.0038
85	0.004
86	0.0052

Example	PDE10A inhibition IC_{50} [µmol/l]
87	0.0055
88	0.0057
89	0.0061
90	0.0061
91	0.0061
92	0.0065
93	0.0083
94	0.0112
95	0.0122
96	0.0126
97	0.0147
98	0.0147
99	0.019
100	0.0218
101	0.022
102	0.0279
103	0.0287
104	0.0296
105	0.0366
106	0.0433
107	0.0519
108	0.0817
109	0.089
110	0.2219

Example	PDE10A inhibition IC_{50} [µmol/l]
111	0.3644
112	0.0013
113	0.0026
114	0.0028
115	0.0051
116	0.0051
117	0.0062
118	0.0119
119	0.0133
120	0.0137
121	0.0167
122	0.0169
123	0.0173
124	0.0177
125	0.0187
126	0.0247
127	0.0259
128	0.026
129	0.0332
130	0.0349
131	0.0351
132	0.0486
133	0.0522
134	0.0576

Example	PDE10A inhibition IC_{50} [µmol/l]
135	0.0641
136	0.0997
137	0.1173
138	0.1305
139	0.1484
140	0.1506
141	0.1509
142	0.1517
143	0.162
144	0.1984
145	0.2105
146	0.2123
147	0.2345
148	0.2439
149	0.2602
150	0.2634
151	0.2875
152	0.3022
153	0.3053
154	0.3148
155	0.346
156	0.359
157	0.3895
158	0.427

Example	PDE10A inhibition IC_{50} [µmol/l]
159	0.4508
160	0.4585
161	0.5471
162	0.6236
163	0.636
164	0.725
165	0.7759
166	0.8121
167	0.8247
168	0.8654
169	0.9633
170	0.9693
171	0.9886

The compounds of formula (I) and/or their pharmaceutically acceptable salts can be used as medicaments, e.g. in the form of pharmaceutical preparations for enteral, parenteral or topical administration. They can be administered, for example, perorally, e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatin capsules, solutions, emulsions or suspensions, rectally, e.g. in the form of suppositories, parenterally, e.g. in the form of injection solutions or suspensions or infusion solutions, or topically, e.g. in the form of ointments, creams or oils.

The production of the pharmaceutical preparations can be effected in a manner which will be familiar to any person skilled in the art by bringing the described compounds of formula (I) and/or their pharmaceutically acceptable salts, optionally in combination with other therapeutically valuable substances, into a galenical administration form together with suitable, non-toxic, inert, therapeutically compatible solid or liquid carrier materials and, if desired, usual pharmaceutical adjuvants.

Suitable carrier materials are not only inorganic carrier materials, but also organic carrier materials. Thus, for example, lactose, corn starch or derivatives thereof, talc, stearic acid or its salts can be used as carrier materials for tablets, coated tablets, dragées and hard gelatin capsules. Suitable carrier materials for soft gelatin capsules are, for example, vegetable oils, waxes, fats and semi-solid and liquid polyols (depending on the nature of the active ingredient no carriers might, however, be required in the case of soft gelatin capsules). Suitable carrier materials for the production of solutions and syrups are, for example, water, polyols, sucrose, invert sugar and the like. Suitable carrier materials for injection solutions are, for example, water, alcohols, polyols, glycerol and vegetable oils. Suitable carrier materials for suppositories are, for example, natural or hardened oils, waxes, fats and semi-liquid or liquid polyols. Suitable carrier materials for topical preparations are glycerides, semi-synthetic and synthetic glycerides, hydrogenated oils, liquid waxes, liquid paraffins, liquid fatty alcohols, sterols, polyethylene glycols and cellulose derivatives.

Usual stabilizers, preservatives, wetting and emulsifying agents, consistency-improving agents, flavour-improving agents, salts for varying the osmotic pressure, buffer substances, solubilizers, colorants and masking agents and antioxidants come into consideration as pharmaceutical adjuvants.

The dosage of the compounds of formula (I) can vary within wide limits depending on the disease to be controlled, the age and the individual condition of the patient and the mode of administration, and will, of course, be fitted to the individual requirements in each particular case. For adult patients a daily dosage of about 0.1 to 2000 mg, especially about 1 to 500 mg, comes into consideration. Depending on severity of the disease and the precise pharmacokinetic profile the compound could be administered with one or several daily dosage units, e.g. in 1 to 3 dosage units.

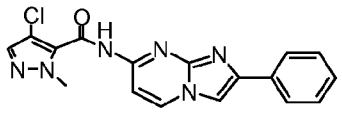
The pharmaceutical preparations conveniently contain about 0.1-500 mg, more specifically 1-200 mg, of a compound of formula (I).

The following examples serve to illustrate the present invention in more detail. They are, however, not intended to limit its scope in any manner.

Examples

Example 1

4-Chloro-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylamine

Bromoacetophenone (2.71 g, 14 mmol) was added to a solution of 2,4-diaminopyrimidine (1.00 g, 9 mmol) in acetone (40 ml), and the mixture was heated to reflux for 5 h. The cooled suspension was filtered, the precipitate was washed (acetone), and then stirred for 15 min in a mixture of 10 ml water and 15 ml NH_4OH (25%). The suspension was filtered, washed (water), and dried under vacuum. The crude product (1.9 g, quant.) was used in the next step without further purification.

MS (m/e) = 211.1 [$M+H^+$].

Step 2: 4-Chloro-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

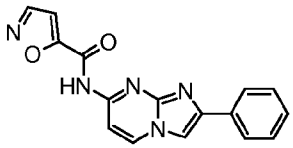
TBTU (2-[1H-benzotriazole-1-yl]-1,1,3,3-tetramethyluronium tetrafluoroborate, 180 mg, 0.56 mmol) and diisopropylethylamine (181 mg, 1.4 mmol) were added to a solution of 4-chlor-2-methyl-2H-pyrazole-3-carboxylsäure (ArtChem, 75 mg, 0.47 mmol) in DMF (2 ml), and the mixture was stirred for 30 min. 2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (100 mg, 0.48 mmol) was added to the black solution, and the mixture was stirred overnight at RT. Due to incomplete conversion, additional amounts of 4-chloro-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide, TBTU, and diisopropylethylamine were added, and the mixture was stirred for an additional 24 h. The reaction mixture was taken up in ethyl acetate, washed (water), dried (Na_2SO_4), and concentrated under reduced pressure. The title compound (17 mg, 10%) was obtained from the residue by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min:

95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 353.2 [$M+H^+$].

Example 2

Isoxazole-5-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

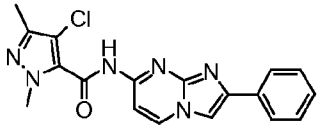


Triethylamine and 5-ethyl-isoxazole-3-carbonyl chloride were added to a solution of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1,) in dichloromethane, and the mixture was stirred at RT overnight. The title compound (29 mg, 16%) was isolated from the mixture by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min: 95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 306.3 [$M+H^+$].

Example 3

4-Chloro-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



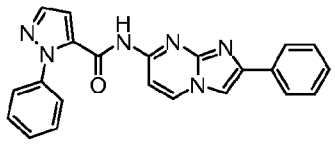
4-Chloro-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (100 mg, 0.57 mmol) and diisopropylethylamine (369 mg, 2.86 mmol) were added to a solution of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1, 100 mg, 0.48 mmol) in ethyl acetate (3 ml). At 0°C, propylphosphonic acid anhydride (1-propanephosphonic acid cyclic anhydride, 50% in ethyl acetate, 0.7 ml, 2.5 eq.) was added dropwise to the mixture. After stirring for 30 min at 0°C, the mixture was stirred overnight at RT. The mixture was taken up in ethyl acetate, washed (water),

dried (Na_2SO_4), and concentrated under reduced pressure. The title compound (16 mg, 9%) was obtained from the residue by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min: 95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 367.1 [$M+H^+$].

Example 4

2-Phenyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

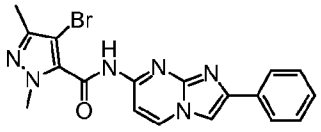


The title compound was obtained in analogy to example 3 from 4-chloro-2,5-dimethyl-2H-pyrazole-3-carboxylic acid.

MS (m/e) = 381.2 [$M+H^+$].

Example 5

4-Bromo-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

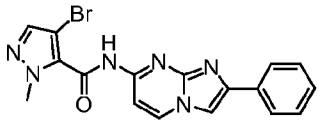


The title compound was obtained in analogy to example 3 from 4-bromo-2,5-dimethyl-2H-pyrazole-3-carboxylic acid.

MS (m/e) = 411.2 [$M+H^+$].

Example 6

4-Bromo-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

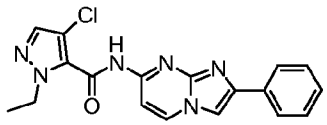


The title compound was obtained in analogy to example 3 from 4-bromo-2-methyl-2H-pyrazole-3-carboxylic acid.

MS (m/e) = 397.2 [M+H$^+$].

Example 7

4-Chloro-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

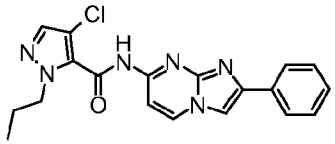


The title compound was obtained in analogy to example 3 from 4-chloro-2-ethyl-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 367.2 [M+H$^+$].

Example 8

4-Chloro-2-propyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

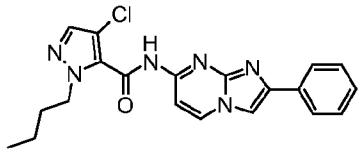


The title compound was obtained in analogy to example 3 from 4-chloro-2-propyl-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 381.2 [M+H$^+$].

Example 9

2-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

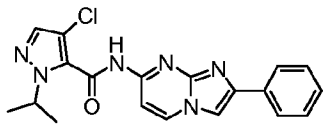


The title compound was obtained in analogy to example 3 from 4-Chloro-2-butyl-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 395.1 [M+H$^+$].

Example 10

4-Chloro-2-isopropyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

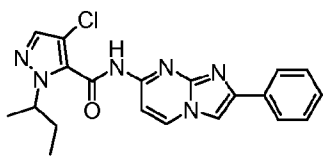


The title compound was obtained in analogy to example 3 from 4-chloro-2-isopropyl-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 381.3 [M+H$^+$].

Example 11

2-sec-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

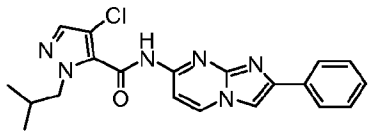


The title compound was obtained in analogy to example 3 from 2-sec-butyl-4-chloro-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 395.2 [M+H$^+$].

Example 12

4-Chloro-2-isobutyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

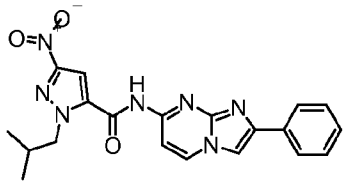


The title compound was obtained in analogy to example 3 from 4-chloro-2-isobutyl-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 395.1 [$M+H^+$].

Example 13

2-Isobutyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

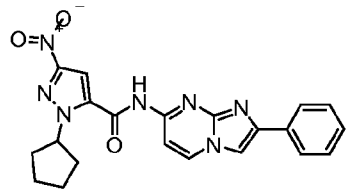


The title compound was obtained in analogy to example 3 from 2-isobutyl-5-nitro-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 406.3 [$M+H^+$].

Example 14

2-Cyclopentyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

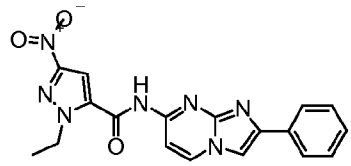


The title compound was obtained in analogy to example 3 from 2-cyclopentyl-5-nitro-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 418.3 [M+H$^+$].

Example 15

2-Ethyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

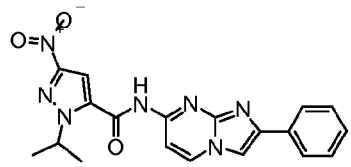


The title compound was obtained in analogy to example 3 from 2-ethyl-5-nitro-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 378.3 [M+H$^+$].

Example 16

2-Isopropyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

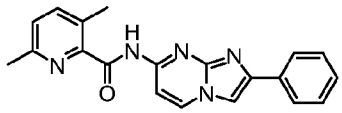


The title compound was obtained in analogy to example 3 from 2-isopropyl-5-nitro-2H-pyrazole-3-carboxylic acid (ArtChem).

MS (m/e) = 392.2 [M+H$^+$].

Example 17

3,6-Dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 3,6-Dimethyl-pyridine-2-carboxylic acid methyl ester

Trimethylsilyldiazomethane 2M in ether (5.7 ml, 11.4 mmole, 1.4 eq.) is added dropwise at RT to a suspension of 3,6-dimethyl-pyridine-2-carboxylic acid (containing potassium chloride) (3.07 g à 25%, 8.12 mmole, 1 eq.) in benzene (24 ml) and methanol (8 ml), and the yellow suspension is stirred at RT for 1.5 h. The yellow mixture is diluted with ethyl actate, washed once with sat. aqueous sodium bicarbonate sol., once with water, once with brine, dried with magnesium sulfate and the solvents are removed in vacuo. Purification of the residue (914 mg) by chromatography on a 20 g Silicycle silica cartridge (eluent heptane / ethyl acetate 5 – 40% 20 min) affords 3,6-dimethyl-pyridine-2-carboxylic acid methyl ester (714 mg, 53.2%) as a colorless liquid.

MS (m/e) = 166.3 [M+H$^+$].

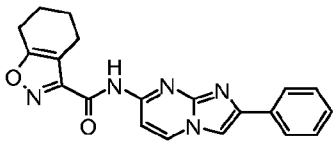
Step 2: 3,6-Dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

To a white suspension of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1, 80 mg, 0.38 mmole) in dioxane (3 ml) is added at RT trimethyl aluminium sol. 2M in toluene (0.8 ml, 1.52 mmole, 4 eq.). The mixture is stirred for 45 min at RT. A solution of 3,6-dimethyl-pyridine-2-carboxylic acid methyl ester (63 mg, 0.38 mmole, 1 eq.) in dioxane (0.4 ml) is then added and the light brown solution is refluxed overnight. The brown solution is loaded on 2 g silica and purified by chromatography on a 12 g RediSep silica cartridge (eluent heptane / ethyl acetate 30 - 70% 15 min) affording 3,6-dimethyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)picolinamide (57 mg, 43.6%) as a white solid.

MS (m/e) = 344.2 [M+H$^+$].

Example 18

4,5,6,7-Tetrahydro-benzo[d]isoxazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

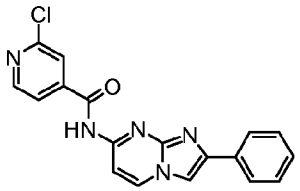


The title compound was obtained in analogy to example 3 from 4,5,6,7-tetrahydro-1,2-benzisoxazole-3-carboxylic acid (ArtChem).

MS (m/e) = 360.3 [$M+H^+$].

Example 19

2-Chloro-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-isonicotinamide

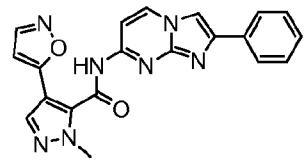


The title compound was obtained in analogy to example 3 from 2-chloroisonicotinic acid.

MS (m/e) = 350.3 [$M+H^+$].

Example 20

4-Isoxazol-5-yl-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

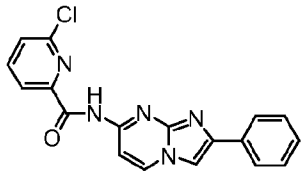


The title compound was obtained in analogy to example 3 from 4-(5-isoxazolyl)-1-methyl-1H-pyrazole-5-carboxylic acid.

MS (m/e) = 386.1 [M+H$^+$].

Example 21

6-Chloro-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

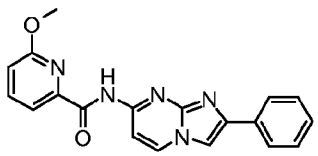


The title compound was obtained in analogy to example 3 from 6-chloropicolinic acid.

MS (m/e) = 350.1 [M+H$^+$].

Example 22

6-Methoxy-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

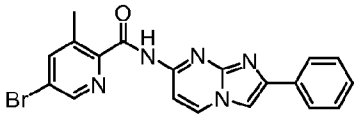


The title compound was obtained in analogy to example 3 from 6-methoxypicolinic acid.

MS (m/e) = 346.1 [M+H$^+$].

Example 23

5-Bromo-3-methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



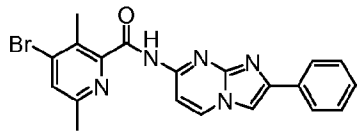
To an argon purged solution of 2-phenylimidazo[1,2-a]pyrimidin-7-amine (example 1, step 1, 80 mg, 0.381 mmol) in dioxane (5 ml) was added trimethyl aluminum solution (0.571 ml, 1.14 mmol, 3 eq). The resulting solution was stirred for 1 hour at RT. Then methyl 5-bromo-3-

methylpicolinate (88 mg, 0.381 mmol) was added and the mixture was heated to reflux and stirred for 18 hours. The title compound (84 mg, 54%) was isolated from the crude product by flash chromatography on a 20 g SiO_2 column using dichloromethane / methanol 0-10 % as eluent.

MS (m/e) = 408.2 [$M+H^+$].

Example 24

4-Bromo-3,6-dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



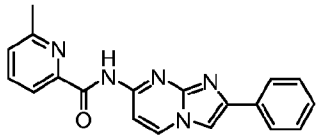
The title compound was obtained in analogy to example 23 from ethyl 4-bromo-3,6-dimethylpicolinate.

(Ethyl 4-bromo-3,6-dimethylpicolinate can be prepared by the method of G. Jaeschke, W. Spooren, E. Vieira, PCT Int. Appl. WO 2007093542.)

MS (m/e) = 424.0 [$M+H^+$].

Example 25

6-Methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

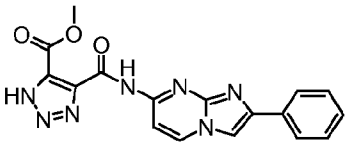


The title compound was obtained in analogy to example 23 from ethyl 4-bromo-3,6-dimethylpicolinate.

MS (m/e) = 330.2 [$M+H^+$].

Example 26

5-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid methyl ester

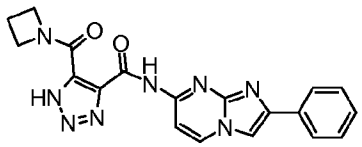


The title compound was obtained in analogy to example 3 from 1H-[1,2,3]triazole-4,5-dicarboxylic acid 5-methyl ester. (1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-methyl ester can be prepared by the method of J. Aszodi, M. Lampilas, B. Musicki, D. A. Rowlands, P. Collette, PCT Int. Appl. WO 2002100860.)

MS (m/e) = 364.1 [M+H$^+$].

Example 27

5-(Azetidine-1-carbonyl)-1H-[1,2,3]triazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 5-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid

NaOH (3N, 1.47 ml) was added to a solution of 5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid methyl ester (example 26, 800 mg, 2.2 mmol) in methanol / THF = 1:1 (16 ml), and the mixture was stirred for 6 h at RT. The mixture was acidified (pH = 3) with HCl (2N), the suspension was stirred for 15 min, and filtered. The precipitated title compound (590 mg, 77%) was dried under vacuum, and used in the next step without further purification.

MS (m/e) = 348.3 [M-H$^+$].

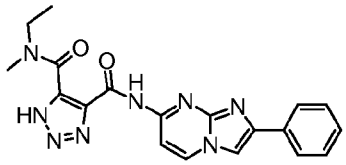
Step 2: 5-(Azetidine-1-carbonyl)-1H-[1,2,3]triazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

Diisopropylethylamine (89 mg, 0.69 mmol) and TBTU (88 mg, 0.27 mmol) were added to a solution of 5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid (80 mg, 0.23 mmol) in DMF (1 ml), and the dark brown solution was stirred for 30 min at RT. Azetidine (39 mg, 0.68 mmol) was added, and the mixture was stirred at RT overnight. The title compound (25 mg, 28%) was obtained from the reaction mixture by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min: 95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 389.3 [$M+H^+$].

Example 28

1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

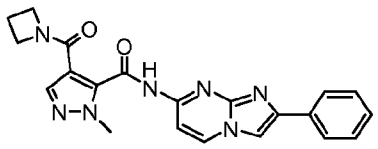


The title compound was obtained in analogy to example 27 from ethylmethylamine.

MS (m/e) = 391.2 [$M+H^+$].

Example 29

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 2-Methyl-2H-pyrazole-3,4-dicarboxylic acid diethyl ester

Under an atmosphere of argon, methylhydrazine (1.15 g, 25 mmol) and HCl (36,5% in water, 2.5 ml) were added to a solution of 2-dimethylaminomethylene-3-oxo-succinic acid diethyl ester

(6.07 g, 25 mmol, obtained by the method of Hanzlowsky et al., *J. Heterocyclic Chem.* **2003**, *40*(3), 487-498) in ethanol (200 ml). The mixture was heated to 60 °C until HPLC analysis indicated the disappearance of the starting material (2 h). The solvent was evaporated, and the residue was taken up in dichloromethane and washed (water). The organic layer was dried (Na_2SO_4), the solvent was evaporated and the title compound (2.06 mg, 36%) was isolated from the mixture by column chromatography (silica gel, heptane : ethyl acetate = 100:0 – 60:40). (The regioisomeric 1-methyl-1H-pyrazole-3,4-dicarboxylic acid diethyl ester can also be isolated, and can be distinguished from the desired product by NOE-^{1}H-NMR.) MS (m/e) = 227.2 [$M+H^+$].

Step 2: 2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethyl ester

(This compound was prepared in close analogy to the method of Pérez et al., Spanish patent appl. ES 493459.) 2-Methyl-2H-pyrazole-3,4-dicarboxylic acid diethyl ester (2.06 g, 9.1 mmol) was suspended in a NaOH solution (0.5M in water, 20 ml, 10 mmol) and heated to reflux (30 min). If the conversion was incomplete after this time, as indicated by HPLC control, small amounts of NaOH were added in 30 min intervals. The reaction mixture was cooled, and HCl was added, and stirred for an additional 30 min (r.t.). The precipitate was filtered, washed (water, small amount) and dried under vacuum. The title compound was obtained as a white solid (1.27 g, 70%), and was used in the next step without further purification. MS (m/e) = 198 [$M+H^+$].

Step 3: 5-Chlorocarbonyl-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester

A mixture of 2-methyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethyl ester (6.00 g) and thionyl chloride (82.8 g) was refluxed for 4 h. Excess thionyl chloride was removed under educed pressure; the obtained crude product (7.26 g, assumed purity ~60%, 66%) was used in the next step without further purification.

Step 4: 1-Methyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester

5-Chlorocarbonyl-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester (3.60g, assumed purity 60%, 10 mmol) was added slowly to a cooled (0°C) solution of 2-phenylimidazo[1,2-a]pyrimidin-7-amine (example 1, step 1, 2.52 g, 12 mmol) and triethylamine (2.02 g, 20 mmol) in dichloromethane (50 ml), and the suspension was stirred overnight at RT. The mixture was

taken up in dichloromethane, and washed with water. The combined organic layers were dried (Na_2SO_4), filtered, and the solvent was evaporated under reduced pressure. The title compound (2.75 g, 71%) was isolated from the residue by column chromatography (silica gel, heptane : ethyl acetate = 100:0 – 60:40).

MS (m/e) = 391.2 [$M+H^+$].

Step 5: 1-Methyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid

NaOH (3N, 6.9 ml) was added to a solution of 1-methyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester (2.70 g, 6.9 mmol) in THF / ethanol = 1:1 (40 ml), an the mixture was stirred at RT overnight. Water (10 ml) and HCl (conc., approx. 3 ml) were added to the cooled (0 °C) mixture, until the mixture had a pH of 3. The suspension was stirred for 15 min, and filtered. The precipitate was washed with a small amount of water, and dried under vacuum. The thus obtained product (910 mg, 36%) was used in the next step without further purification.

MS (m/e) = 361.3 [$M-H^+$].

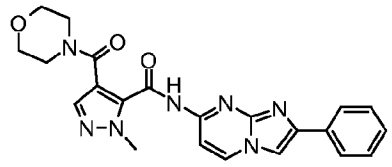
Step 6: 4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

TBTU (213 mg, 0.66 mmol) and diisopropylethylamine (214 mg, 1.66 mmol) were added to a solution of 1-methyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid (200 mg, 0.55 mmol) in DMF (2 ml), and the mixture was stirred for 30 min. Azetidine (95 mg, 1.66 mmol) was added, and the mixture was stirred at RT overnight. Water (6 ml) was added, and the suspension was stirred for 15 min at RT, and then filtered. The precipitate was suspended in a mixture of DMF (2 ml) and methanol (1 ml). The suspension was stirred for 15 min, and filtered. The obtained title compound was dried under vacuum.

MS (m/e) = 402.4 [$M+H^+$].

Example 30

2-Methyl-4-(morpholine-4-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

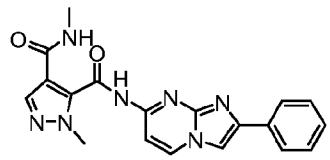


The title compound was obtained in analogy to example 29, using morpholine in the last step.

MS (m/e) = 432.3 [M+H$^+$].

Example 31

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

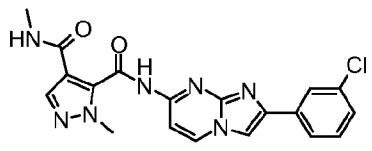


Methylamine (2N in methanol, 1.54 ml, 3.1 mmol) was added to a solution of 1-methyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester (example 29, Step 4, 100 mg, 0.26 mmol) in THF (1.5 ml), and the mixture was stirred over the weekend at RT. The solvent was evaporated, DMF (1.5 ml) was added to the residue, and the mixture was stirred for 5 min. The precipitated title compound (20 mg, 21%) was collected by filtration, and residual DMF was removed under vacuum.

MS (m/e) = 376.4 [M+H$^+$].

Example 32

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide

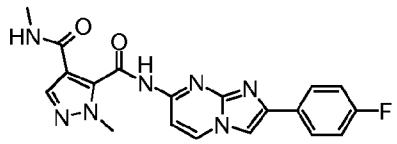


The title compound was prepared in analogy to example 31 from 5-[2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl]-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester. 5-[2-(3-Chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl]-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester was prepared in analogy to example 29, using 2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine in step 4. 2-(3-Chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine was prepared in analogy to example 1, step 1, from 2-bromo-1-(3-chloro-phenyl)-ethanone.

MS (m/e) = 410.2 [M+H$^+$].

Example 33

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(4-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide

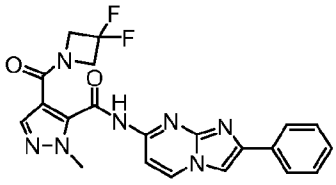


The title compound was prepared in analogy to example 31 from 5-[2-(4-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl]-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester. 5-[2-(4-Fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl]-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester was prepared in analogy to example 29, using 2-(4-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine in step 4. 2-(4-Fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine was prepared in analogy to example 1, step 1, from 2-bromo-1-(4-fluoro-phenyl)-ethanone.

MS (m/e) = 394.1 [M+H$^+$].

Example 34

4-(3,3-Difluoro-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

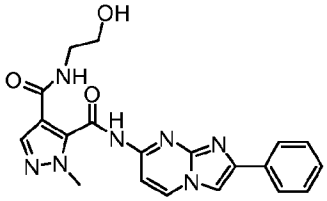


The title compound was obtained in analogy to example 29, using 3,3-difluoro-azetidine in the last step.

MS (m/e) = 438.3 [M+H$^+$].

Example 35

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

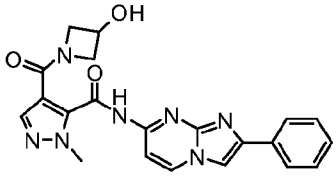


The title compound was obtained in analogy to example 29, using 2-amino-ethanol in the last step.

MS (m/e) = 406.4 [M+H$^+$].

Example 36

4-(3-Hydroxy-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

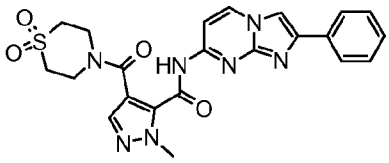


The title compound was obtained in analogy to example 29, using azetidin-3-ol in the last step.

MS (m/e) = 418.3 [M+H$^+$].

Example 37

4-(1,1-Dioxo-1λ6-thiomorpholine-4-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

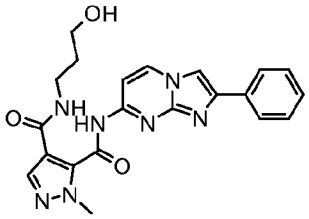


The title compound was obtained in analogy to example 29, using thiomorpholine 1,1-dioxide in the last step.

MS (m/e) = 480.2 [M+H$^+$].

Example 38

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

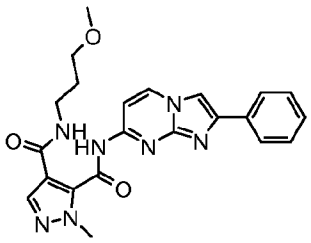


The title compound was obtained in analogy to example 29, using 3-amino-propan-1-ol in the last step.

MS (m/e) = 420.2 [M+H$^+$].

Example 39

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-methoxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

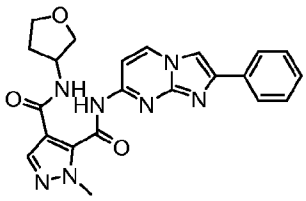


The title compound was obtained in analogy to example 29, using 3-methoxy-propylamine in the last step.

MS (m/e) = 434.3 [M+H$^+$].

Example 40

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-[(tetrahydro-furan-3-yl)-amide]

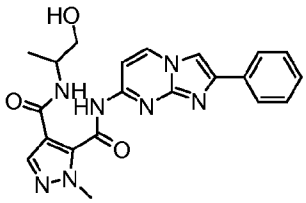


The title compound was obtained in analogy to example 29, using tetrahydro-furan-3-ylamine in the last step.

MS (m/e) = 432.3 [M+H$^+$].

Example 41

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-1-methyl-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

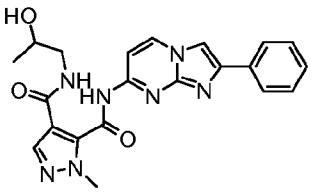


The title compound was obtained in analogy to example 29, using 2-amino-propan-1-ol in the last step.

MS (m/e) = 420.1 [M+H$^+$].

Example 42

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

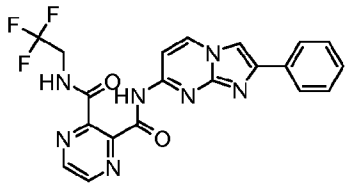


The title compound was obtained in analogy to example 29, using 1-amino-propan-2-ol in the last step.

MS (m/e) = 420.2 [M+H$^+$].

Example 43

Pyrazine-2,3-dicarboxylic acid 2-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 3-[(2,2,2-trifluoro-ethyl)-amide]



Step 1: 3-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-pyrazine-2-carboxylic acid

Furo[3,4-b]pyrazine-5,7-dione (736 mg, 4.9 mmol) and DMAP (58 mg, cat.) were added to a solution of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1, 1.00 g, 4.8 mmol) in DMF (25 ml). The mixture was heated to 78°C overnight, and cooled to RT. The formed precipitate was collected by filtration, and residual solvent was removed under vacuum. The thus obtained crude product (800 mg, 47%) was used in the next step without further purification.

MS (m/e) = 361.3 [M+H$^+$].

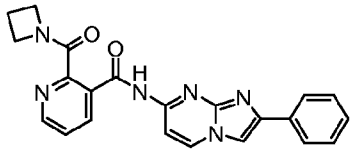
Step 2: Pyrazine-2,3-dicarboxylic acid 2-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 3-[(2,2,2-trifluoro-ethyl)-amide]

In a sealable tube, TBTU (75 mg, 0.23 mmol), 3-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-pyrazine-2-carboxylic acid (70 mg, 0.19 mmol), and diisopropylethylamine (75 mg, 0.58 mmol) were dissolved in DMF (2 ml) and shaken for 1 h at RT. Trifluoroethylamine (23 mg, 0.23 mmol) was then added, and the mixture was shaken at RT overnight. The title compound was isolated from the reaction mixture by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min: 95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 442.2 [$M+H^+$].

Example 44

2-(Azetidine-1-carbonyl)-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-nicotinamide



Step 1: 3-Chlorocarbonyl-pyridine-2-carboxylic acid methyl ester

Pyridine-2,3-dicarboxylic acid 2-methyl ester (500 mg, 2.76 mmol) was dissolved in thionyl chloride (8.21 g, 68 mmol) and heated to reflux for 4 h. Excess thionyl chloride was removed under vacuum. The obtained crude product (620 mg, assumed purity 60%, 68% yield) was used in the next step without further purification.

Step 2: 3-[(2-Phenyl-imidazo[1,2-a]pyrimidin-7-yl)-(pyridine-2-[carboxylic acid methyl ester]-3-carbonyl)-carbamoyl]-pyridine-2-carboxylic acid methyl ester

3-Chlorocarbonyl-pyridine-2-carboxylic acid methyl ester (620 mg, 3.1 mmol) was added slowly to a solution of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (step 1, example 1, 470 mg, 2.2 mmol) and triethylamine (566 mg) in dichloromethane (7 ml), and the mixture was stirred overnight at RT. The mixture was diluted with additional dichloromethane, and washed with water. The combined organic layers were dried (Na_2SO_4), the solvent was evaporated, and the

title compound (490 mg, 49%) was obtained from the residue by by column chromatography (silica gel, dichloromethane : methanol = 50:50 – 0:100).

MS (m/e) = 374.2 [$M+H^+$].

Step 3: 3-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-pyridine-2-carboxylic acid

NaOH (3N, 2.2 ml, 6.6 mmol) was added to a solution of 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-(pyridine-2-[carboxylic acid methyl ester]-3-carbonyl)-carbamoyl]-pyridine-2-carboxylic acid methyl ester (1.18 g, 2.2 mmol) in methanol / THF = 1:1, and the mixture was stirred for 5 h at RT. The mixture was acidified to pH = 3 by addition of HCl (conc.), and the volatile solvents were evaporated under reduced pressure. Water was added to the obtained suspension, and the mixture was stirred for 15 min at RT. The precipitate was collected by filtration, washed with water, and dried under vacuum. The thus obtained product (290 mg, 37%) was used in the next step without further purification.

MS (m/e) = 358.3 [$M-H^+$].

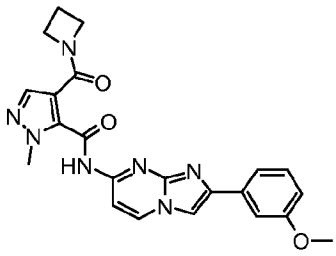
Step 4: 2-(Azetidine-1-carbonyl)-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-nicotinamide

TBTU (107 mg, 0.33 mmol), 3-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-pyridine-2-carboxylic acid (70 mg, 0.19 mmol), and diisopropylethylamine (108 mg, 0.3 mmol) were dissolved in DMF (1 ml) and shaken for 30 min at RT. Azetidine (48 mg, 0.84 mmol) was then added, and the mixture was shaken at RT overnight. The title compound (9 mg, 8%) was isolated from the reaction mixture by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min: 95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 399.2 [$M+H^+$].

Example 45

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide

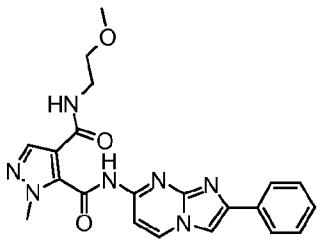


The title compound was prepared in analogy to example 29, using 2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine in the first step. 2-(3-Methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine can be prepared in analogy to example 1, step 1, from 2-bromo-1-(3-methoxy-phenyl)-ethanone.

MS (m/e) = 432.2 [M+H$^+$].

Example 46

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

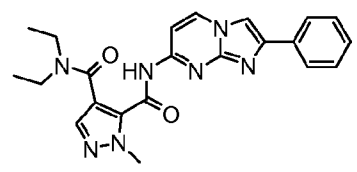


The title compound was obtained in analogy to example 29, using 2-methoxy-ethylamine in the last step.

MS (m/e) = 420.2 [M+H$^+$].

Example 47

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-diethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

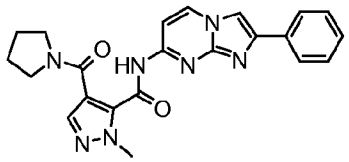


The title compound was obtained in analogy to example 29, using diethylamine in the last step.

MS (m/e) = 418.3 [M+H$^+$].

Example 48

2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

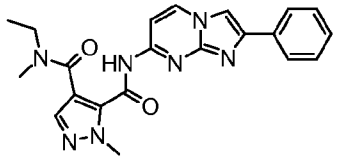


The title compound was obtained in analogy to example 29, using pyrrolidine in the last step.

MS (m/e) = 416.3 [M+H$^+$].

Example 49

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

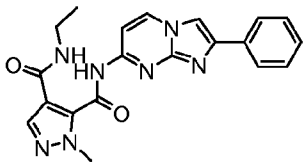


The title compound was obtained in analogy to example 29, using ethylmethylamine in the last step.

MS (m/e) = 404.4 [M+H$^+$].

Example 50

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

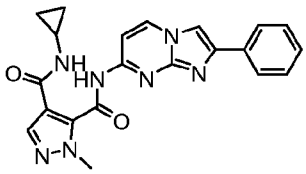


The title compound was obtained in analogy to example 29, using ethylamine in the last step.

MS (m/e) = 390.3 [M+H$^+$].

Example 51

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

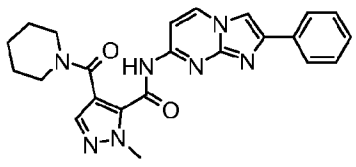


The title compound was obtained in analogy to example 29, using cyclopropylamine in the last step.

MS (m/e) = 402.4 [M+H$^+$].

Example 52

2-Methyl-4-(piperidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

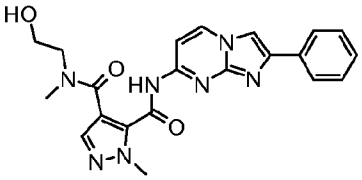


The title compound was obtained in analogy to example 29, using piperidine in the last step.

MS (m/e) = 430.4 [M+H$^+$].

Example 53

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

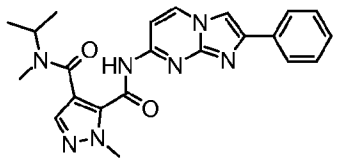


The title compound was obtained in analogy to example 29, using 2-methylamino-ethanol in the last step.

MS (m/e) = 420.2 [M+H$^+$].

Example 54

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isopropyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

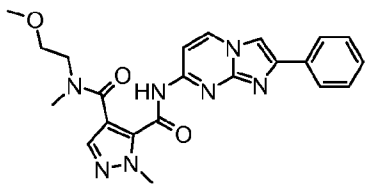


The title compound was obtained in analogy to example 29, using isopropyl-methyl-amine in the last step.

MS (m/e) = 418.3 [M+H$^+$].

Example 55

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

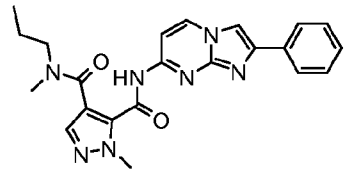


The title compound was obtained in analogy to example 29, using (2-methoxy-ethyl)-methyl-amine in the last step.

MS (m/e) = 434.4 [M+H$^+$].

Example 56

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(methyl-propyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

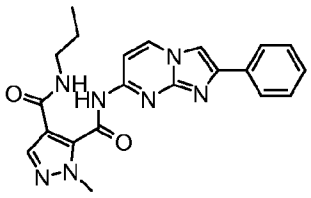


The title compound was obtained in analogy to example 29, using methyl-propyl-amine in the last step.

MS (m/e) = 418.3 [M+H$^+$].

Example 57

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-propylamide

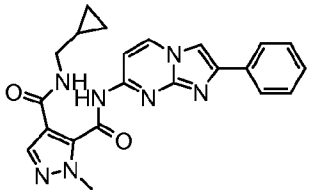


The title compound was obtained in analogy to example 29, using propylamine in the last step.

MS (m/e) = 404.4 [M+H$^+$].

Example 58

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylmethyl-amide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

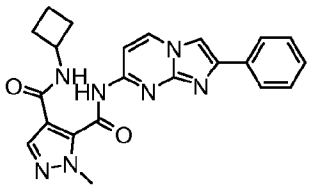


The title compound was obtained in analogy to example 29, using cyclopropylmethylamine in the last step.

MS (m/e) = 416.4 [M+H$^+$].

Example 59

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclobutylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

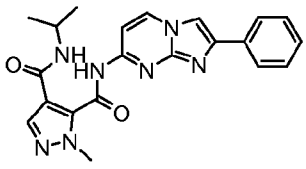


The title compound was obtained in analogy to example 29, using cyclobutylamine in the last step.

MS (m/e) = 416.4 [M+H$^+$].

Example 60

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-isopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

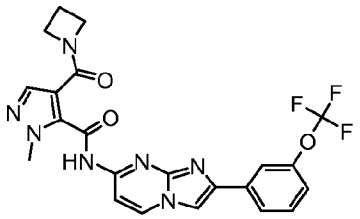


The title compound was obtained in analogy to example 29, using isopropylamine in the last step.

MS (m/e) = 404.4 [M+H$^+$].

Example 61

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-trifluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide

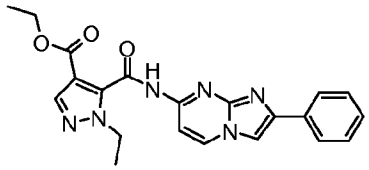


The title compound was prepared in analogy to example 29, using 2-(3-trifluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine. 2-(3-Trifluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine can be prepared in analogy to example 1, step 1, from 2-bromo-1-(3-trifluoromethoxy-phenyl)-ethanone.

MS (m/e) = 486.3 [$M+H^+$].

Example 62

1-Ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester



Step 1: 2H-Pyrazole-3,4-dicarboxylic acid diethyl ester

Under an atmosphere of argon, hydrazine monohydrate hydrochloride (1.91 g, 28 mmol) and HCl (36,5% in water, 2.8 ml) were added to a solution of 2-dimethylaminomethylene-3-oxo-succinic acid diethyl ester (6.8 g, 28 mmol) in ethanol (100 ml). The mixture was heated to 60 °C (3 h). The solvent was evaporated, and the residue was taken up in dichloromethane and washed (water). The organic layer was dried (Na_2SO_4), the solvent was evaporated and the title compound (1.81 mg, 31%) was isolated from the mixture by column chromatography (silica gel, heptane : ethyl acetate = 100:0 – 60:40).

MS (m/e) = 383.3 [$M+H^+$].

Step 2: 2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid diethyl ester

Sodium ethanolate solution was freshly prepared by dissolving sodium (240 mg) in ethanol (30 ml). 2H-Pyrazole-3,4-dicarboxylic acid diethyl ester (800 mg, 3.77 mmol) was dissolved in this sodium ethanolate solution (11 ml) and stirred for 10 min at RT, before ethyl iodide (1.4 g, 9 mmol) was added dropwise. After the completion of the addition, the mixture was heated to reflux until all starting material was consumed (1 h). The solvent was then evaporated, the residue was taken up in ethyl acetate and washed (water). The organic layer was dried (Na_2SO_4), evaporated, and the title compound (280 mg, 31%) was isolated from the mixture by column chromatography (silica gel, heptane : ethyl acetate = 100:0 – 60:40). (The regioisomeric 1-ethyl-1H-pyrazole-3,4-dicarboxylic acid diethyl ester can also be isolated, and can be distinguished from the desired product by NOE-^{1}H-NMR.)

MS (m/e) = 241.1 [$M+H^+$].

Step 3: 2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethyl ester

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid diethyl ester (280 mg, 1.2 mmol) was suspended in a NaOH solution (0.5 M in water, 2.8 ml) and stirred at RT until HPLC analysis indicated the consumption of the starting material (4 h). HCl (1 N, 1 ml) was added, and the mixture was extracted with ethyl acetate. The combined organic layers were dried (Na_2SO_4), evaporated, and the title compound (200 mg, 81%) was isolated from the mixture by column chromatography (silica gel, heptane : ethyl acetate = 100:0 – 60:40). MS (m/e) = 211.1 [$M-H^+$].

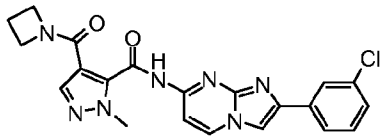
Step 4: 1-Ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester

TBTU (1.1 g) and diisopropylethylamine (1.1 g) were added to a solution of 2-ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethyl ester (610 mg) in DMF (7 ml), and the mixture was stirred for 30 min at RT. 2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1, 725 mg) was added to the light yellow solution, and the mixture was stirred over the weekend at RT. Water (15 ml) was added, and the mixture was stirred for an additional 15 min. For purification, the precipitate was suspended in DMF (5 ml) and water (10 ml), and filtered; this process was repeated 4 times. The thus obtained title compound (150 mg, 13%) was dried under vacuum.

MS (m/e) = 405.4 [M+H$^+$].

Example 63

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide

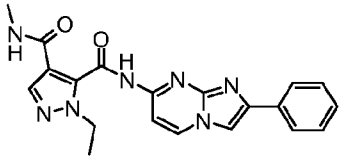


The title compound was prepared in analogy to example 29, using 2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine in the first step. 2-(3-Chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine can be prepared in analogy to example 1, step 1, from 2-Bromo-1-(3-chloro-phenyl)-ethanone.

MS (m/e) = 436.2 [M+H$^+$].

Example 64

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]



Step 1: Ethyl 5-(chlorocarbonyl)-1-ethyl-1H-pyrazole-4-carboxylate

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethyl ester (example 62, step 3, 1.47 g, 6.93 mmol) and thionyl chloride (19.0 g, 11.6 ml, 159 mmol) were combined to give a light yellow solution. The reaction mixture was stirred at reflux for 5 h. Excess thionyl chloride was removed under reduced pressure, and residual thionyl chloride was removed under vacuum. The title compound (1.6 g, estimated purity 37%, 37% yield) was used without further purification in the next step.

MS (m/e) = 390.3 [M+H$^+$].

Step 2: Ethyl 1-ethyl-5-(2-phenylimidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylate

2-Phenylimidazo[1,2-a]pyrimidin-7-amine (example 1, step 1, 648 mg, 3.08 mmol) and triethylamine (519 mg, 715 µl, 5.13 mmol) were combined with dichloromethane (15 ml) to give a light brown solution. Ethyl 5-(chlorocarbonyl)-1-ethyl-1H-pyrazole-4-carboxylate (1.6 g, 2.57 mmol) was diluted in dichloromethan and was added dropwise at 0°C. The reaction was stirred overnight. The reaction mixture was poured into 20 mL water and extracted with dichloromethan (2 x 50 mL). The organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude material was purified by flash chromatography (silica gel, 50g, 50% to 100% EtOAc in heptane). The obtained product contained the imide (2 acid chlorides added to amine) as an impurity, but was used in the next step (where the title compound and the impurity give the same product). The title compound was obtained as a light brown solid (510mg, 49.1 %).

MS (m/e) =405.4 [$M+H^+$].

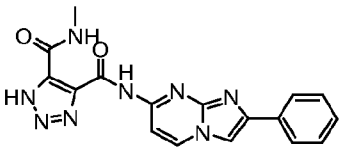
Step 3: 2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

Methylamine (2N solution in methanol, 0.61 ml)was added to a solution of ethyl 1-ethyl-5-(2-phenylimidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylate (33 mg) in THF (0.6 ml), and the mixture was stirred at RT overnight. The solvent was evaporated, and the title compound (16 mg, 50%) was isolated from the residue by preparative HPLC (254nm, Agilent Zorbax XdB-C18, Run: 7 min, Flow: 30 ml/min, Gradient: 0.0 min: 95/5 H_2O/CH_3CN; 0.5min: 95/5 H_2O/CH_3CN 4.5 min: 5/95 H_2O/CH_3CN; 6.9 min 5/95 H_2O/CH_3CN; 7 min 95/5 H_2O/CH_3CN).

MS (m/e) = 390.3 [$M+H^+$].

Example 65

1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-methylamide 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

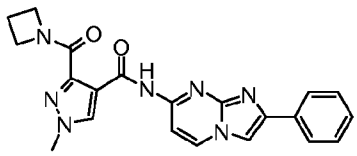


The title compound was obtained in analogy to example 31 from 5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid methyl ester (example 26).

MS (m/e) = 363.2 [M+H$^+$].

Example 66

3-(Azetidine-1-carbonyl)-1-methyl-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 1-Methyl-4-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-3-carboxylic acid ethyl ester

At 0°C, propylphosphonic acid anhydride (1-propanephosphonic acid cyclic anhydride, 50% in ethyl acetate, 7.4 ml, 2.5 eq.) was added slowly to a solution of 2-phenylimidazo[1,2-a]pyrimidin-7-amine (example 1, step 1, 1.27 g, 6 mmol), 1-methyl-1H-pyrazole-3,4-dicarboxylic acid 3-ethyl ester (1.00 g, 5 mmol), and ethyldiisopropylethylamine (2.0 ml, 15 mmol) in ethyl acetate (20 ml). The mixture was stirred for 30 min at 0°C, and subsequently at RT for 48 h. The mixture was taken up in ethyl acetate, and washed with water. The combined water layers were adjusted to pH = 9 (NaOH), and extracted with dichloromethane. All organic layers were combined, dried (Na_2SO_4), and evaporated. The title compound (580 mg , 29%) was obtained from the residue by column chromatography (silica gel, heptane : ethyl acetate = 100:0 – 80:20). (1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 3-ethyl ester was obtained by the method of Pérez et al., Spanish patent appl. ES 493459.)

MS (m/e) = 391.2 [M+H$^+$].

Step 2: 1-Methyl-4-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-3-carboxylic acid

NaOH (3N, 1.5 ml) was added to a solution of 1-methyl-4-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-3-carboxylic acid ethyl ester (390 mg, 1.5 mmol) in a mixture of THF (5 ml) and methanol (5 ml), and the mixture was stirred for 3 h at RT. Water (10 ml) was added, and the mixture was acidified (pH = 3) by addition of HCl. The mixture was stirred for 30 min and filtered. The obtained precipitate was washed with a small amount of water, and was dried under vacuum. The thus obtained title compound (240 mg, 45%) was pure enough to be used in the next step.

MS (m/e) = 363.3 [M+H$^+$].

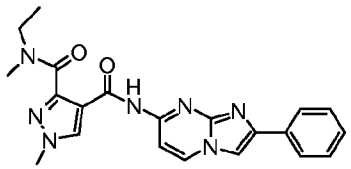
Step 3: 3-(Azetidine-1-carbonyl)-1-methyl-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

The title compound was obtained in analogy to example 29, step 6, from 1-Methyl-4-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-3-carboxylic acid.

MS (m/e) = 402.3 [M+H$^+$].

Example 67

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 3-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

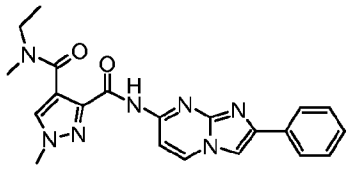


The title compound was prepared in analogy to example 66 from ethyl-methyl-amine.

MS (m/e) = 404.2 [M+H$^+$].

Example 68

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

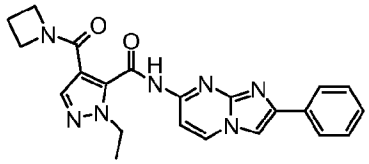


The title compound was obtained as a by-product during the preparation of example 67, presumably via an imide-type intermediate during the final coupling step.

MS (m/e) = 404.2 [M+H$^+$].

Example 69

4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 1-Ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid

The title compound was prepared in analogy to example 29, step 5, from ethyl 1-ethyl-5-(2-phenylimidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylate (example 56, step 2).

MS (m/e) = 377.3 [M+H$^+$].

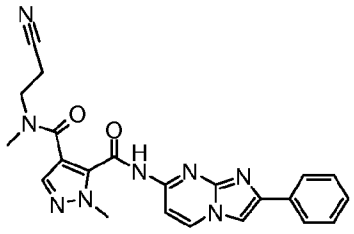
Step 2: 4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

The title compound was prepared in analogy to example 29, step 6, from 1-ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid.

MS (m/e) = 416.3 [M+H$^+$].

Example 70

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-cyano-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

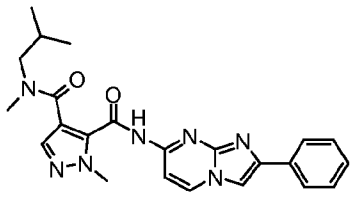


The title compound was prepared in analogy to example 29, step 6, from (2-cyano-ethyl)-methyl-amine.

MS (m/e) = 429.3 [M+H$^+$].

Example 71

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isobutyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

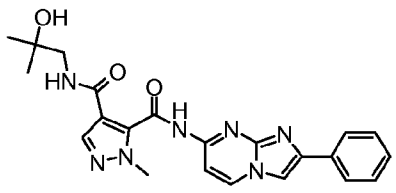


The title compound was prepared in analogy to example 29, step 6, from isobutyl-methyl-amine.

MS (m/e) = 432.4 [M+H$^+$].

Example 72

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-2-methyl-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

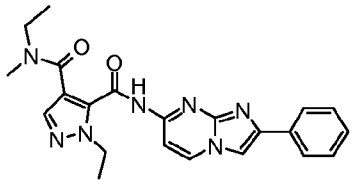


The title compound was prepared in analogy to example 29, step 6, from 2-hydroxy-2-methyl-propyl-amine.

MS (m/e) = 434.3 [M+H$^+$].

Example 73

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

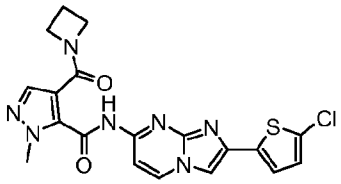


The title compound was prepared in analogy to example 69, step 2, from ethyl-methyl-amine.

MS (m/e) = 418.3 [M+H$^+$].

Example 74

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide

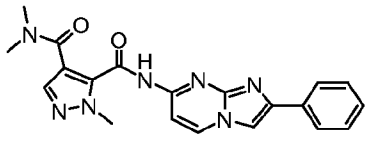


The title compound was prepared in analogy to example 29, using 2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-ylamine. 2-(5-Chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-ylamine can be prepared in analogy to example 1, step 1, from 2-bromo-1-(5-chloro-thiophen-2-yl)-ethanone.

MS (m/e) = 442.2 [M+H$^+$].

Example 75

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide]

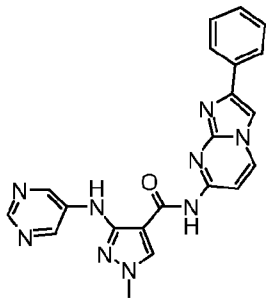


The title compound was prepared in analogy to example 29, step 6, from dimethylamine hydrochloride.

MS (m/e) = 390.3 [M+H$^+$].

Example 76

1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid ethyl ester

Under an atmosphere of argon, palladium(II) acetate (79 mg), and subsequently xantphos (4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, 256 mg) was added to a mixture of 5-bromopyridine (2.0 g), 3-amino-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester (1.5 g), K_2CO_3 (2.2 g), water (0.33 ml), and o-xylene (20 ml). The mixture was heated to 140°C for 17 h. Upon cooling and addition of dichloromethane (50 ml), the mixture was filtered and concentrated under vacuum. The title compound (1.52 g, 69%) was obtained from the residue by column chromatography (silica gel, cyclohexane / ethyl acetate gradient).

MS (m/e) = 248.2 [M+H$^+$].

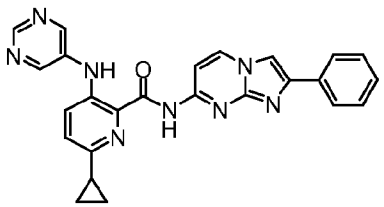
Step 2: 1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

Trimethylaluminum (2M solution in toluene, 0.3 ml) was added to a stirred suspension of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1, 128 mg) in dioxane (5 ml), and the mixture was stirred for 2 h at RT. 1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid ethyl ester (50 mg) was then added in one portion, and the mixture was heated to 100 °C for 17 h. Upon cooling, water (0.5 ml) was added, followed by small amounts of methanol and dichloromethane to get an almost clear solution. Some $MgSO_4$ was added, the mixture was stirred for 15 min, and filtered. The filtrate was concentrated, and the title compound (23 mg, 28%) was isolated from the residue by column chromatography (silica gel, dichloromethane / methanol gradient), followed by trituration (methanol).

MS (m/e) = 412.2 [$M+H^+$].

Example 77

6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide



Step 1: 6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid ethyl ester

Under an atmosphere of argon, palladium(II) acetate (101 mg), and subsequently xantphos (4,5-bis(diphenylphosphino)-9,9-dimethylxanthene, 325 mg) was added to a mixture of 5-bromopyridine (2.5 g), 3-amino-6-cyclopropyl-pyridine-2-carboxylic acid ethyl ester (2.32 g), K_2CO_3 (2.8 g), water (0.43 ml), and o-xylene (30 ml). The mixture was heated to 140°C for 17 h. Upon cooling and addition of dichloromethane (50 ml), the mixture was filtered and concentrated under vacuum. The title compound (2.59 g, 81%) was obtained from the residue by column chromatography (silica gel, cyclohexane / ethyl acetate gradient).

(3-Amino-6-cyclopropyl-pyridine-2-carboxylic acid ethyl ester can be prepared by the method of Georg Jaeschke et al., U.S. Pat. Appl. Publ. (2006) US 2006199960.)

MS (m/e) = 285.2 [M+H$^+$].

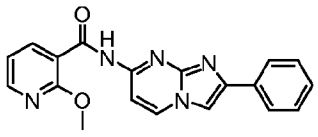
Step 2: 6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide

Trimethylaluminum (2M solution in toluene, 0.26 ml) was added to a stirred suspension of 2-phenyl-imidazo[1,2-a]pyrimidin-7-ylamine (example 1, step 1, 111 mg) in dioxane (5 ml), and the mixture was stirred for 2 h at RT. 6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid ethyl ester (50 mg) was then added in one portion, and the mixture was heated to 100 °C for 17 h. Upon cooling, water (0.5 ml) was added, followed by small amounts of methanol and dichloromethane to get an almost clear solution. Some $MgSO_4$ was added, the mixture was stirred for 15 min, and filtered. The filtrate was concentrated, and the title compound (44 mg, 56%) was isolated from the residue by column chromatography (silica gel, dichloromethane / methanol gradient), followed by trituration (methanol).

MS (m/e) = 449.2 [M+H$^+$].

Example 78

2-Methoxy-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)nicotinamide

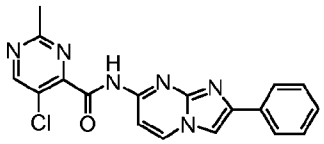


A mixture of 2-phenylimidazo[1,2-a]pyrimidin-7-amine (200 mg, 951 µmol, Eq: 1.00), 2-methoxynicotinic acid (146 mg, 951 µmol, Eq: 1.00), diisopropylethylamine (369 mg, 498 µl, 2.85 mmol, Eq: 3) and propylphosphonic anhydride in ethyl acetate 50% (1.21 g, 1.12 ml, 1.9 mmol, Eq: 2) in tetrahydrofuran (10 ml) is stirred for 18 hours at 60 °C. The mixture is diluted with ethyl acetate and washed 2 times with water and once with brine, the organic layer was separated, dried over magnesium sulfate, filtrated and evaporated. The crude material was

applied on silicagel and purified by flash chromatography over a 20 g silicagel column using ethyl acetate / methanol 0-10 % as eluent affording 2-methoxy-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)nicotinamide (36 mg, 11 %) as a light yellow solid. MS: m/e = 346.1 (M+H+), mp: 225-226 °C

Example 79

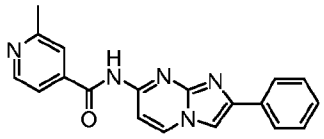
5-Chloro-2-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)pyrimidine-4-carboxamide



A mixture of 5-chloro-2-methylpyrimidine-4-carboxylic acid (100 mg, 0.579 mmol), 2-phenylimidazo[1,2-a]pyrimidin-7-amine (146 mg, 0.695 mmol, 1.2 eq), diisopropylethylamine (304 ul, 1.74 mmol, 3 eq) and propylphosphonic anhydride in ethyl acetate 50 % (854 ul, 1.45 mmol, 2.5 eq) in tetrahydrofuran (6 ml) is stirred for 1 day at 25 °C. The mixture is diluted with ethyl acetate and washed 2 times with water, the organic layer is dried over magnesium sulfate and evapoarted. The crude material was purified by flash chromatography over a 20 g silicagel column using ethyl acetate 100 % as eluent to afford 5-chloro-2-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)pyrimidine-4-carboxamide (64 mg, 30.3%) as a yellow solid. MS: m/e = 365.1 (M+H+), mp: >250 °C

Example 80

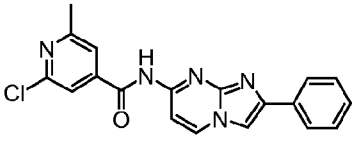
2-Methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)isonicotinamide



A mixture of 2-phenylimidazo[1,2-a]pyrimidin-7-amine (156 mg, 0.766 mmol, 1 eq.), 2-methylisonicotinic acid (116 mg, 0.842 mmol, 1.1 eq.), propylphosphonic anhydride in ethyl acetate 50% (1.13 ml, 1.91 mmol, 2.5 eq) and ethyldiisopropylamine (0.535 ml, 3.06 mmol, 4 eq) in tetrahydrofuran (10 ml) is stirred for 18 hours at roomtemperature. The solution is then refluxed for 4 hours. The mixture is diluted with ethyl acetate and washed with sat. aqueous sodium bicarbonate, with water, dried over magnesium sulfate and the solvent is removed in vacuo. Purification of the residue by chromatography on a 12 g RediSep silica cartridge using dichloromethane + 5% methanol as eluent affords 2-methyl-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-isonicotinamide (45 mg, 17.8%) as a yellow solid. MS: m/e = 330.2 (M+H+) mp.: 255-7°C.

Example 81

2-Chloro-6-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)isonicotinamide

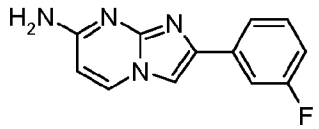


A mixture of 2-phenylimidazo[1,2-a]pyrimidin-7-amine (141 mg, 0.671 mmol, 1 eq.), 2-chroro-6-methylisonicotinic acid (127 mg, 0.738 mmol, 1.1 eq.), propylphosphonic anhydride in ethyl

acetate 50% (0.98 ml, 1.68 mmol, 2.5 eq) and ethyldiisopropylamine (0.47 ml, 2.68 mmol, 4 eq) in tetrahydrofurane (10 ml) is refluxed for 4 hours. The mixture is diluted with ethyl acetate and washed with sat. aqueous sodium bicarbonate, twice with water, dried over magnesium sulfate and the solvent is removed in vacuo. Purification of the residue by chromatography on a 20 g Silicycle silica cartridge using ethyl acetate a eluent affords 2-chloro-6-methyl-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-isonicotinamide (129 mg, 52.9%) as a yellow solid (cryst. fom heptane / ethlyl acetate 7/3). MS: m/e = 364.0 (M+H+), mp.: 148-151°C.

Intermediate compounds of formula 3, used in Examples 82 - 111

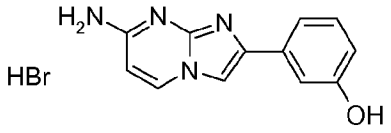
2-(3-Fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine



2-Bromo-1-(3-fluorophenyl)ethanone (10.9 g, 50 mmol) was added to a solution of 2,4-diaminopyrimidine (3.70 g, 34 mmol) in acetone (185 ml), and the mixture was heated to reflux for 6 h. The cooled suspension was filtered and the precipitate was washed with acetone (50 ml). The solid was re-suspended in water (35 ml) and NH4OHaq. (25%, 50 ml), then it was collected over a glass fiber paper and the filtrate was washed with H_2O (75 ml). After drying under vacuum, the product was obtained (5.56 g, 72%) as a yellow solid.

MS (m/z) = 229.1 [M+H+].

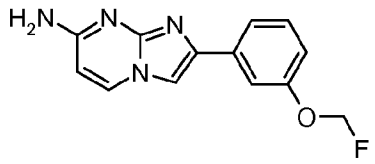
3-(7-Amino-imidazo[1,2-a]pyrimidin-2-yl)-phenol hydrobromide



2-(3-Methoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-ylamine (2.5 g, 10.4 mmol; intermediate to example 45) was combined with 25 ml $HBr_{aq.}$ (48%) to give a light yellow suspension. The reaction mixture was refluxed for 48 h. After cooling to RT, H_2O was added and the brown suspension was filtered. The solid was washed with H_2O and dried in HV at 40 °C to yield the title compound (2.75 g, 86%) as a white solid.

MS (m/z) = 227.2 [M+H+].

2-(3-Fluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine

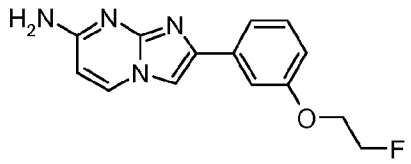


In a sealed tube 3-(7-aminoimidazo[1,2-*a*]pyrimidin-2-yl)phenol hydrobromide (260 mg, 0.85 mmol) was combined in DMF (3 ml) to give a brown solution. Toluene-4-sulfonic acid fluoromethyl ester (249 mg, 1.22 mmol; CAS Nr. 114435-86-8) was dissolved in DMF and added. Cs_2CO_3 (527 mg, 1.62 mmol) was added. The reaction mixture was heated under argon to 70 °C for 9 h, then stirring was continued overnight at RT. The reaction mixture was diluted with H_2O (30 ml) and extracted with EtOAc (3x 30 ml).The combined organic layers were dried ($MgSO_4$) and concentrated under vacuum and the crude product was purified by flash

chromatography (50 g SiO_2, DCM/MeOH/$NH_{3aq.}$ 140:10:1). The title compound (105 mg, 48%) was obtained as a yellow solid.

MS (m/z) = 259.1 [M+H+].

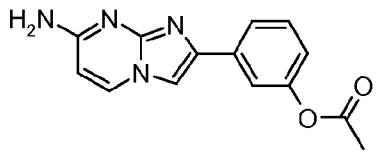
2-[3-(2-Fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-ylamine



In a sealed tube 3-(7-aminoimidazo[1,2-*a*]pyrimidin-2-yl)phenol hydrobromide (800 mg, 2.6 mmol) was combined with DMF (4.0 ml) to give a light brown solution. 1-Bromo-2-fluoroethane (476 mg, 3.75 mmol) dissolved in DMF (4.0ml) and Cs_2CO_3 (1.62 g, 4.97 mmol) were added. The reaction mixture was stirred 23 h at 70 °C. H_2O (50ml) was added to the reaction mixture and the product was extracted with EtOAc (3x 40ml). After drying over $MgSO_4$, filtration and concentration in vacuum, the crude product (orange oil) was purified by flash chromatography (50g SiO_2- NH_2 cartridge, eluent: CH_2Cl_2 to CH_2Cl_2/MeOH 95:5) to yield the title compound (150 mg, 21%).

MS (m/z) = 273.1 [M+H+].

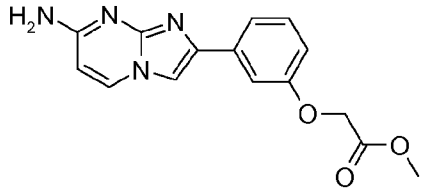
Acetic acid 3-(7-amino-imidazo[1,2-a]pyrimidin-2-yl)-phenyl ester



To a microwave vial were added 3-(7-aminoimidazo[1,2-*a*]pyrimidin-2-yl)phenol hydrobromide (500 mg, 1.63 mmol), acetic anhydride (199 mg, 185 µl, 1.95 mmol) and pyridine (5.00 ml). The vial was capped and heated in the microwave at 120 °C for 15 min. H_2O was added to the reaction mixture and the pH was installed around 7-8 by addition of 10% $NaHCO_3$ aq. solution. The product was extracted with CH_2Cl_2, then the solvent was partially evaporated and the formed solid was collected and purified by flash chromatography (SiO_2 cartridge; eluent: CH_2Cl_2/MeOH/NH_3aq. 140:10:1). White solid (207 mg, 45%).

MS (m/z) = 269.1 [M+H+].

[3-(7-Amino-imidazo[1,2-a]pyrimidin-2-yl)-phenoxy]-acetic acid methyl ester

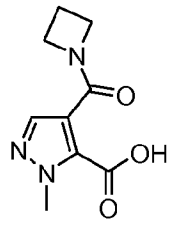


3-(7-Aminoimidazo[1,2-*a*]pyrimidin-2-yl)phenol hydrobromide (100 mg, 0.33 mmol) was combined with DMF (0.2 ml) to give a light brown suspension. Methyl-2-bromoacetate (55 mg, 0.36 mmol) and Cs_2CO_3 (424 mg, 1.3 mmol) were added, and the reaction mixture was stirred 2 h in a sealed tube at 65 °C. The reaction mixture was directly put on a column and the product was isolated by flash chromatography (SiO_2-NH_2 cartridge; eluent: CH_2Cl_2/MeOH 95:05) to yield the title compound (57 mg, 58%) as a light yellow solid.

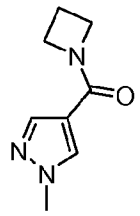
MS (m/z) = 299.1 [M+H+].

Carboxylic acid intermediates used in Examples 82 - 111

4-(Azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



*Step 1: Azetidin-1-yl-(1-methyl-1*H*-pyrazol-4-yl)-methanone*



1-Methyl-1H-pyrazole-4-carboxylic acid (1.0 g, 7.93 mmol; CAS Nr. 5952-92-1) was combined with DMF (10.0 ml) to give a colorless solution. Et_3N (2.41 g, 3.32 ml, 23.8 mmol) and 2-(1*H*-benzo[d][1,2,3]triazol-1-yl)-1,1,3,3-tetramethylisouronium tetrafluoroborate (TBTU, 2.8 g, 8.72 mmol) were added and the reaction mixture was stirred at RT for 1 h. Azetidine (475 mg, 8.33 mmol) was added and the stirring was continued overnight. DMF was partially removed under high vacuum, H_2O and 10% $NaHCO_3$ aq. solution were added to the residue, and the compound was extracted with EtOAc. After drying over Na_2SO_4, filtration and concentration under vacuum,

the crude product was purified by flash chromatography (50g SiO_2-NH_2 cartridge; eluent: CH_2Cl_2/MeOH 95:05). More product was isolated from the aqueous phase by full evaporation and a second chromatography. White solid (971 mg, 74%).

MS (m/z) = 166.2 [M+H+].

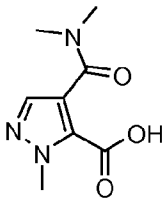
*Step 2: 4-(Azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid*

Azetidin-1-yl(1-methyl-1*H*-pyrazol-4-yl)methanone (467.2 mg, 2.83 mmol) was combined under N_2 with THF (10.0 ml) to give a colorless solution. 1,1,4,7,7-Pentamethyldiethylenetriamine (539 mg, 650 µl, 3.11 mmol) was added, the solution was cooled to -78 °C and 1.6 M *t*BuLi in heptane (2.65 ml, 4.24 mmol, Eq: 1.50) was added drop by drop. After stirring 30min an excess of dry ice was added carefully. After 5 min at -78 °C the yellow suspension was allowed to warm up to RT. After stirring 1 h H_2O was added to the reaction mixture and an extraction (CH_2Cl_2) was performed. The H_2O layer was acidified using 1N HCl solution, and the acid was extracted (CH_2Cl_2). After drying over Na_2SO_4, filtration and concentration under vacuum, the product was dried under high vacuum. Off-white solid (496 mg, 84%).

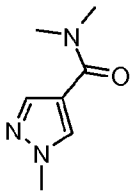
MS (m/z) = 210.1 [M+H+].

The following calboxylic acid intermediates were prepared in analogy to 4-(azetidine-1-carbonyl)-1-methyl-1H-pyrazole-5-carboxylic acid:

4-(Dimethylcarbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



*Step 1: N,N-1-Trimethyl-1*H*-pyrazole-4-carboxamide*



From 1-methyl-1*H*-pyrazole-4-carboxylic acid (1.00 g, 7.93 mmol) and dimethylamine hydrochloride (679 mg, 8.33 mmol). Off-white solid (1.12 g, 92%).

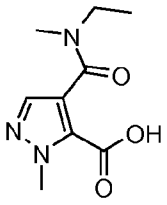
MS (m/z) = 154.1 [M+H+].

Step 2: 4-(Dimethylcarbamoyl)-1-methyl-1H-pyrazole-5-carboxylic acid

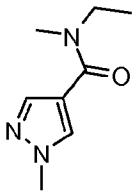
From N,N-1-trimethyl-1*H*-pyrazole-4-carboxamide (300 mg, 1.96 mmol). White solid (329 mg, 82%).

MS (m/z) = 198.1 [M+H+].

4-(Ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



*Step 1: N-Ethyl-N-1-dimethyl-1*H*-pyrazole-4-carboxamide*



From 1-methyl-1*H*-pyrazole-4-carboxylic acid (1 g, 7.93 mmol) and N-methylethanamine (492 mg, 715 µl, 8.33 mmol). Off.white solid (995 mg, 75%).

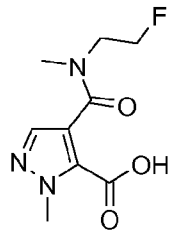
MS (m/z) = 168.1 [M+H+].

*Step 2: 4-(Ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid*

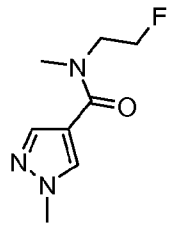
From N-ethyl-N-1-dimethyl-1*H*-pyrazole-4-carboxamide (514.4 mg, 3.08 mmol). Light brown solid (460 mg, 69%).

MS (m/z) = 212.1 [M+H+].

4-((2-Fluoroethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



*Step 1: 1-Methyl-1*H*-pyrazole-4-carboxylic acid (2-fluoro-ethyl)-methyl-amide*



From 1-methyl-1*H*-pyrazole-4-carboxylic acid (1.0 g, 7.93 mmol) and 2-fluoro-N-methylethanamine hydrochloride (991 mg, 8.72 mmol). Yellow oil (1.41 g, 92%).

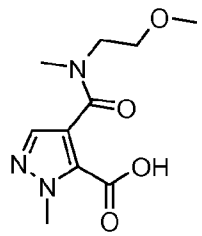
MS (m/z) = 186.1 [M+H+].

*Step 2: 4-((2-Fluoroethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid*

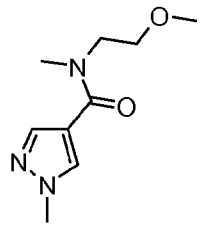
From 1-methyl-1*H*-pyrazole-4-carboxylic acid (2-fluoro-ethyl)-methyl-amide (500 mg, 2.7 mmol). Light brown viscous oil (307 mg, 50%).

MS (m/z) = 230.2 [M+H+].

4-((2-Methoxyethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



*Step 1: N-(2-Methoxyethyl)-N-1-dimethyl-1*H*-pyrazole-4-carboxamide*



From 1-methyl-1*H*-pyrazole-4-carboxylic acid (500 mg, 3.96 mmol) and 2-methoxy-N-methylethanamine (389 mg, 4.36 mmol). Colorless liquid (580mg, 74%).

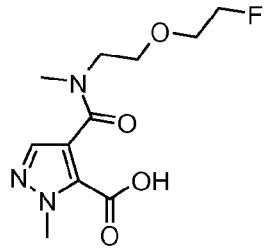
MS (m/z) = 198.2 [M+H+].

*Step 2: 4-((2-Methoxyethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid*

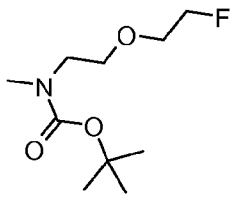
From N-(2-methoxyethyl)-N-1-dimethyl-1*H*-pyrazole-4-carboxamide (550 mg, 2.79 mmol). Colorless waxy solid (590 mg, 88%).

MS (m/z) = 240.1 [M-H-].

4-((2-(2-Fluoroethoxy)ethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



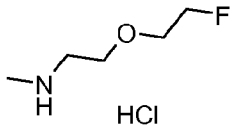
Step 1: [2-(2-Fluoro-ethoxy)-ethyl]-methyl-carbamic acid tert-butyl ester



To a solution of (2-hydroxy-ethyl)-methyl-carbamic acid tert-butyl ester (CAS Nr. 57561-39-4; 2.50 g, 14.3 mmol) in toluene (35 ml) was added powered KOH (2.8 g, 50 mmol) and Bu_4NHSO_4 (0.97 mg, 2.86 mmol). The reaction mixture was stirred vigorously and heated to 50 °C while neat 1-bromo-2-fluoro-ethane (2.72 g, 21.4 mmol) was added slowly. The temperature was increased to 80 °C and maintained for 3-5 h. The reaction mixture was cooled to RT, water was added (50ml) and the pH was adjusted to 7 with 1N HCl solution. Extraction with EtOAc (2x150 ml), washing with brine, drying with Na_2SO_4 and concentrating under vacuum yielded the crude product. The crude material was subjected to column chromatography on silica by EtOAc: hexane (10:90 to 20:80) to give the desired product as light yellow liquid (1.2 g, 38%).

MS (m/z) = 122.0 [M-Boc+]; 166.2 [M-tBu+].

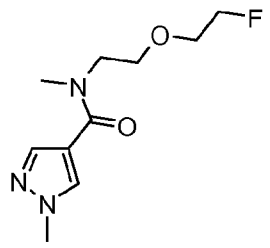
Step 2: [2-(2-Fluoro-ethoxy)-ethyl]-methyl-amine hydrochloride



To a stirred solution of [2-(2-fluoro-ethoxy)-ethyl]-methyl-carbamic acid tert-butyl ester (2.00 g, 0.05 mmol) in dry 1, 4-dioxane (20 ml) was added 4M HCl in 1,4-dioxane (22.6 ml, 90 mmol) dropwise at 0 °C. The reaction mixture was stirred at RT for 5 h. Volatiles were removed under vacuum. The crude material was washed with hexane and dried under vacuum to give desired product [2-(2-fluoro-ethoxy)-ethyl]-methyl-amine hydrochloride as pale yellow solid (1.2 g, 84%).

MS (m/z) = 122.0 [M+H+].

*Step 3: N-(2-(2-Fluoroethoxy)ethyl)-N-1-dimethyl-1*H*-pyrazole-4-carboxamide*



From 1-methyl-1*H*-pyrazole-4-carboxylic acid (1.00 g, 7.93 mmol) and [2-(2-fluoro-ethoxy)-ethyl]-methyl-amine hydrochloride. Light yellow oil (1.82 g, 95%).

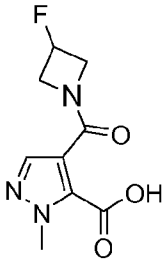
MS (m/z) = 230.2 [M+H+].

*Step 4: 4-((2-(2-Fluoroethoxy)ethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid*

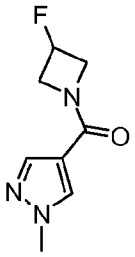
From N-(2-(2-fluoroethoxy)ethyl)-N-1-dimethyl-1*H*-pyrazole-4-carboxamide (500 mg, 2.18 mmol). Yellow oil (448 mg, 88%).

MS (m/z) = 272.1 [M-H-].

4-(3-Fluoroazetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid



*Step 1: (3-Fluoroazetidin-1-yl)(1-methyl-1*H*-pyrazol-4-yl)methanone*



From 1-methyl-1*H*-pyrazole-4-carboxylic acid (1.0 g, 7.93 mmol) and 3-fluoroazetidine hydrochloride (884 mg, 7.93 mmol). Off-white solid (597 mg, 41%).

MS (m/z) = 184.1 [M+H+].

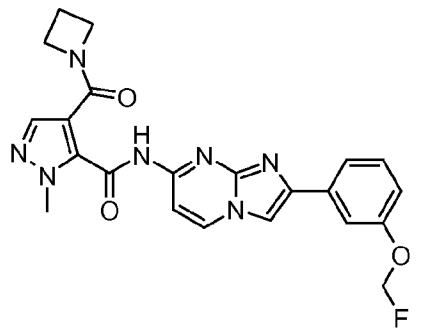
*Step 2: 4-(3-Fluoroazetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid*

From (3-fluoroazetidin-1-yl)(1-methyl-1*H*-pyrazol-4-yl)methanone (500 mg, 2.73 mmol). White Solid (352 mg, 57%).

MS (m/z) = 226.2 [M+H+].

Example 82

4-(Azetidine-1-carbonyl)-N-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-yl)-1-methyl-1*H*-pyrazole-5-carboxamide

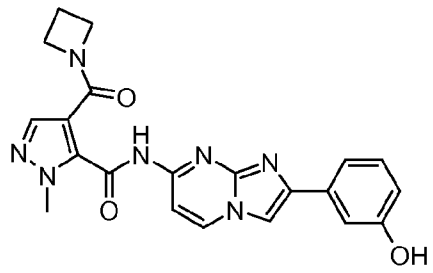


2-(3-Fluoromethoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-ylamine (100 mg, 0.387 µmol) was combined with EtOAc (2.0 ml) to give a light yellow suspension. 4-(Azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (97 mg, 465 µmol) and DIPEA (300 mg, 406 µl, 2.32 mmol) were added. The reaction mixture was cooled down to 0 °C and *n*-propylphosphonic acid anhydride, cyclic trimer (616 mg, 582 µl, 968 µmol) was added drop by drop. After stirring at 0 °C for 30 min the reaction mixture was allowed to warm-up and stirred at RT overnight. The reaction mixture was then diluted with and 10% $NaHCO_3$ aq. solution and extracted with EtOAc (3x). The combined organic layers were dried ($MgSO_4$) and concentrated under vacuum. The crude product was purified by flash chromatography (10g SiO_2; eluent: CH_2Cl_2 to CH_2Cl_2/MeOH/NH_3 140:10:1). The obtain material was dissolved in CH_2Cl_2 and the product was precipitated with Et_2O, filtered off, washed with Et_2O, and dried overnight at HV. Yellow solid (89 mg, 47%).

MS (m/z) = 450.2 [M+H+].

Example 83

4-(Azetidine-1-carbonyl)-2-methyl-2*H*-pyrazole-3-carboxylic acid [2-(3-hydroxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide

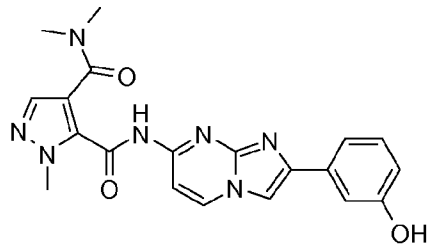


3-(7-(4-(Azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxamido)imidazo[1,2-*a*]pyrimidin-2-yl)phenyl acetate (Example 105; 25 mg, 54.4 µmol) was combined with MeOH (0.7 ml), CH_2Cl_2 (0.2 ml) and H_2O to give a yellow solution. $NaHCO_3$ (4.57 mg, 54.4 µmol) was added and the reaction mixture was stirred at RT over night. The precipitated light yellow solid was filtered and washed with MeOH and H_2O. After drying over night under high vacuum, the product (13 mg, 56%) was obtained as light yellow solid.

MS (m/z) = 418.2 [M+H+].

Example 84

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-{[2-(3-hydroxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

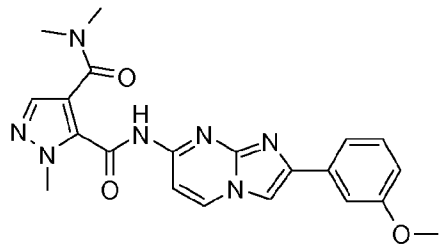


3-(7-(4-(Dimethylcarbamoyl)-1-methyl-1*H*-pyrazole-5-carboxamido)imidazo[1,2-*a*]pyrimidin-2-yl)phenyl acetate (Example 93, 46.7 mg, 104 µmol) was combined with MeOH (1.5 ml), and H_2O to give a yellow solution. $NaHCO_3$ (8.77 mg, 0.75 ml, 104 µmol) was added and the reaction mixture was stirred at RT over night. The reaction mixture was quenched to pH 7 with 0.1N HCl solution, the solvents were evaporated until dryness and the residue was purified by two consecutive flash chromatographies (10g SiO_2 cartridge; eluent CH_2Cl_2/MeOH/NH_3aq. 140:10:1; then 10g SiO_2-NH_2 cartridge; eluent: CH_2Cl_2). Light yellow solid (18 mg, 42%).

MS (m/z) = 406.3 [M+H+].

Example 85

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

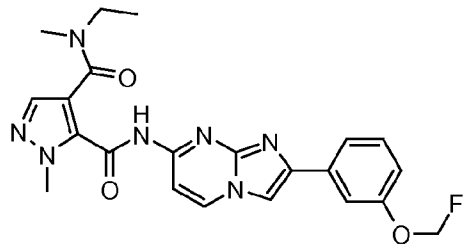


The title compound was prepared in analogy to example 82 from 2-(3-methoxyphenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 416 µmol) and 4-(dimethylcarbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (98.5 mg, 499 µmol). Yellow solid (86 mg, 48%).

MS (m/z) = 420.2 [M+H+].

Example 86

N-4-Ethyl-N-5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-yl)-N4,1-dimethyl-1*H*-pyrazole-4,5-dicarboxamide

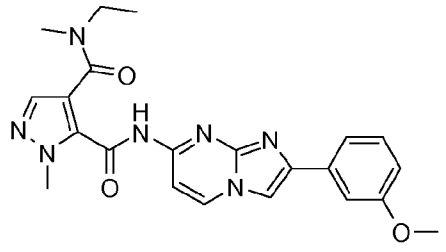


The title compound was prepared in analogy to example 82 from 2-(3-(fluoromethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (67.0 mg, 259 µmol) and 4-(ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (65.8 mg, 311 µmol). Yellow solid (24 mg, 20%).

MS (m/z) = 452.2 [M+H+].

Example 87

N-4-ethyl-N-5-(2-(3-methoxyphenyl)imidazo[1,2-*a*]pyrimidin-7-yl)-N-4,1-dimethyl-1*H*-pyrazole-4,5-dicarboxamide

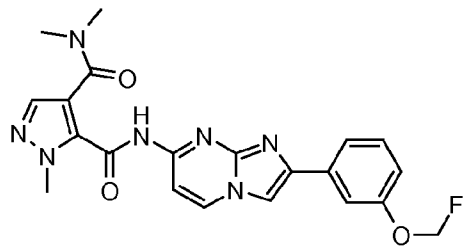


The title compound was prepared in analogy to example 82 from 2-(3-methoxyphenyl)imidazo[1,2-*a*]pyrimidin-7-amine (65 mg, 271 µmol) and 4-(ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (68.6 mg, 325 µmol). Off-white solid (72 mg, 60%).

MS (m/z) = 434.9 [M+H+].

Example 88

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-{[2-(3-fluoromethoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}



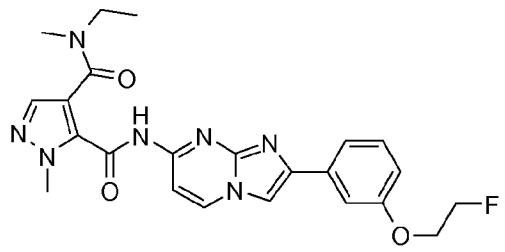
The title compound was prepared in analogy to example 82 from 2-(3-(fluoromethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (105 mg, 407 µmol) and 4-

(dimethylcarbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (96.2 mg, 488 µmol). Light yellow solid (114 mg, 64%).

MS (m/z) = 438.2 [M+H+].

Example 89

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-yl}-amide)

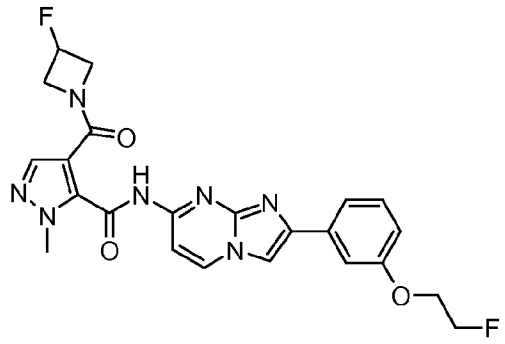


The title compound was prepared in analogy to example 82 from 2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 367 µmol) and 4-(ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (93.1 mg, 441 µmol). Yellow solid (49 mg, 29%).

MS (m/z) = 466.2 [M+H+].

Example 90

4-(3-Fluoro-azetidine-1-carbonyl)-2-methyl-2*H*-pyrazole-3-carboxylic acid {2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-yl}-amide

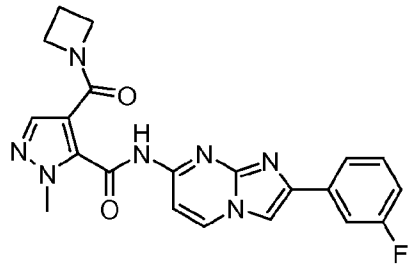


The title compound was prepared in analogy to example 82 from 2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-amine (120 mg) and 4-(3-fluoroazetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 440 µmol). Light brown solid (132 mg, 60%).

MS (m/z) = 482.2 [M+H+].

Example 91

4-(Azetidine-1-carbonyl)-2-methyl-2*H*-pyrazole-3-carboxylic acid [2-(3-fluoro-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide

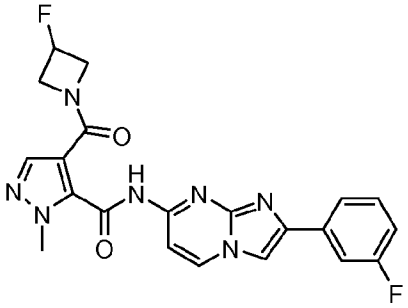


The title compound was prepared in analogy to example 82 from 4-(azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (91.7 mg, 438 µmol) and 2-(3-fluorophenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 438 µmol). Yellow solid (6.5 mg, 3.5%).

MS (m/z) = 420.1 [M+H+].

Example 92

4-(3-Fluoro-azetidine-1-carbonyl)-2-methyl-2*H*-pyrazole-3-carboxylic acid [2-(3-fluoro-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide

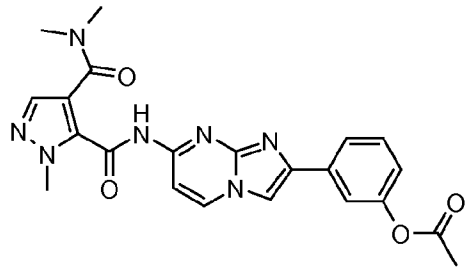


The title compound was prepared in analogy to example 82 from 2-(3-fluorophenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg) and 4-(3-fluoroazetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 440 µmol). Yellow solid (76mg, 39%).

MS (m/z) = 438.1 [M+H+].

Example 93

3-(7-(4-(dimethylcarbamoyl)-1-methyl-1*H*-pyrazole-5-carboxamido)imidazo[1,2-*a*]pyrimidin-2-yl)phenyl acetate

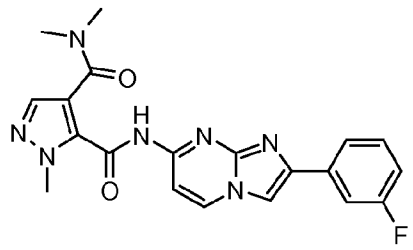


The title compound was prepared in analogy to example 82, step 3, from 4-dimethylcarbamoyl-2-methyl-2H-pyrazole-3-carboxylic acid (step 2, example 85; 44.1 mg, 224 µmol,) and acetic acid 3-(7-amino-imidazo[1,2-a]pyrimidin-2-yl)-phenyl ester (50 mg, 186 µmol). Yield: 53 mg (60%). Yellow solid.

MS (m/z) = 448.2 [M+H+].

Example 94

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-{[2-(3-fluoro-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

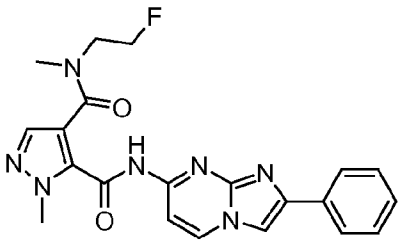


The title compound was prepared in analogy to example 82 from 2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-amine (95 mg, 416 µmol) and 4-(dimethylcarbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (98.5 mg, 500 µmol). Light yellow solid (31.9 mg, 19%).

MS (m/z) = 408.1 [M+H+].

Example 95

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-[(2-fluoro-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-*a*]pyrimidin-7-yl)-amide]

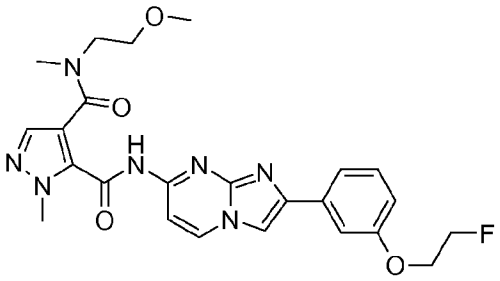


The title compound was prepared in analogy to example 82 from 2-phenylimidazo[1,2-*a*]pyrimidin-7-amine (90 mg, 428 µmol) and 4-((2-fluoroethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (118 mg, 514 µmol). Light yellow solid (60 mg, 31%).

MS (m/z) = 422.2 [M+H+].

Example 96

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-yl}-amide) 4-[(2-methoxy-ethyl)-methyl-amide]

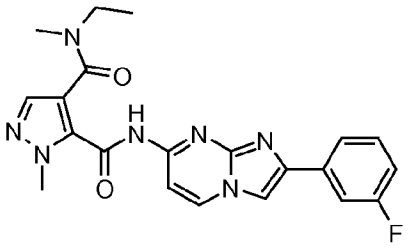


The title compound was prepared in analogy to example 82 from 2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 367 µmol) and 4-[(2-methyl-ethyl)-methyl-carbamoyl]-2-methyl-2*H*-pyrazole-3-carboxylic acid (106 mg, 441 µmol). Yellow solid (6.7 mg, 3.1%).

MS (m/z) = 496.2 [M+H+].

Example 97

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-{[2-(3-fluoro-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

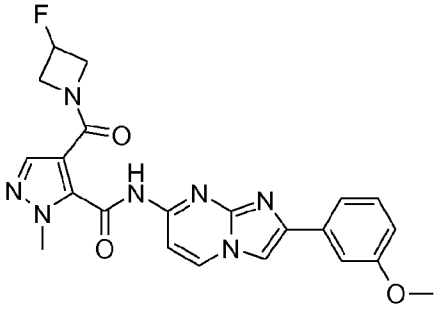


The title compound was prepared in analogy to example 82 from 2-(3-fluorophenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 438 µmol) and 4-(ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (111 mg, 526 µmol). Light yellow solid (7.2 mg, 3.9%).

MS (m/z) = 422.2 [M+H+].

Example 98

4-(3-Fluoro-azetidine-1-carbonyl)-2-methyl-2*H*-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide

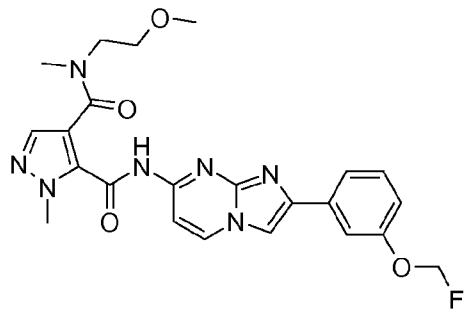


The title compound was prepared in analogy to example 82 from 4-(3-fluoroazetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 440 µmol) and 2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-amine (106). Yellow solid (142 mg, 72%).

MS (m/z) = 450.2 [M+H+].

Example 99

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-fluoromethoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide} 4-[(2-methoxy-ethyl)-methyl-amide]

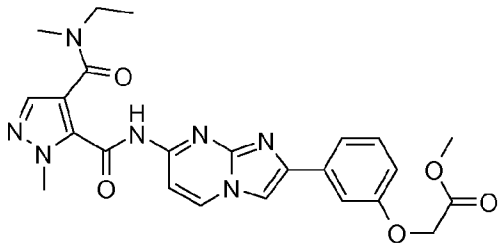


The title compound was prepared in analogy to example 82 from 2-(3-(fluoromethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 387 µmol) and 4-[(2-methyl-ethyl)-methyl-carbamoyl]-2-methyl-2*H*-pyrazole-3-carboxylic acid (112 mg, 465 µmol). Yellow solid (41 mg, 20%).

MS (m/z) = 482.3 [M+H+].

Example 100

[3-(7-{[4-(Ethyl-methyl-carbamoyl)-2-methyl-2*H*-pyrazole-3-carbonyl]-amino}-imidazo[1,2-*a*]pyrimidin-2-yl)-phenoxy]-acetic acid methyl ester



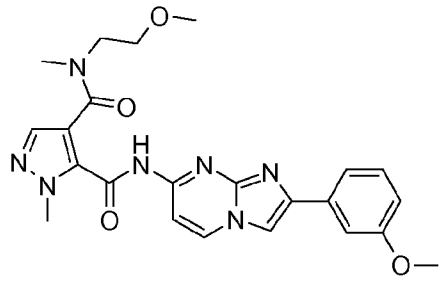
The title compound was prepared in analogy to example 82 from methyl 2-(3-(7-aminoimidazo[1,2-*a*]pyrimidin-2-yl)phenoxy)acetate (105 mg, 352 µmol) and 4-

(ethyl(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (74.3 mg, 352 µmol). Light yellow solid (30 mg, 16%).

MS (m/z) = 492.2 [M+H+].

Example 101

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

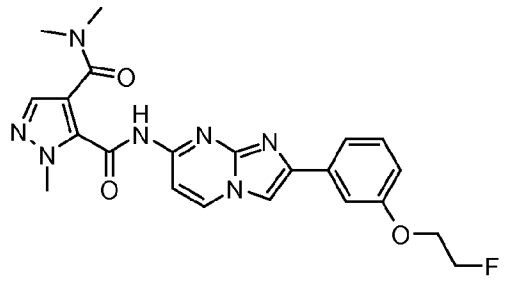


The title compound was prepared in analogy to example 82 from 2-(3-methoxyphenyl)imidazol[1,2-a]pyrimidin-7-amine (100 mg, 416 µmol) and 4-[(2-methyl-ethyl)-methyl-carbamoyl]-2-methyl-2*H*-pyrazole-3-carboxylic acid (120 mg, 499 µmol). Light yellow solid (79 mg, 38%).

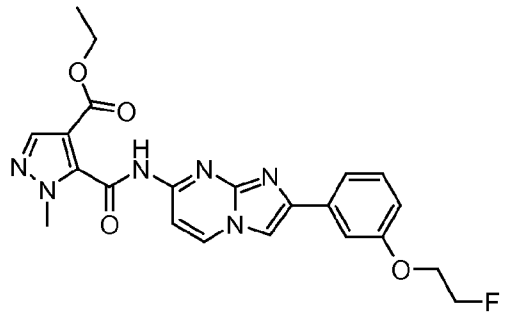
MS (m/z) = 464.2 [M+H+].

Example 102

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-yl}-amide)



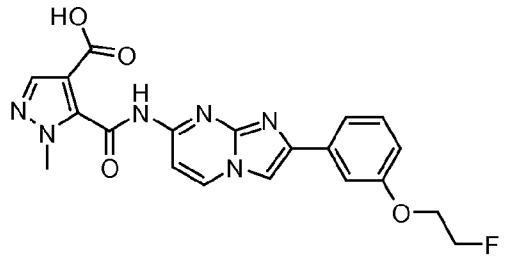
Step 1: 5-{2-[3-(2-Fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl}-1-methyl-1H-pyrazole-4-carboxylic acid ethyl ester



2-(3-(2-Fluoroethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (1 eq.) was combined with EtOAc (7.50 ml) to give a light yellow suspension. 4-(Ethoxycarbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (1 eq.) and DIPEA (6 eq.) were added. The reaction mixture was cooled down to 0 °C and *n*-propylphosphonic acid anhydride, cyclic trimer (1.17g, 1.1ml, 1,84mmol, 2.50 eq.) was added dropwise. After stirring at 0 °C during 30 min, the reaction mixture was stirred and allowed to warm-up to RT overnight. The reaction mixture (yellow solution) was poured into 50 ml EtOAc and extracted with H_2O (1 x 30 ml). The aqueous layer was back-extracted with DCM (3 x 20 ml). The organic layers were combined and washed with sat. NaCl-solution (1x30 ml), dried over $MgSO_4$, filtrated and concentrated under vacuum to give a yellow solid (207mg). The crude material was purified by flash chromatography (silica gel, 20g, CH_2Cl_2 to 50% CH_2Cl_2/MeOH/$NH_{3\,aq.}$ 140:10:1). Yellow solid (332 mg, 31%).

MS (m/z) = 453.2 [M+H+].

Step 2: 5-{2-[3-(2-Fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl}-1-methyl-1H-pyrazole-4-carboxylic acid



Ethyl 5-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-ylcarbamoyl)-1-methyl-1*H*-pyrazole-4-carboxylate (100 mg, 221 µmol) was combined with Ethanol (0.570 ml) and THF (0.570) to give a yellow solution. The reaction was stirred at RT for 6 h. H_2O was added to the suspension and then HCl 1N was added until the mixture was acidic (pH=3). The suspension was stirred for 30 min and then the reaction mixture was filtered. The residual solvent was removed under vacuum. The title compound was obtained as a light yellow solid (73mg, 78%).

MS (m/z) = 425.2 [M+H+].

Step 3: 2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide)

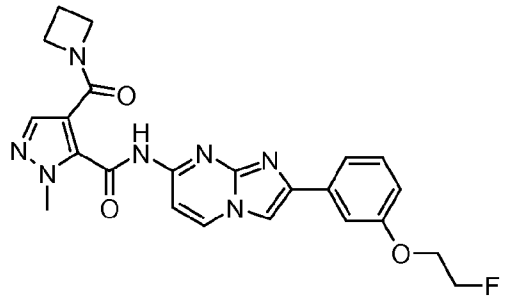
Dimethylamine hydrochloride (5.76 mg, 70.7 µmol) was combined with EtOAc (0.700 ml) to give a colorless solution. 5-(2-(3-(2-Fluoroethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-ylcarbamoyl)-1-methyl-1*H*-pyrazole-4-carboxylic acid (30.0 mg, 70.7 µmol) and DIPEA (54.8 mg, 74.1 µl, 424 µml) were added. The light yellow suspension was cooled down to 0 °C, and *n*-propylphosphonic acid anhydride, cyclic trimer (112 mg, 177 µmol) was added dropwise. After stirring at 0 °C for 30 min, the reaction mixture was stirred and allowed to warm-up to RT

overnight. After dilution with H_2O the product was extracted with EtOAc. Drying ($MgSO_4$) and evaporation of the solvent yielded the crude product. Purification by preparative TLC (silica gel, 1.0 mm, CH_2Cl_2/MeOH/NH_4OH 140:10:1) yielded the title compound (7.5 mg, 23%) as yellow solid.

MS (m/z) = 452.2 [M+H+].

Example 103

4-(Azetidine-1-carbonyl)-2-methyl-2*H*-pyrazole-3-carboxylic acid {2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-yl}-amide

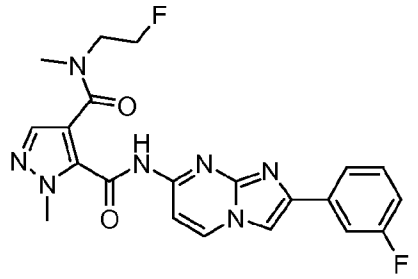


The title compound was prepared in analogy to example 102 from 2-[3-(2-Fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-ylamine. Yellow solid.

MS (m/z) = 464.3 [M+H+].

Example 104

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-[(2-fluoro-ethyl)-methyl-amide] 3-{[2-(3-fluoro-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

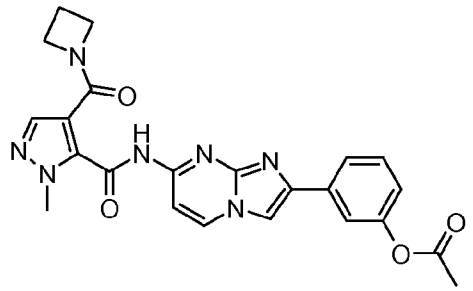


The title compound was prepared in analogy to example 82 from 2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-amine (99 mg, 436 µmol) and 4-((2-fluoroethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 436 µmol) Yellow solid (37 mg, 17%).

MS (m/z) = 440.2 [M+H+].

Example 105

3-(7-(4-(azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxamido)imidazo[1,2-*a*]pyrimidin-2-yl)phenyl acetate



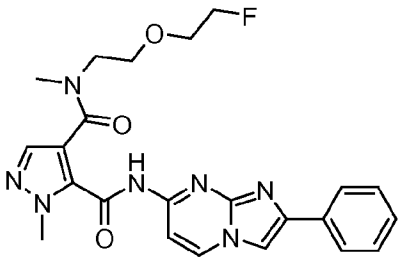
The title compound was prepared in analogy to example 82, step 3, from 4-(azetidine-1-carbonyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (156 mg, 746 µmol) and acetic acid 3-(7-

amino-imidazo[1,2-*a*]pyrimidin-2-yl)-phenyl ester (200 mg, 746 µmol). Yield: 158 mg (42%). Yellow foam.

MS (m/z) = 459.2 [M+H+].

Example 106

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-{[2-(2-fluoro-ethoxy)-ethyl]-methyl-amide} 3-[(2-phenyl-imidazo[1,2-*a*]pyrimidin-7-yl)-amide]

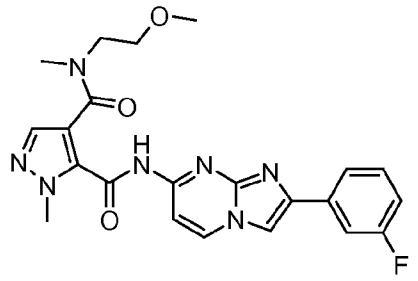


The title compound was prepared in analogy to example 82 from 2-phenylimidazo[1,2-a]pyrimidin-7-amine (77, 366 µmol) and 4-((2-(2-fluoroethoxy)ethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 366 µmol). Light yellow foam (15 mg, 8.1%).

MS (m/z) = 466.2 [M+H+].

Example 107

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-fluoro-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide} 4-[(2-methoxy-ethyl)-methyl-amide]

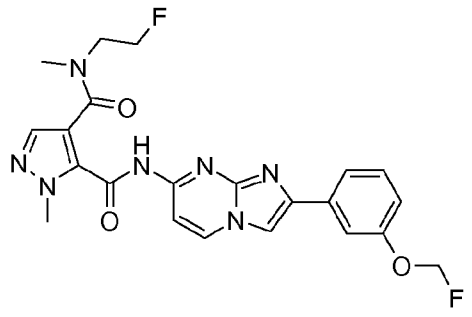


The title compound was prepared in analogy to example 82 from 2-(3-fluorophenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 438 µmol) and 4-[(2-methyl-ethyl)-methyl-carbamoyl]-2-methyl-2*H*-pyrazole-3-carboxylic acid (127 mg, 526 µmol). Yellow solid (17 mg, 8%).

MS (m/z) = 452.2 [M+H+].

Example 108

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-[(2-fluoro-ethyl)-methyl-amide] 3-{[2-(3-fluoromethoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

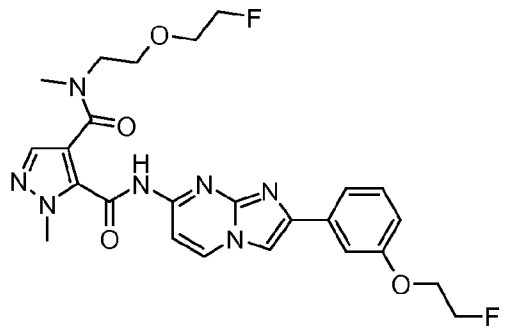


The title compound was prepared in analogy to example 82 from 4-((2-fluoroethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (89 mg, 387 µmol and 2-(3-(fluoromethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100 mg, 387 µmol). Yellow solid (4.7 mg, 2%).

MS (m/z) = 470.1 [M+H+].

Example 109

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-{[2-(2-fluoro-ethoxy)-ethyl]-methyl-amide} 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-*a*]pyrimidin-7-yl}-amide)

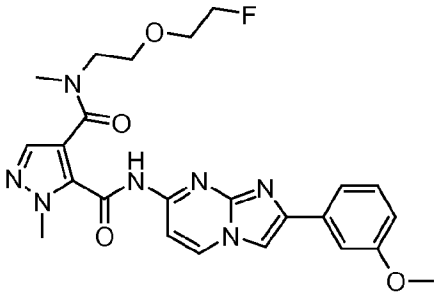


The title compound was prepared in analogy to example 82 from 2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-*a*]pyrimidin-7-amine (100, 366 µmol) and 4-((2-(2-fluoroethoxy)ethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 366 µmol). Light yellow foam (18 mg, 9%).

MS (m/z) = 528.2 [M+H+].

Example 110

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-{[2-(2-fluoro-ethoxy)-ethyl]-methyl-amide} 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}

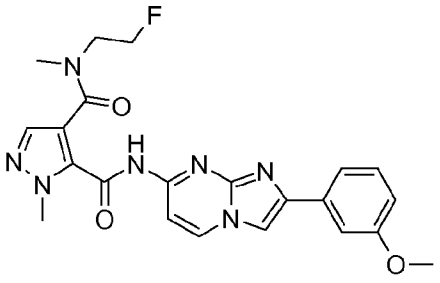


The title compound was prepared in analogy to example 82 from 2-(3-methoxyphenyl)imidazo[1,2-*a*]pyrimidin-7-amine (88, 366 µmol) and 4-((2-(2-fluoroethoxy)ethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 366 µmol). Light yellow foam (36 mg, 19%).

MS (m/z) = 496.2 [M+H+].

Example 111

2-Methyl-2*H*-pyrazole-3,4-dicarboxylic acid 4-[(2-fluoro-ethyl)-methyl-amide] 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-*a*]pyrimidin-7-yl]-amide}



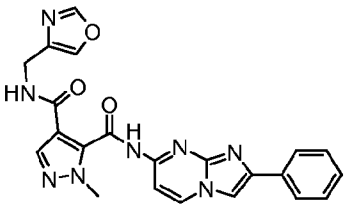
The title compound was prepared in analogy to example 82 from 2-(3-methoxyphenyl)imidazo[1,2-*a*]pyrimidin-7-amine (105, 436 µmol) and 4-((2-

fluoroethyl)(methyl)carbamoyl)-1-methyl-1*H*-pyrazole-5-carboxylic acid (100 mg, 436 µmol). Color solid (17 mg, 9%).

MS (m/z) = 452.2 [M+H+].

Example 112

1-methyl-N4-(oxazol-4-ylmethyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

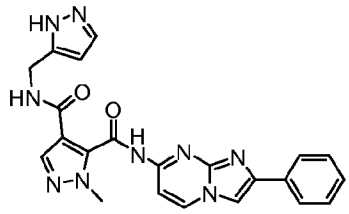


The title compound was obtained in analogy to example 29, using C-oxazol-4-yl-methylamine in the last step.

MS (m/e) = 443.3 [M+H$^+$].

Example 113

N4-((1H-pyrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

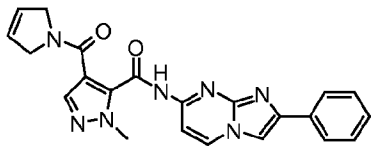


The title compound was obtained in analogy to example 29, using C-(2H-pyrazol-3-yl)-methylamine in the last step.

MS (m/e) = 442.3 [M+H$^+$].

Example 114

4-(2,5-dihydro-1H-pyrrole-1-carbonyl)-1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide

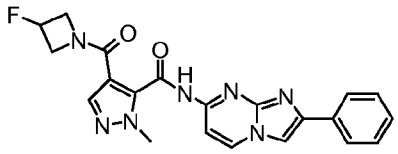


The title compound was obtained in analogy to example 29, using 2,5-dihydro-1H-pyrrole in the last step.

MS (m/e) = 414.3 [M-H$^+$].

Example 115

4-(3-fluoroazetidine-1-carbonyl)-1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide

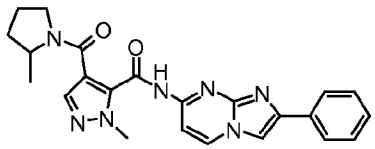


The title compound was obtained in analogy to example 29, using 3-fluoro-azetidine in the last step.

MS (m/e) = 420.2 [M+H$^+$].

Example 116

1-methyl-4-(2-methylpyrrolidine-1-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide

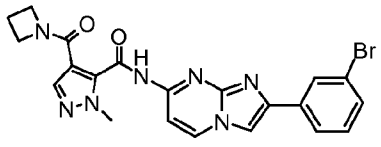


The title compound was obtained in analogy to example 29, using 2-methyl-pyrrolidine in the last step.

MS (m/e) = 430.3 [M+H$^+$].

Example 117

4-(azetidine-1-carbonyl)-N-(2-(3-bromophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide

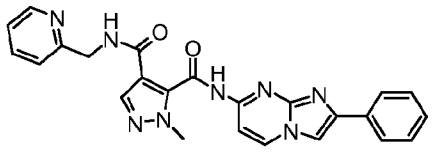


The title compound was obtained in analogy to example 29, using 2-(3-bromo-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine in step 4. 2-(3-Bromo-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine was prepared in analogy to example 1, step 1, from 2-bromo-1-(3-chloro-phenyl)-ethanone.

MS (m/e) = 480.2 [$M+H^+$].

Example 118

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-2-ylmethyl)-1H-pyrazole-4,5-dicarboxamide

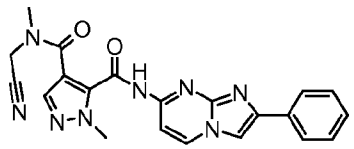


The title compound was obtained in analogy to example 29, using C-pyridin-2-yl-methylamine in the last step.

MS (m/e) = 453.2 [$M+H^+$].

Example 119

N4-(cyanomethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

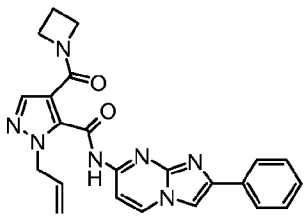


The title compound was obtained in analogy to example 29, using methylamino-acetonitrile in the last step.

MS (m/e) = 415.3 [$M+H^+$].

Example 120

1-allyl-4-(azetidine-1-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide



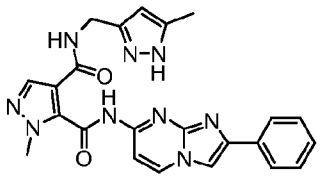
The title compound was obtained in analogy to example 64 from 2-allyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethyl ester (step 1) and azetidine (step 2). 2-Allyl-2H-pyrazole-3,4-

dicarboxylic acid 4-ethyl ester was prepared in analogy to example 62, using allyl bromide in step 2.

MS (m/e) = 428.3 [M+H$^+$].

Example 121

1-methyl-N4-((5-methyl-1H-pyrazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

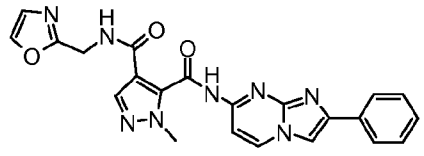


The title compound was obtained in analogy to example 29, using C-(5-methyl-1H-pyrazol-3-yl)-methyl amine in the last step.

MS (m/e) = 456.4 [M+H$^+$].

Example 122

1-methyl-N4-(oxazol-2-ylmethyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

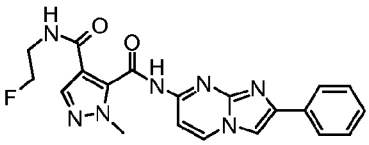


The title compound was obtained in analogy to example 29, using C-oxazol-2-yl-methylamine in the last step.

MS (m/e) = 443.3 [M+H$^+$].

Example 123

N4-(2-fluoroethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

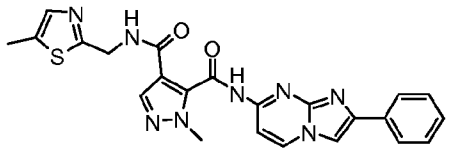


The title compound was obtained in analogy to example 29, using 2-fluoro-ethylamine in the last step.

MS (m/e) = 408.3 [M+H$^+$].

Example 124

1-methyl-N4-((5-methylthiazol-2-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

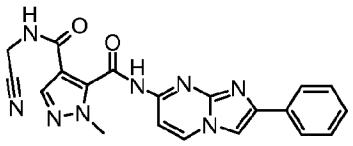


The title compound was obtained in analogy to example 29, using C-(5-methyl-thiazol-2-yl)-methylamine in the last step.

MS (m/e) = 473.2 [M+H$^+$].

Example 125

N4-(cyanomethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

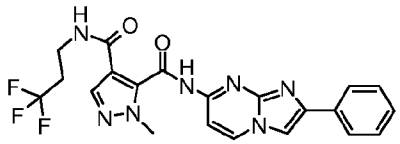


The title compound was obtained in analogy to example 29, using amino-acetonitrile in the last step.

MS (m/e) = 401.3 [M+H$^+$].

Example 126

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(3,3,3-trifluoropropyl)-1H-pyrazole-4,5-dicarboxamide

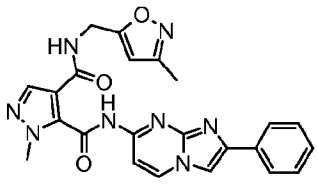


The title compound was obtained in analogy to example 29, using 3,3,3-trifluoro-propylamine in the last step.

MS (m/e) = 458.2 [M+H$^+$].

Example 127

1-methyl-N4-((3-methylisoxazol-5-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

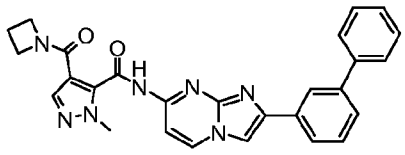


The title compound was obtained in analogy to example 29, using C-(3-methyl-isoxazol-5-yl)-methylamine in the last step.

MS (m/e) = 457.3 [M+H$^+$].

Example 128

4-(azetidine-1-carbonyl)-N-(2-(biphenyl-3-yl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide

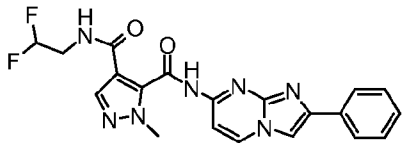


Under an atmosphere of argon, in a 25 mL round-bottomed flask, 4-(azetidine-1-carbonyl)-N-(2-(3-bromophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide (85mg, 177 µmol, Eq: 1.00, example 117), phenylboronic acid (43.2 mg, 354 µmol, Eq: 2), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (14.5 mg, 17.7 µmol, Eq: 0.1) and potassium carbonate (73.4 mg, 531 µmol, Eq: 3) were combined with DMF (2 ml) and water (0.2ml) to give a brown solution. The reaction was stirred for 1h at 100°C. The HPLC-MS showed complete conversion. The reaction mixture was poured into 20 mL water and extracted with EtOAc (2 x 25 mL).The organic layers were dried over Na_2SO_4 and concentrated in vacuo. After the addition of 2ml Methanol the desired product crystallised. The suspensnion was filtered off and washed with 0.5ml MeOH. The residual solvent was removed under vacuum.The title compound was obtained as a light brown solid (42mg, 49.7 %). 4-(Azetidine-1-carbonyl)-N-(2-(3-bromophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide was prepared in analogy to example 29, using 2-(3-bromo-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine in the first step. 2-(3-Bromo-phenyl)-imidazo[1,2-a]pyrimidin-7-ylamine can be prepared in analogy to example 1, step 1, from 2-bromo-1-(3-bromo-phenyl)-ethanone.

MS (m/e) = 478.2 $[M+H^+]$.

Example 129

N4-(2,2-difluoroethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

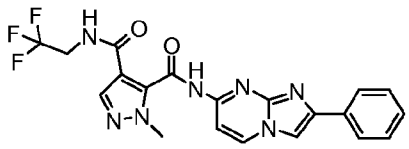


The title compound was obtained in analogy to example 29, using 2,2-difluoro-ethylamine in the last step.

MS (m/e) = 426.1 [$M+H^+$].

Example 130

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(2,2,2-trifluoroethyl)-1H-pyrazole-4,5-dicarboxamide

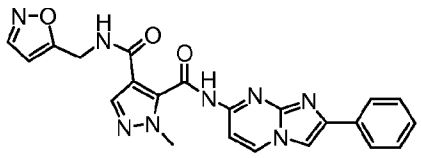


The title compound was obtained in analogy to example 29, using 2,2,2-trifluoro-ethylamine in the last step.

MS (m/e) = 444.2 [$M+H^+$].

Example 131

N4-(isoxazol-5-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

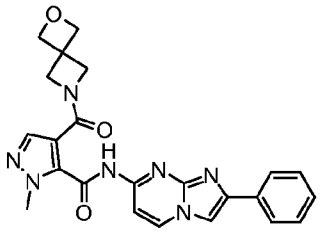


The title compound was obtained in analogy to example 29, using C-isoxazol-5-yl-methylamine in the last step.

MS (m/e) = 443.4 [M+H$^+$].

Example 132

1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-4-(2-oxa-6-azaspiro[3.3]heptane-6-carbonyl)-1H-pyrazole-5-carboxamide

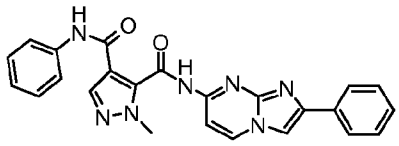


The title compound was obtained in analogy to example 29, using 2-oxa-6-aza-spiro[3.3]heptane in the last step.

MS (m/e) = 444.3 [M+H$^+$].

Example 133

1-methyl-N4-phenyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

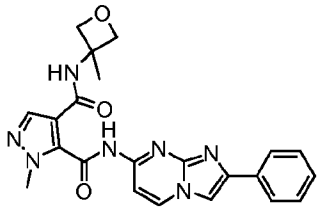


The title compound was obtained in analogy to example 29, using aniline in the last step.

MS (m/e) = 438.2 [$M+H^+$].

Example 134

1-methyl-N4-(3-methyloxetan-3-yl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

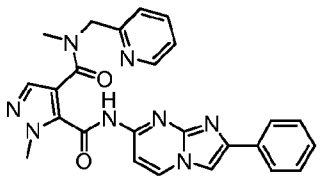


The title compound was obtained in analogy to example 29, using 3-methyl-oxetan-3-ylamine in the last step.

MS (m/e) = 432.3 [$M+H^+$].

Example 135

N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-2-ylmethyl)-1H-pyrazole-4,5-dicarboxamide

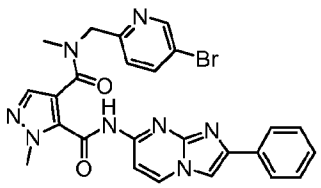


The title compound was obtained in analogy to example 29, using methyl-pyridin-2-ylmethyl-amine in the last step.

MS (m/e) = 467.3 [$M+H^+$].

Example 136

N4-((5-bromopyridin-2-yl)methyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

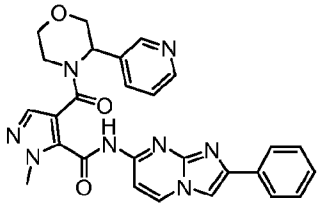


The title compound was obtained in analogy to example 29, using (5-bromo-pyridin-2-ylmethyl)-methyl-amine in the last step.

MS (m/e) = 547.1 [$M+H^+$].

Example 137

1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-4-(3-(pyridin-3-yl)morpholine-4-carbonyl)-1H-pyrazole-5-carboxamide

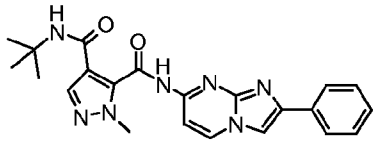


The title compound was obtained in analogy to example 29, using 3-pyridin-3-yl-morpholine in the last step.

MS (m/e) = 509.4 [$M+H^+$].

Example 138

N4-tert-butyl-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

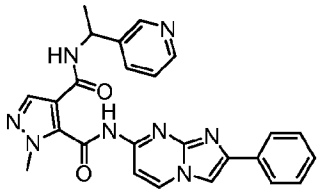


The title compound was obtained in analogy to example 29, using tert-butylamine in the last step.

MS (m/e) = 418.3 [$M+H^+$].

Example 139

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(1-(pyridin-3-yl)ethyl)-1H-pyrazole-4,5-dicarboxamide

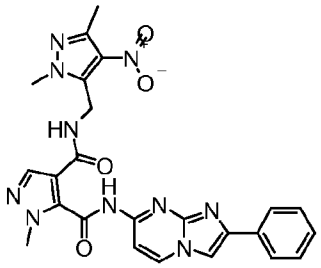


The title compound was obtained in analogy to example 29, using methyl-(1-pyridin-3-yl-ethyl)-amine in the last step.

MS (m/e) = 467.3 [$M+H^+$].

Example 140

N4-((1,3-dimethyl-4-nitro-1H-pyrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

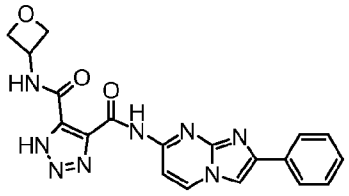


The title compound was obtained in analogy to example 29, using C-(2,5-dimethyl-4-nitro-2H-pyrazol-3-yl)-methylamine in the last step.

MS (m/e) = 515.3 [$M+H^+$].

Example 141

N5-(oxetan-3-yl)-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide

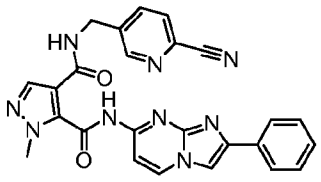


The title compound was obtained in analogy to example 29, using oxetan-3-ylamine in the last step.

MS (m/e) = 405.3 [$M+H^+$].

Example 142

N4-((6-cyanopyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

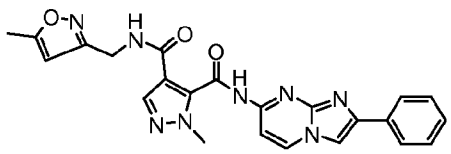


The title compound was obtained in analogy to example 29, using 5-aminomethyl-pyridine-2-carbonitrile in the last step.

MS (m/e) = 490.3 [M+H$^+$].

Example 143

1-methyl-N4-((5-methylisoxazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

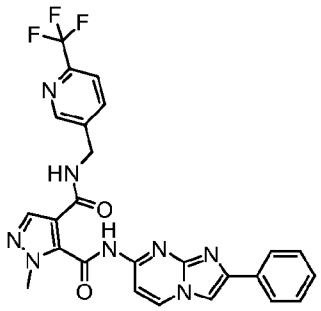


The title compound was obtained in analogy to example 29, using C-(5-methyl-isoxazol-3-yl)-methylamine in the last step.

MS (m/e) = 457.3 [M+H$^+$].

Example 144

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-pyrazole-4,5-dicarboxamide

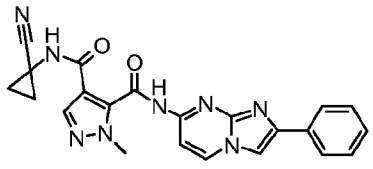


The title compound was obtained in analogy to example 29, using C-(6-trifluoromethyl-pyridin-3-yl)-methylamine in the last step.

MS (m/e) = 521.3 [$M+H^+$].

Example 145

N4-(1-cyanocyclopropyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

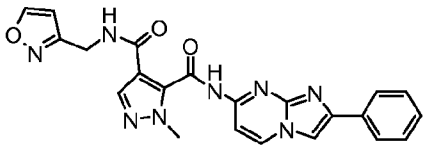


The title compound was obtained in analogy to example 29, using 1-amino-cyclopropanecarbonitrile in the last step.

MS (m/e) = 427.2 [$M+H^+$].

Example 146

N4-(isoxazol-3-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

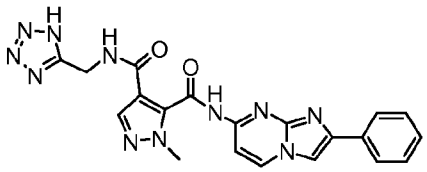


The title compound was obtained in analogy to example 29, using C-isoxazol-3-yl-methylamine in the last step.

MS (m/e) = 443.3 [M+H$^+$].

Example 147

N4-((1H-tetrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

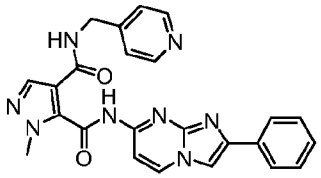


The title compound was obtained in analogy to example 29, using C-(1H-tetrazol-5-yl)-methylamine in the last step.

MS (m/e) = 444.4 [M+H$^+$].

Example 148

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-4-ylmethyl)-1H-pyrazole-4,5-dicarboxamide

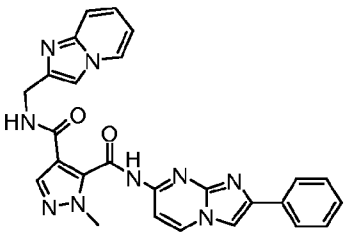


The title compound was obtained in analogy to example 29, using C-pyridin-4-yl-methylamine in the last step.

MS (m/e) = 453.3 [$M+H^+$].

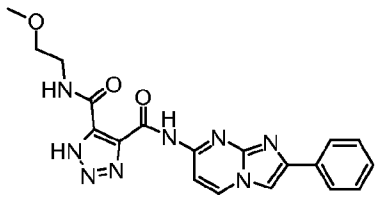
Example 149

N4-(imidazo[1,2-a]pyridin-2-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide



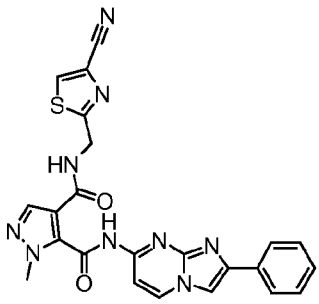
Example 150

N5-(2-methoxyethyl)-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide



Example 151

N4-((4-cyanothiazol-2-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

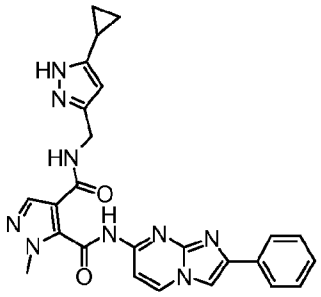


The title compound was obtained in analogy to example 29, using 2-aminomethyl-thiazole-4-carbonitrile in the last step.

MS (m/e) = 484.3 [$M+H^+$].

Example 152

N4-((5-cyclopropyl-1H-pyrazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

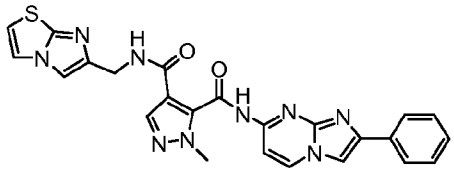


The title compound was obtained in analogy to example 29, using C-(5-cyclopropyl-1H-pyrazol-3-yl)-methylamine in the last step.

MS (m/e) = 456.4 [$M+H^+$].

Example 153

N4-(imidazo[2,1-b]thiazol-6-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

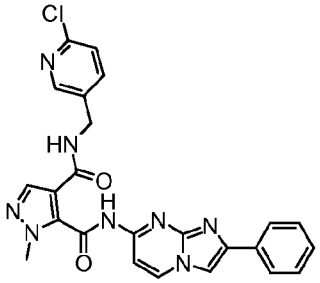


The title compound was obtained in analogy to example 29, using C-imidazo[2,1-b]thiazol-6-yl-methyl amine in the last step.

MS (m/e) = 498.4 [$M+H^+$].

Example 154

N4-((6-chloropyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

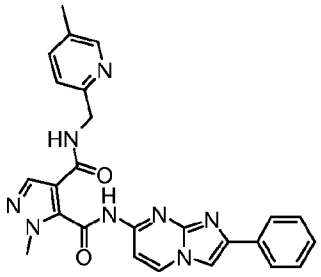


The title compound was obtained in analogy to example 29, using C-(6-chloro-pyridin-3-yl)-methylamine in the last step.

MS (m/e) = 487.3 [$M+H^+$].

Example 155

1-methyl-N4-((5-methylpyridin-2-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

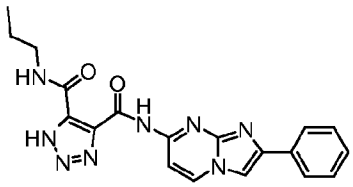


The title compound was obtained in analogy to example 29, using C-(5-methyl-pyridin-2-yl)-methylamine in the last step.

MS (m/e) = 467.3 [M+H$^+$].

Example 156

N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N5-propyl-1H-1,2,3-triazole-4,5-dicarboxamide

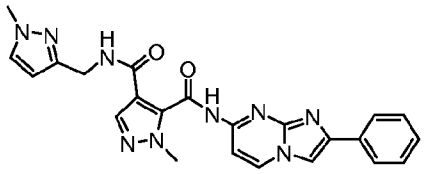


The title compound was obtained in analogy to example 27, using propylamine in the last step.

MS (m/e) = 391.2 [M+H$^+$].

Example 157

1-methyl-N4-((1-methyl-1H-pyrazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

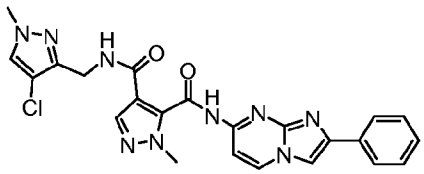


The title compound was obtained in analogy to example 29, using C-(1-methyl-1H-pyrazol-3-yl)-methylamine in the last step.

MS (m/e) = 456.3 [M+H$^+$].

Example 158

N4-((4-chloro-1-methyl-1H-pyrazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

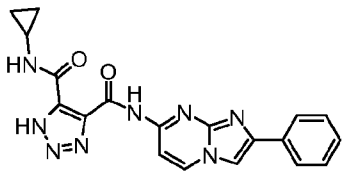


The title compound was obtained in analogy to example 29, using C-(4-chloro-1-methyl-1H-pyrazol-3-yl)-methylaminein the last step.

MS (m/e) = 490.3 [M+H$^+$].

Example 159

N5-cyclopropyl-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide

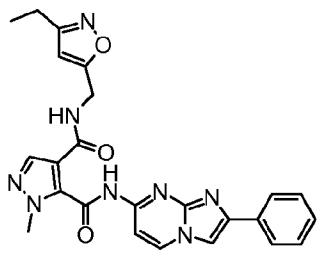


The title compound was obtained in analogy to example 27, using cyclopropylamine in the last step.

MS (m/e) = 391.2 [$M+H^+$].

Example 160

N4-((3-ethylisoxazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

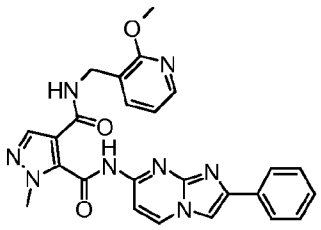


The title compound was obtained in analogy to example 29, using C-(3-ethyl-isoxazol-5-yl)-methylamine in the last step.

MS (m/e) = 471.2 [$M+H^+$].

Example 161

N4-((2-methoxypyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

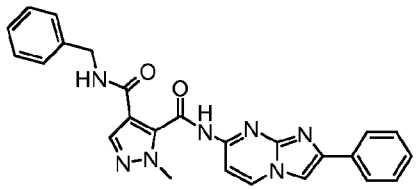


The title compound was obtained in analogy to example 29, using C-(2-methoxy-pyridin-3-yl)-methylamine in the last step.

MS (m/e) = 483.3 [$M+H^+$].

Example 162

N4-benzyl-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

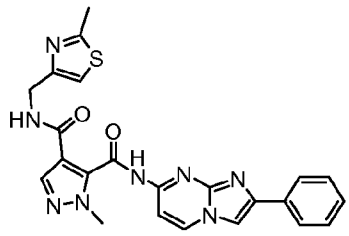


The title compound was obtained in analogy to example 29, using benzylamine in the last step.

MS (m/e) = 452.2 [M+H$^+$].

Example 163

1-methyl-N4-((2-methylthiazol-4-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

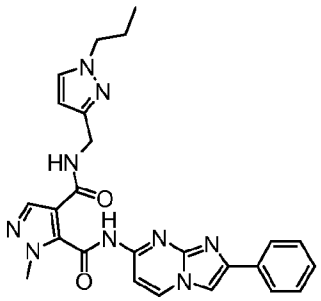


The title compound was obtained in analogy to example 29, using C-(2-methyl-thiazol-4-yl)-methylamine in the last step.

MS (m/e) = 473.2 [M+H$^+$].

Example 164

1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-((1-propyl-1H-pyrazol-3-yl)methyl)-1H-pyrazole-4,5-dicarboxamide

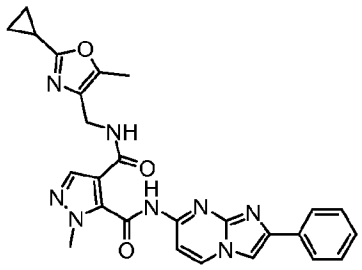


The title compound was obtained in analogy to example 29, using C-(1-propyl-1H-pyrazol-3-yl)-methylamine in the last step.

MS (m/e) = 484.4 [M+H$^+$].

Example 165

N4-((2-cyclopropyl-5-methyloxazol-4-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

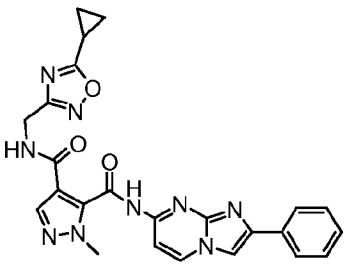


The title compound was obtained in analogy to example 29, using (2-cyclopropyl-5-methyloxazol-4-yl)methanamine in the last step.

MS (m/e) = 497.3 [M+H$^+$].

Example 166

N4-((5-cyclopropyl-1,2,4-oxadiazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

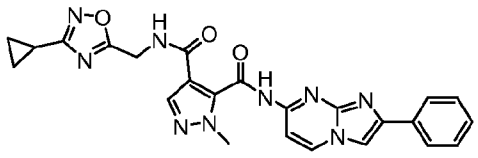


The title compound was obtained in analogy to example 29, using C-(5-cyclopropyl-[1,2,4]oxadiazol-3-yl)-methylamine in the last step.

MS (m/e) = 484.4 [$M+H^+$].

Example 167

N4-((3-cyclopropyl-1,2,4-oxadiazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

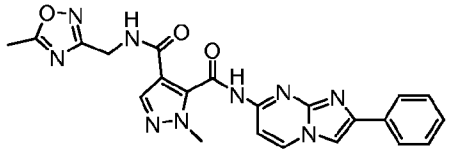


The title compound was obtained in analogy to example 29, using C-(3-cyclopropyl-[1,2,4]oxadiazol-5-yl)-methylamine in the last step.

MS (m/e) = 484.4 [$M+H^+$].

Example 168

1-methyl-N4-((5-methyl-1,2,4-oxadiazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

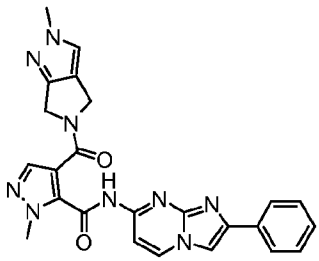


The title compound was obtained in analogy to example 29, using C-(5-methyl-[1,2,4]oxadiazol-3-yl)-methylamine in the last step.

MS (m/e) = 458.4 [$M+H^+$].

Example 169

1-methyl-4-(2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole-5-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide

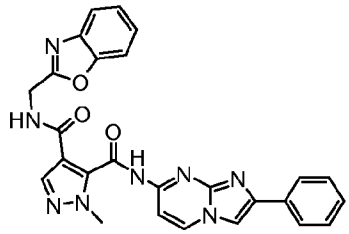


The title compound was obtained in analogy to example 29, using 2-methyl-2,4,5,6-tetrahydro-pyrrolo[3,4-c]pyrazole in the last step.

MS (m/e) = 468.3 [M+H$^+$].

Example 170

N4-(benzo[d]oxazol-2-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide

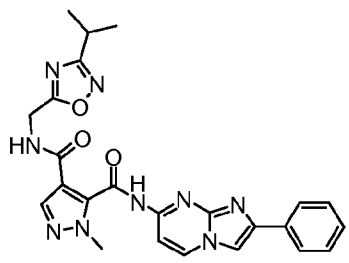


The title compound was obtained in analogy to example 29, using C-benzooxazol-2-yl-methylamine in the last step.

MS (m/e) = 493.3 [M+H$^+$].

Example 171

N4-((3-isopropyl-1,2,4-oxadiazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide



The title compound was obtained in analogy to example 29, using C-(3-isopropyl-[1,2,4]oxadiazol-5-yl)-methylamine in the last step.

MS (m/e) = 486.5 [$M+H^+$].

5

Example A

Film coated tablets containing the following ingredients can be manufactured in a conventional manner:

Ingredients	Per tablet	
Kernel:		
Compound of formula (I)	10.0 mg	200.0 mg
Microcrystalline cellulose	23.5 mg	43.5 mg
Lactose hydrous	60.0 mg	70.0 mg
Povidone K30	12.5 mg	15.0 mg
Sodium starch glycolate	12.5 mg	17.0 mg
Magnesium stearate	1.5 mg	4.5 mg
(Kernel Weight)	120.0 mg	350.0 mg
Film Coat:		
Hydroxypropyl methyl cellulose	3.5 mg	7.0 mg
Polyethylene glycol 6000	0.8 mg	1.6 mg
Talc	1.3 mg	2.6 mg
Iron oxyde (yellow)	0.8 mg	1.6 mg
Titan dioxide	0.8 mg	1.6 mg

The active ingredient is sieved and mixed with microcristalline cellulose and the mixture is granulated with a solution of polyvinylpyrrolidon in water. The granulate is mixed with sodium starch glycolate and magesiumstearate and compressed to yield kernels of 120 or 350 mg respectively. The kernels are lacquered with an aqueous solution / suspension of the above mentioned film coat.

Example B

Capsules containing the following ingredients can be manufactured in a conventional manner:

Ingredients	Per capsule
Compound of formula (I)	25.0 mg
Lactose	150.0 mg
Maize starch	20.0 mg
Talc	5.0 mg

The components are sieved and mixed and filled into capsules of size 2.

Example C

Injection solutions can have the following composition:

Compound of formula (I)	3.0 mg
Polyethylene Glycol 400	150.0 mg
Acetic Acid	q.s. ad pH 5.0
Water for injection solutions	ad 1.0 mL

The active ingredient is dissolved in a mixture of Polyethylene Glycol 400 and water for injection (part). The pH is adjusted to 5.0 by Acetic Acid. The volume is adjusted to 1.0 mL by addition of the residual amount of water. The solution is filtered, filled into vials using an appropriate overage and sterilized.

Example D

Soft gelatin capsules containing the following ingredients can be manufactured in a conventional manner:

Capsule contents

Compound of formula (I)	5.0 mg
Yellow wax	8.0 mg
Hydrogenated Soya bean oil	8.0 mg
Partially hydrogenated plant oils	34.0 mg
Soya bean oil	110.0 mg
Weight of capsule contents	165.0 mg
Gelatin capsule	
Gelatin	75.0 mg
Glycerol 85 %	32.0 mg
Karion 83	8.0 mg (dry matter)
Titan dioxide	0.4 mg
Iron oxide yellow	1.1 mg

The active ingredient is dissolved in a warm melting of the other ingredients and the mixture is filled into soft gelatin capsules of appropriate size. The filled soft gelatin capsules are treated according to the usual procedures.

Example E

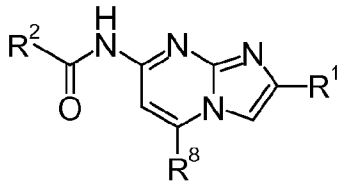
Sachets containing the following ingredients can be manufactured in a conventional manner:

Compound of formula (I)	50.0 mg
Lactose, fine powder	1015.0 mg
Microcristalline cellulose (AVICEL PH 102)	1400.0 mg
Sodium carboxymethyl cellulose	14.0 mg
Polyvinylpyrrolidon K 30	10.0 mg
Magnesiumstearate	10.0 mg
Flavoring additives	1.0 mg

The active ingredient is mixed with lactose, microcristalline cellulose and sodium carboxymethyl cellulose and granulated with a mixture of polyvinylpyrrolidon in water. The granulate is mixed with magnesiumstearate and the flavouring additives and filled into sachets.

Claims

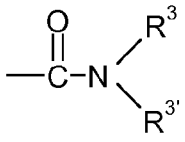
1. A compound of formula (I)



(I)

wherein

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of hydroxyl, halogen, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy, lower alkoxy lower alkyl, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy and phenyl;

R^2 is 5- or 6-membered monocyclic heteroaryl having 1 to 3 heteroatoms independently selected from N and O, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of , halogen, hydroxyl, nitro, lower alkyl, lower alkenyl, lower alkoxy, lower alkoxy-C(O)-, lower hydroxyalkyl, lower haloalkyl, lower alkoxy lower alkyl, lower alkyl-C(O)-, cycloalkyl, heterocyclyl, aryl, heteroaryl and amino optionally substituted by heteroaryl, wherein two substituents of R^2, together with said heteroaryl to which they are attached, may form a 9- or 10-membered bicyclic ring;

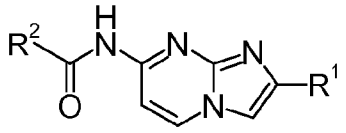
R^3 and $R^{3'}$ are independently hydrogen, lower alkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl, cyanocycloalkyl, heterocyclyl or aryl, wherein said lower alkyl is optionally substituted by lower haloalkoxy, cycloalkyl, aryl or heteroaryl, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, lower alkyl, lower haloalkyl, lower alkoxy and cycloalkyl, and wherein said heterocyclyl is optionally substituted by lower alkyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl, 2,5-dihydro-1H-pyrrole, 2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole or 2-oxa-6-azaspiro[3.3]heptane, wherein said heterocyclyl is optionally substituted by 1 to 3 halogen, hydroxyl, oxo, lower alkyl or heteroaryl;

R^8 is hydrogen, lower alkyl, lower alkoxy or lower alkoxy lower alkyl;

or a pharmaceutically acceptable salt thereof.

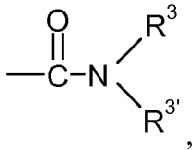
2. A compound of formula (I')



(I')

wherein

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, lower alkyl, lower alkoxy, lower haloalkyl, lower haloalkoxy and lower alkoxy lower alkyl;

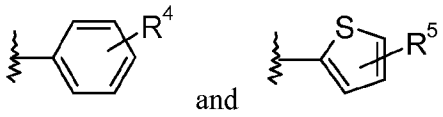
R^2 is 5- or 6-membered monocyclic heteroaryl having 1 to 3 heteroatoms independently selected from N and O, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of , halogen, hydroxyl, nitro, lower alkyl, lower alkoxy, lower alkoxy-C(O)-, lower hydroxyalkyl, lower haloalkyl, lower alkoxy lower alkyl, lower alkyl-C(O)-, cycloalkyl, heterocyclyl, aryl, heteroaryl and amino optionally substituted by heteroaryl, wherein two substituents of R^2, together with said heteroaryl to which they are attached, may form a 9- or 10-membered bicyclic ring;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl optionally substituted by cycloalkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl or heterocyclyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl optionally substituted by 1 to 3 halogen, hydroxyl or oxo;

or a pharmaceutically acceptable salt thereof.

3. A compound or a pharmaceutically acceptable salt thereof according to claim 1, wherein R^1 is selected from the group consisting of:



and

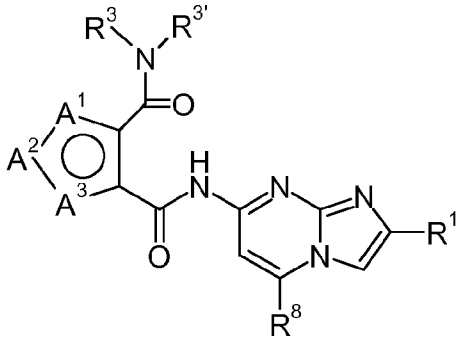
wherein

R^4 is hydrogen, hydroxyl, halogen, lower alkoxy, lower haloalkoxy, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy or phenyl;

R^5 is halogen.

4. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1 and 3, wherein R^8 is hydrogen or lower alkoxy lower alkyl.

5. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1, 3 and 4, having formula (Ia)



(Ia)

wherein

A^1 is -NH-, -N=, -NR^6- or -CH=;

A^2 is -N= or -$NR^{6'}$-;

A^3 is -N=, -$NR^{6''}$- or -CH=;

R^6 is lower alkyl;

$R^{6'}$ is lower alkyl;

$R^{6''}$ is lower alkyl or lower alkenyl;

R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by 1 to 3 substituents independently selected from the group consisting of hydroxyl, halogen, lower alkoxy, lower haloalkoxy, -OC(O)-lower alkyl, -OCH2C(O)-lower alkoxy and phenyl;

R^3 and $R^{3'}$ are independently hydrogen, lower alkyl, lower hydroxyalkyl, lower cyanoalkyl, lower haloalkyl, lower alkoxy lower alkyl, cycloalkyl, cyanocycloalkyl, heterocyclyl or aryl, wherein said lower alkyl is optionally substituted by lower haloalkoxy, cycloalkyl, aryl or heteroaryl, wherein said heteroaryl is optionally substituted by 1 to 3 substituents independently selected from the group consisting of halogen, nitro, cyano, lower alkyl,

lower haloalkyl, lower alkoxy and cycloalkyl, and wherein said heterocyclyl is optionally substituted by lower alkyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form a heterocyclyl, 2,5-dihydro-1H-pyrrole, 2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole or 2-oxa-6-azaspiro[3.3]heptane, wherein said heterocyclyl is optionally substituted by 1 to 3 halogen, hydroxyl, oxo, lower alkyl or heteroaryl;

R^8 is hydrogen, lower alkyl, lower alkoxy or lower alkoxy lower alkyl.

6. A compound according to claim 5, selected from the group consisting of:
5-(Azetidine-1-carbonyl)-1H-[1,2,3]triazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-4-(morpholine-4-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(4-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-methylamide,
4-(3,3-Difluoro-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(3-Hydroxy-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-(1,1-Dioxo-1λ6-thiomorpholine-4-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(3-methoxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-[(tetrahydro-furan-3-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-1-methyl-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-diethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-ethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-4-(piperidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isopropyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(methyl-propyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 4-propylamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclopropylmethyl-amide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-cyclobutylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-isopropylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-trifluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-methylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

1H-[1,2,3]Triazole-4,5-dicarboxylic acid 5-methylamide 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

3-(Azetidine-1-carbonyl)-1-methyl-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 3-(ethyl-methyl-amide) 4-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

1-Methyl-1H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-cyano-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(isobutyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-hydroxy-2-methyl-propyl)-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(azetidine-1-carbonyl)-N-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-hydroxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,

N5-(2-(3-hydroxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,N4,1-trimethyl-1H-pyrazole-4,5-dicarboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide},

N4-ethyl-N5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-ethyl-N5-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,N4,1-trimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-ethyl-N5-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

4-(3-fluoroazetidine-1-carbonyl)-N-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

4-(azetidine-1-carbonyl)-N-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

4-(3-fluoroazetidine-1-carbonyl)-N-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

3-(7-(4-(dimethylcarbamoyl)-1-methyl-1H-pyrazole-5-carboxamido)imidazo[1,2-a]pyrimidin-2-yl)phenyl acetate,

N5-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,N4,1-trimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-fluoroethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide) 4-[(2-methoxy-ethyl)-methyl-amide],

N4-ethyl-N5-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

4-(3-fluoroazetidine-1-carbonyl)-N-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-fluoromethoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-[(2-methoxy-ethyl)-methyl-amide],

methyl 2-(3-(7-(4-(ethyl(methyl)carbamoyl)-1-methyl-1H-pyrazole-5-carboxamido)imidazo[1,2-a]pyrimidin-2-yl)phenoxy)acetate,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-{[2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide},

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-({2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide),

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid {2-[3-(2-fluoro-ethoxy)-phenyl]-imidazo[1,2-a]pyrimidin-7-yl}-amide,

N4-(2-fluoroethyl)-N5-(2-(3-fluorophenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

3-(7-(4-(azetidine-1-carbonyl)-1-methyl-1H-pyrazole-5-carboxamido)imidazo[1,2-a]pyrimidin-2-yl)phenyl acetate,

N4-(2-(2-fluoroethoxy)ethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 3-{[2-(3-fluoro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide} 4-[(2-methoxy-ethyl)-methyl-amide],

N4-(2-fluoroethyl)-N5-(2-(3-(fluoromethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-(2-fluoroethoxy)ethyl)-N5-(2-(3-(2-fluoroethoxy)phenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-(2-fluoroethoxy)ethyl)-N5-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,

N4-(2-fluoroethyl)-N5-(2-(3-methoxyphenyl)imidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-(oxazol-4-ylmethyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((1H-pyrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
4-(2,5-dihydro-1H-pyrrole-1-carbonyl)-1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
4-(3-fluoroazetidine-1-carbonyl)-1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
1-methyl-4-(2-methylpyrrolidine-1-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
4-(azetidine-1-carbonyl)-N-(2-(3-bromophenyl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-2-ylmethyl)-1H-pyrazole-4,5-dicarboxamide,
N4-(cyanomethyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-allyl-4-(azetidine-1-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
1-methyl-N4-((5-methyl-1H-pyrazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-(oxazol-2-ylmethyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-(2-fluoroethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((5-methylthiazol-2-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-(cyanomethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(3,3,3-trifluoropropyl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-((3-methylisoxazol-5-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
4-(azetidine-1-carbonyl)-N-(2-(biphenyl-3-yl)imidazo[1,2-a]pyrimidin-7-yl)-1-methyl-1H-pyrazole-5-carboxamide,
N4-(2,2-difluoroethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(2,2,2-trifluoroethyl)-1H-pyrazole-4,5-dicarboxamide,
N4-(isoxazol-5-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-4-(2-oxa-6-azaspiro[3.3]heptane-6-carbonyl)-1H-pyrazole-5-carboxamide,
1-methyl-N4-phenyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-(3-methyloxetan-3-yl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-2-ylmethyl)-1H-pyrazole-4,5-dicarboxamide,
N4-((5-bromopyridin-2-yl)methyl)-N4,1-dimethyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-4-(3-(pyridin-3-yl)morpholine-4-carbonyl)-1H-pyrazole-5-carboxamide,
N4-tert-butyl-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(1-(pyridin-3-yl)ethyl)-1H-pyrazole-4,5-dicarboxamide,
N4-((1,3-dimethyl-4-nitro-1H-pyrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N5-(oxetan-3-yl)-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide,
N4-((6-cyanopyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,

1-methyl-N4-((5-methylisoxazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1H-pyrazole-4,5-dicarboxamide,
N4-(1-cyanocyclopropyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N5-(5-(methoxymethyl)-2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4,1-dimethyl-1H-pyrazole-4,5-dicarboxamide,
N4-((1H-tetrazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-(pyridin-4-ylmethyl)-1H-pyrazole-4,5-dicarboxamide,
N4-(imidazo[1,2-a]pyridin-2-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N5-(2-methoxyethyl)-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide,
N4-((4-cyanothiazol-2-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((5-cyclopropyl-1H-pyrazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-(imidazo[2,1-b]thiazol-6-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((6-chloropyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((5-methylpyridin-2-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N5-propyl-1H-1,2,3-triazole-4,5-dicarboxamide,
1-methyl-N4-((1-methyl-1H-pyrazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((4-chloro-1-methyl-1H-pyrazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N5-cyclopropyl-N4-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-1,2,3-triazole-4,5-dicarboxamide,

N4-((3-ethylisoxazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((2-methoxypyridin-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-benzyl-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((2-methylthiazol-4-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-N4-((1-propyl-1H-pyrazol-3-yl)methyl)-1H-pyrazole-4,5-dicarboxamide,
N4-((2-cyclopropyl-5-methyloxazol-4-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((5-cyclopropyl-1,2,4-oxadiazol-3-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((3-cyclopropyl-1,2,4-oxadiazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-N4-((5-methyl-1,2,4-oxadiazol-3-yl)methyl)-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
1-methyl-4-(2-methyl-2,4,5,6-tetrahydropyrrolo[3,4-c]pyrazole-5-carbonyl)-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-5-carboxamide,
N4-(benzo[d]oxazol-2-ylmethyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
N4-((3-isopropyl-1,2,4-oxadiazol-5-yl)methyl)-1-methyl-N5-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)-1H-pyrazole-4,5-dicarboxamide,
or a pharmaceutically acceptable salt thereof.

7. A compound or a pharmaceutically acceptable salt thereof according to claim 5, wherein

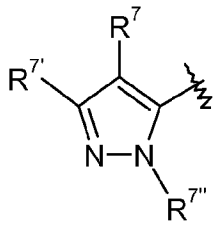
R^1 is phenyl or thienyl, wherein said phenyl and said thienyl are optionally substituted by halogen or lower alkoxy;

R^3 and $R^{3'}$ are independently lower alkyl or lower alkoxy lower alkyl, or

R^3 and $R^{3'}$, together with the nitrogen atom to which they are attached, form an azetidine ring, pyrrolidine ring or piperidine ring, wherein said azetizine ring is optionally substituted by 1 or 2 substituents independently selected from the group consisting of hydroxyl and halogen.

8. A compound according to claim 7, selected from the group consisting of:
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-4-(morpholine-4-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-(3,3-Difluoro-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-(3-Hydroxy-azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-methoxy-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
2-Methyl-4-(pyrrolidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
2-Methyl-4-(piperidine-1-carbonyl)-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-[(2-methoxy-ethyl)-methyl-amide] 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(3-chloro-phenyl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
4-(Azetidine-1-carbonyl)-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Ethyl-2H-pyrazole-3,4-dicarboxylic acid 4-(ethyl-methyl-amide) 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],

4-(Azetidine-1-carbonyl)-2-methyl-2H-pyrazole-3-carboxylic acid [2-(5-chloro-thiophen-2-yl)-imidazo[1,2-a]pyrimidin-7-yl]-amide,
2-Methyl-2H-pyrazole-3,4-dicarboxylic acid 4-dimethylamide 3-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide],
or a pharmaceutically acceptable salt thereof.

9. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1, 3 and 4, wherein R^2 is ,

wherein

R^7 is hydrogen, halogen, lower alkoxy-C(O)- or heteroaryl;

$R^{7'}$ is hydrogen, lower alkyl or nitro;

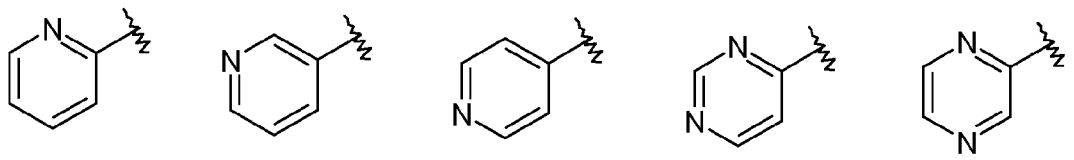
$R^{7''}$ is lower alkyl, cycloalkyl or aryl.

10. A compound according to claim 9, selected from the group consisting of:
4-Chloro-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Phenyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-2,5-dimethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-ethyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-propyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,

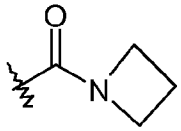
2-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-isopropyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-sec-Butyl-4-chloro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Chloro-2-isobutyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Isobutyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Cyclopentyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Ethyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Isopropyl-5-nitro-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Isoxazol-5-yl-2-methyl-2H-pyrazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
1-Ethyl-5-(2-phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-1H-pyrazole-4-carboxylic acid ethyl ester,
or a pharmaceutically acceptable salt thereof.

11. A compound according to any of claims 1, 3 and 4, selected from the group consisting of:
Isoxazole-5-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4,5,6,7-Tetrahydro-benzo[d]isoxazole-3-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
5-(2-Phenyl-imidazo[1,2-a]pyrimidin-7-ylcarbamoyl)-3H-[1,2,3]triazole-4-carboxylic acid methyl ester,
1-Methyl-3-(pyrimidin-5-ylamino)-1H-pyrazole-4-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
or a pharmaceutically acceptable salt thereof.

12. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1, 3 and 4, wherein R^2 is 6-membered heteroaryl selected from the group consisting of:



wherein said heteroaryl is substituted by 1 to 3 substituents independently selected from the group consisting of bromo, chloro, methyl, methoxy, cyclopropyl, $-C(O)NHCH_2CF_3$,

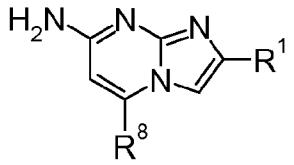


and pyrimidin-5-ylamino.

13. A compound according to claim 12, selected from the group consisting of:
3,6-Dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-Chloro-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-isonicotinamide,
6-Chloro-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
6-Methoxy-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
5-Bromo-3-methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
4-Bromo-3,6-dimethyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
6-Methyl-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
Pyrazine-2,3-dicarboxylic acid 2-[(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide] 3-[(2,2,2-trifluoro-ethyl)-amide],
2-(Azetidine-1-carbonyl)-N-(2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-nicotinamide,
6-Cyclopropyl-3-(pyrimidin-5-ylamino)-pyridine-2-carboxylic acid (2-phenyl-imidazo[1,2-a]pyrimidin-7-yl)-amide,
2-methoxy-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)nicotinamide,
5-chloro-2-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)pyrimidine-4-carboxamide,
2-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)isonicotinamide,
2-chloro-6-methyl-N-(2-phenylimidazo[1,2-a]pyrimidin-7-yl)isonicotinamide,
or a pharmaceutically acceptable salt thereof.

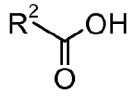
14. A process for the manufacture of a compound of formula (I) as defined in any of claims 1 - 13, which process comprises

reacting a compound of formula 3



3

with a compound of formula 2



2

wherein R^1, R^2 and R^8 are as defined in any of claims 1 - 12, and if desired, converting the compound into a pharmaceutically acceptable salt thereof.

15. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13, when manufactured by a process according to claim 14.

16. A pharmaceutical composition comprising a compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 and a pharmaceutically acceptable carrier and/or adjuvant.

17. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for use as therapeutic active substances.

18. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for use as a therapeutic active substance for the treatment and/or prophylaxis of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome,

cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma or breast cancer.

19. A method for the therapeutic and/or prophylactic treatment of diseases which are modulated by PDE10A inhibitors, particularly for the therapeutic and/or prophylactic treatment of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma or breast cancer, which method comprises administering a compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 to a human being or animal.

20. The use of a compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for the therapeutic and/or prophylactic treatment of diseases which are modulated by PDE10A inhibitors.

21. The use of a compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for the therapeutic and/or prophylactic treatment of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder,

attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma or breast cancer.

22. The use of a compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for the preparation of a medicament for the therapeutic and/or prophylactic treatment of diseases which are modulated by PDE10A inhibitors.

23. The use of a compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for the preparation of a medicament for the therapeutic and/or prophylactic treatment of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma or breast cancer.

24. A compound or a pharmaceutically acceptable salt thereof according to any of claims 1 - 13 for the treatment or prophylaxis of psychotic disorders, schizophrenia, positive, negative and/or cognitive symptoms associated with schizophrenia, delusional disorder, substance-induced psychotic disorder, anxiety disorders, panic disorder, obsessive/compulsive disorders, acute stress disorder, generalized anxiety disorder, drug addictions, movement disorders, Parkinson's disease, restless leg syndrome, cognition deficiency disorders, Alzheimer's disease, multi-infarct dementia, mood disorders, depression, bipolar disorders, neuropsychiatric conditions, psychosis, attention-deficit/hyperactivity disorder, attentional disorders, diabetes and related disorders, type 2 diabetes mellitus, neurodegenerative disorders, Huntington's disease, multiple sclerosis, stroke, spinal cord injury, solid tumors, hematological malignancies, renal cell carcinoma or breast cancer.

25. The invention as hereinbefore defined.