

INHIBITORS OF PHOSPHODIESTERASE TYPE 10A

The present invention relates to novel compounds which are inhibitors of phosphodiesterase type 10A and to their use for the manufacture of a medicament and
5 which thus are suitable for treating or controlling of medical disorders selected from neurological disorders and psychiatric disorders, for ameliorating the symptoms associated with such disorders and for reducing the risk of such disorders.

Background of the Invention

10 Phosphodiesterase type 10A (hereinafter PDE10A) is a dual-substrate phosphodiesterase that can convert both cAMP to AMP and cGMP to GMP. PDE10A is highly prominent in the mammalian brain. In the rat, as well as in other mammalian species, PDE10A and the mRNA of PDE10A are highly enriched in the GABAergic
15 medium spiny projection neurons (MSNs) of the striatal complex (caudate nucleus, nucleus accumbens, and olfactory tubercle) where the output is regulated by the effect of PDE10A on cAMP and cGMP signalling cascades (see e.g. C. J. Schmidt et al, The Journal of Pharmacology and Experimental Therapeutics 325 (2008) 681-690, A. Nishi, The Journal of Neuroscience 2008, 28, 10450-10471).

20 MSNs express two functional classes of neurons: the D₁ class expressing D₁ dopamine receptors and the D₂ class expressing D₂ dopamine receptors. The D₁ class of neurons is part of the 'direct' striatal output pathway, which broadly functions to facilitate behavioral responses. The D₂ class of neurons is part of the 'indirect' striatal output pathway, which functions to suppress behavioral responses that compete with
25 those being facilitated by the 'direct' pathway. PDE10A regulation of cAMP and/or cGMP signaling in the dendritic compartment of these neurons may be involved in filtering the cortico/thalamic input into the MSN. Furthermore, PDE10A may be involved in the regulation of GABA release in the substantia nigra and globus pallidus (Seeger, T.F. et al. Brain Research, 2003, 985, 1 13-126). Inhibition of PDE10A results
30 in striatal activation and behavioral suppression such as dampened locomotion, inhibition of conditioned avoidance response (CAR), and activity in the rat auditory

gating model, suggesting that inhibitors of phosphodiesterase type 10A represent a novel class of antipsychotic agents.

The hypotheses around the physiological role of PDE10A and the therapeutic utility of PDE10A inhibitors derive in part from studies with papaverine (J. A. Siuciak et al. loc. cit.), the first extensively profiled pharmacological tool compound for this target. The PDE10A inhibitor papaverine was shown to be active in several antipsychotic models. Papaverine potentiated the cataleptic effect of the D₂ receptor antagonist haloperidol in rats, but did not cause catalepsy on its own (WO 03/093499). Papaverine reduced hyperactivity in rats induced by PCP, while reduction of amphetamine-induced hyperactivity was insignificant (WO 03/093499). These models suggest that PDE10A inhibition has the classic antipsychotic potential that would be expected from theoretical considerations. Papaverine, however has significant limitations in this regard with relatively poor potency and selectivity and a very short exposure half-life after systemic administration. It was found that inhibition of PDE10A reverses subchronic PCP-induced deficits in attentional set-shifting in rats suggesting that PDE10A inhibitors might alleviate cognitive deficits associated with schizophrenia. (Rodefer et al., Eur. J. Neurosci., 4 (2005) 1070-1076).

The discovery of a new class of PDE10A inhibitors with improved potency, selectivity, and pharmacokinetic properties, provided an opportunity to further explore the physiology of PDE10A and the potential therapeutic utility of inhibiting this enzyme. The new class of inhibitors are exemplified by MP-10 (PF-2545920: 2-{4-[1-methylpyridine-4-yl-1-H-pyrazol-3-3ly]phenoxyethyl}-quinoline) and TP-10, i.e. 2-{4-[pyridine-4-yl-1-(2,2,2-trifluoroethyl)-1-H-pyrazol-3-3ly]phenoxyethyl}-quinoline. The compounds offer a therapeutic approach to the treatment of schizophrenia (see C. J. Schmidt et al., loc cit.; S.M. Grauer et al., Journal of Pharmacology and Experimental Therapeutics, fast forward DOI 10.1124 JPET 109.155994). Positive signals in rodent models of schizophrenia include the: attenuation of conditioned avoidance response (CAR), inhibition of hyperactivity caused by amphetamine-induced dopamine release or phencyclidine (PCP) mediated NMDA receptor blockade, attenuation of pharmacologically impaired social or object recognition, and antagonism of apomorphine-induced climbing. Taken together, these data suggest a broad suppression of all 3 symptoms clusters (positive symptoms,

negative symptoms & cognitive dysfunctions) linked to schizophrenia (see C. J. Schmidt et al., loc cit.; S.M. Grauer et al., loc. cit).

Beyond schizophrenia, selective PDE10 inhibitors may have the potential for the treatment of Huntington's disease (S. H. Francis et al., *Physiol. Rev.*, 91 (2011) 651-690) and they may be a therapeutic option for substance abuse disorders (F. Sotty et al., *J. Neurochem.*, 109 (2009) 766-775). Furthermore, it has been suggested that PDE10A inhibitors may be useful for treatment of obesity and non-insulin dependent diabetes (see e.g. WO 2005/120514, WO 2005/012485, Cantin et al, *Bioorganic & Medicinal Chemistry Letters* 17 (2007) 2869-2873).

In summary, inhibitors of PDE10A offer a promising therapeutic approach to the treatment or prevention of neurological and psychiatric disorders, in particular schizophrenia and related disorders, including symptoms linked to schizophrenia such as cognitive dysfunction.

Several classes of compounds which are inhibitors of PDE10A have been described in the art, the recent compound groups are:

Pyrido[3,2-e]pyridazines - see WO 2007/137819, WO 2007/137820, WO 2009/068246, WO 2009/068320, WO 2009/070583 and WO 2009/070584;

4-substituted phthalazines and quinazolines WO 2007/085954, WO 2007/022280, WO 2007/096743, WO 2007/103370, WO 2008/020302, WO 2008/006372 and WO 2009/036766;

4-substituted cinnazolines - see WO 2006/028957, WO 2007/098169, WO 2007/098214, WO 2007/103554, WO 2009/025823 and WO 2009/025839;

Isoquinolines and isoquinolinones - see WO 2007/100880 and WO 2009/029214

MP10 and MP10 like compounds: US 2007/0155779, WO 2008/001182 and WO 2008/004117; and

Benzodiazepines - see WO 2007/082546.

For a further review see also T. Chappie et al. *Current Opinion in Drug Discovery & Development* 12(4), (2009) 458-467) and the literature cited therein.

Although some of the compounds of prior art are known to inhibit PDE10A effectively having IC₅₀ values of less than 50 nM, there is still an ongoing need for compounds which inhibit PDE10A. In particular, there is an ongoing need for compounds which have one of the following characteristics:

- i. Selective inhibition of PDE10A, in particular vis-à-vis inhibition of the other ten phosphodiesterase families PDE1-9, 11 and their different gene variants; suitable selectivity with regard to molecular receptors, transporters channels, enzymes or other biomolecules whose interaction with the PDE10A ligand might cause undesired side effects;
- 5 ii. metabolic stability, in particular microsomal stability, e.g. measured in vitro, in liver microsomes from various species (e.g. rat or human) in human cells, such as hepatocytes;
- 10 iii. no or only low inhibition of cytochrome P450 (CYP) enzymes: cytochrome P450 (CYP) is the name for a superfamily of heme proteins having enzymatic activity (oxidase). They are also particularly important for the degradation (metabolism) of foreign substances such as drugs or xenobiotics in mammalian organisms. The principal representatives of the types and subtypes of CYP in the human body are: CYP 1A2, CYP 2C9, CYP 2D6 and CYP 3A4. If CYP 3A4 inhibitors (e.g. grapefruit juice, cimetidine, erythromycin) are used at the same time as medicinal substances which are degraded by this enzyme system and thus compete for the same binding site on the enzyme, the degradation thereof may be slowed down and thus effects and side effects of the administered medicinal substance may be undesirably enhanced;
- 15 20 iv. a suitable solubility in water (in mg/ml);
- v. suitable pharmacokinetics (time course of the concentration of the compound of the invention in plasma or in tissue, for example brain). The pharmacokinetics can be described by the following parameters: half-life, volume of distribution (in $\text{l} \cdot \text{kg}^{-1}$), plasma clearance (in $\text{l} \cdot \text{h}^{-1} \cdot \text{kg}^{-1}$), AUC (area under the curve, area under the concentration-time curve (in $\text{ng} \cdot \text{h} \cdot \text{l}^{-1}$), oral bioavailability, (the dose-normalized ratio of AUC after oral administration and AUC after intravenous administration), the so-called brain-plasma ratio (the ratio of AUC in brain tissue and AUC in plasma);
- 25 30 vi. no or only low blockade of the hERG channel: compounds which block the hERG channel may cause a prolongation of the QT interval and thus lead to serious disturbances of cardiac rhythm (for example so-called "torsade de

pointes"). The potential of compounds to block the hERG channel can be determined by means of the displacement assay with radiolabelled dofetilide which is described in the literature (G. J. Diaz et al., Journal of Pharmacological and Toxicological Methods, 50 (2004), 187-199). A smaller IC₅₀ in this dofetilide assay means a greater probability of potent hERG blockade. In addition, the blockade of the hERG channel can be measured by electrophysiological experiments on cells which have been transfected with the hERG channel, by so-called whole-cell patch clamping (G. J. Diaz et al., Journal of Pharmacological and Toxicological Methods, 50 (2004), 187-199).

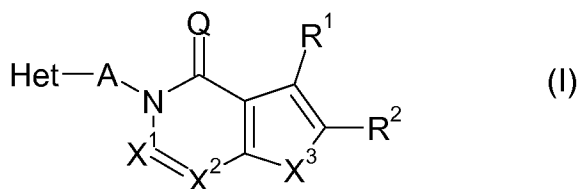
- vii. high free fraction in brain, i.e. the fraction of the compound bound to proteins should be low.
- viii. low lipophilicity.

Brief Description of the Invention

The present invention is thus based on the object of providing compounds which inhibit PDE10A at low concentrations.

The compounds are further intended to display at least one of the properties i. to viii. mentioned above, in particular high selectivity with regard to inhibition of PDE10A, high selectivity vis-à-vis other phosphodiesterases such as , enhanced metabolic stability, in particular microsomal and/or cytosolic stability, low affinity to the HERG receptor, low inhibition of cytochrome P450 (CYP) enzymes, suitable solubility in water and suitable pharmacokinetics.

This object and further objects are achieved by the compounds of the general formula I described below, the N-oxides, the prodrugs, the hydrates and the tautomers thereof and the pharmaceutically suitable salts thereof:



wherein

Q is O or S;

X¹ is N or CH;

X² is N or C-R⁷;

5 X³ is O, S, -X⁴=C(R⁸)-, where C(R⁸) is bound to the carbon atom which carries R², or

-X⁵=C(R⁹)-, where X⁵ is bound to the carbon atom which carries R²;

X⁴ is N or C-R⁹;

X⁵ is N;

10

Het is selected from

i. monocyclic hetaryl having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, which is unsubstituted or may carry 1, 2, 3 or 4 identical or
15 different substituents R^x,

ii. fused bicyclic hetaryl having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, benzothienyl or benzofuryl, where bicyclic hetaryl, benzothienyl and benzofuryl are, independently of each other,
20 unsubstituted or may carry 1, 2, 3 or 4 identical or different substituents R^x, and

iii. phenyl, which carries a monocyclic hetaryl radical having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, which in addition to
25 monocyclic hetaryl, may carry 1, 2 or 3 identical or different substituents R^x,

where

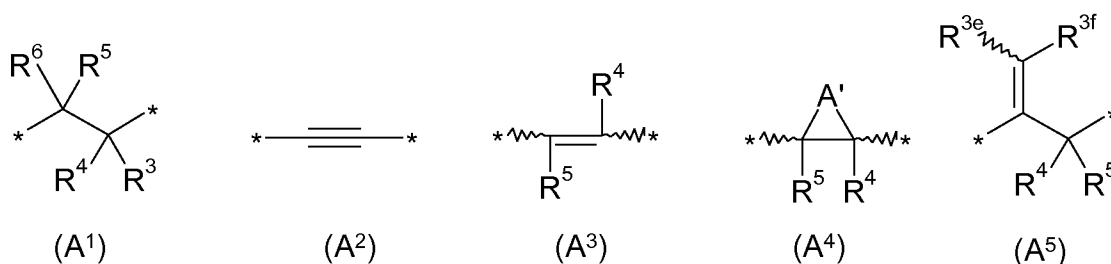
R^x is selected from the group consisting of H, halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, C₃-C₆-cycloalkyl, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkyl, OH, hydroxy-C₁-C₄-alkyl, O-C₃-C₆-cycloalkyl, benzyloxy, C(O)O-(C₁-C₄-alkyl), O-(C₁-C₄-alkyl)-CO₂H,
30

$N(R^{x1})(R^{x2})$, $C(O)N(R^{x1})(R^{x2})$, C_1 - C_4 -alkyl- $N(R^{x1})(R^{x2})$,
 $-NR^{x3}-C(O)-N(R^{x1})(R^{x2})$, $NR^{x3}-C(O)O-(C_1-C_4\text{-alkyl})$,
 $-N(R^{x3})-SO_2-R^{x4}$, phenyl, CN, $-SF_5$, $-OSF_5$, $-SO_2R^{x4}$, $-SR^{x4}$ and
 trimethylsilyl, where R^{x1} , R^{x2} , R^{x3} and R^{x4} , independently of
 5 each other are selected from the group consisting of hydrogen,
 C_1 - C_4 -alkyl, C_1 - C_4 -fluoroalkyl and C_3 - C_6 -cycloalkyl or R^{x1} and
 R^{x2} form together with the N atom to which they are attached a
 3- to 7-membered, nitrogen heterocycle which may have 1, 2 or
 3 further different or identical heteroatoms or heteroatom
 10 containing groups selected from the group of O, N, S, SO and
 SO_2 as ring members and which may carry 1, 2, 3, 4, 5 or 6
 substituents selected from C_1 - C_4 -alkyl,
 or two radicals R^x which are bound at adjacent carbon atoms
 may form a fused 5- or 6-membered saturated carbocyclic
 15 radical or a fused 5- or 6-membered heterocyclic radical having
 1, 2 or 3 heteroatoms as ring members, which are selected from
 O, S and N;

R^1 is selected from the group consisting of hydrogen, halogen, OH, C_1 -
 20 C_4 -alkyl, trimethylsilyl, C_1 - C_4 -alkylsulfanyl, C_1 - C_4 -alkoxy- C_1 - C_4 -
 alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_1 - C_4 -alkylsulfanyl-
 C_1 - C_4 -alkoxy, C_2 - C_4 -alkenyloxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -
 fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl
 groups, fluorinated cyclopropyl, CN, $NR^{x1}R^{x2}$, $NR^{x1}R^{x2}-C_1$ - C_4 -alkoxy
 25 and the moiety Y^1 -Cyc¹;

R^2 is selected from the group consisting of hydrogen, halogen, OH, C_1 -
 C_4 -alkyl, trimethylsilyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 -
 C_4 -alkoxy- C_1 - C_4 -alkoxy, C_2 - C_4 -alkenyloxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -
 30 fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl
 groups, fluorinated cyclopropyl, CN and $NR^{x1}R^{x2}$;

A represents one of the following groups A¹, A², A³, A⁴ or A⁵:



5 where * indicates the points of attachment to Het and to the nitrogen atom, respectively;

R³, R⁴, R⁵, R⁶ independently of each other are selected from the group consisting of hydrogen, halogen, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, C₃-C₆-cycloalkyl, or the radicals together with the carbon atoms to which they are bound form a saturated 3- to 6-membered carbocycle or a saturated 3- to 6-membered heterocycle having 1 or 2 non-adjacent heteroatoms as ring members, where the carbocycle and the heterocycle are unsubstituted or may carry 1, 2, 3 or 4 substituents selected from fluorine and methyl or either the radicals R³, R⁴ or the radicals R⁵, R⁶ together with the carbon atom to which they are bound form a saturated 3- to 6-membered carbocycle or a saturated 3- to 6-membered heterocycle having 1 or 2 non-adjacent heteroatoms as ring members, where the carbocycle and the heterocycle are unsubstituted or may carry 1, 2, 3 or 4 substituents selected from fluorine and methyl;

A' is a O, NR^{3a}, CR^{3b}R^{3c} or linear C₂-C₃-alkandiyl, where one of the CH₂-moieties of C₂-C₃-alkandiyl may be replaced by oxygen or NR^{3a}, and where 1, 2, 3, or 4 of the hydrogen atoms of C₂-C₃-alkandiyl may be replaced by a radical R^{3d}, where R^{3a} is hydrogen or C₁-C₄-alkyl,

- R^{3b} , R^{3c} independently of each other are selected from the group consisting of hydrogen, halogen, C_1 - C_4 -alkyl or R^{3b} and R^{3c} together form C_2 - C_3 -alkandiyl;
- R^{3d} is selected from the group consisting of halogen and C_1 - C_4 -alkyl;
- R^{3e} , R^{3f} independently of each other are selected from the group consisting of hydrogen and C_1 - C_4 -alkyl;
- R^7 is selected from the group consisting of hydrogen, halogen, OH, C_1 - C_4 -alkyl, trimethylsilyl, C_1 - C_4 -alkylsulfanyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_1 - C_4 -alkylsulfanyl- C_1 - C_4 -alkoxy, C_2 - C_4 -alkenyloxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN, $NR^{x1}R^{x2}$, $NR^{x1}R^{x2}$ - C_1 - C_4 -alkoxy and the moiety Y^2 -Cyc²;
- R^8 is selected from the group consisting of hydrogen, halogen, OH, C_1 - C_4 -alkyl, trimethylsilyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_2 - C_4 -alkenyloxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN and $NR^{x1}R^{x2}$;
- R^9 is selected from the group consisting of hydrogen, halogen, OH, C_1 - C_4 -alkyl, trimethylsilyl, C_1 - C_4 -alkylsulfanyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_1 - C_4 -alkylsulfanyl- C_1 - C_4 -alkoxy, C_2 - C_4 -alkenyloxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN, $NR^{x1}R^{x2}$, $NR^{x1}R^{x2}$ - C_1 - C_4 -alkoxy and the moiety Y^3 -Cyc³;

Y¹, Y², Y³ independently of each other are selected from a chemical bond, CH₂, O, O-CH₂, NR^y, NR^y-CH₂, NR^y-S(O)₂, S, S(O), S(O)₂, 1,2-ethandiyl, 1,2-ethendiyl or 1,2-ethyndiyl, where R^y is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl, C₁-C₄-alkylsulfonyl, C₁-C₄-fluoroalkylsulfonyl;

Cyc¹, Cyc², Cyc³ independently of each other are selected from the group consisting of phenyl, naphthyl, 4- to 8-membered saturated or partially unsaturated heteromonocyclic radicals, saturated or partially unsaturated 7- to 10 membered heterobicyclic radicals, 5- or 6-membered monocyclic hetaryl, and 8- to 10 membered bicyclic hetaryl, where the saturated or partially unsaturated heteromonocyclic and heterobicyclic radicals have 1, 2, 3 or 4 heteroatoms or heteroatom containing groups as ring members, which are selected from O, S, SO, SO₂ and N, and where the 5- or 6-membered monocyclic hetaryl and the 8- to 10-membered bicyclic hetaryl have 1, 2, 3 or 4 heteroatoms as ring members, which are selected from O, S and N, where phenyl, naphthyl, the saturated or partially unsaturated heteromonocyclic and heterobicyclic radicals and the mono and bicyclic heteroaromatic radicals are unsubstituted or carry 1, 2, 3, 4 or 5 radicals R^{C1} or one radical Y¹-R^{C2} and 0, 1, 2, 3 or 4 radicals R^{C1}; where

R^{C1} is selected from hydrogen, halogen, OH, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkylsulfanyl, hydroxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkoxy, cyano-C₁-C₄-alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, C₁-C₄-alkylsulfonyl, C(O)R^a, Z-C(O)OR^b, Z-C(O)NR^cR^d, S(O)₂NR^cR^d and Z-NR^eR^f, where

R^a is selected from the group consisting of C₁-C₄-alkyl and C₁-C₄-fluoroalkyl,

11

- R^b is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₂-C₄-alkenyl and C₁-C₄-fluoroalkyl,
- R^c, R^d is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-alkoxy and C₁-C₄-fluoroalkoxy,
- R^e, R^f is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-alkoxy and C₁-C₄-fluoroalkoxy,
- Z is a covalent bond or C₁-C₄-alkandiyl,
- or two radicals R^{C1} which are bound at adjacent carbon atoms may form a fused 5- or 6-membered carbocyclic radical or a fused 5- or 6-membered heterocyclic radical having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N;
- or two radicals R^{C1} which are bound at the same carbon atom may form a spiro 5- or 6-membered carbocyclic radical or a spiro 5- or 6-membered heterocyclic radical having 1 or 2 heteroatoms as ring members, which are selected from O, S and N,
- or two radicals R^{C1} which are bound at the same carbon atom may form an oxygen atom,
- where the fused and the spiro radicals are unsubstituted or carry 1, 2, 3 or 4 radicals R^{C3} ;
- Y' is a chemical bond, CH₂, O, O-CH₂, S(O)₂, NR^{y'}, NR^{y'}-CH₂ or NR^{y'}-S(O)₂, where R^{y'} is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl, C₁-C₄-alkylsulfonyl, C₁-C₄-fluoroalkylsulfonyl;
- R^{C2} is a carbocyclic or heterocyclic radical selected from the group consisting of phenyl, 3- to 7-membered saturated or partially unsaturated monocarbocyclic radicals, 3- to 7-membered

12

5 saturated or partially unsaturated heteromonocyclic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, and 5- or 6-membered heteroaromatic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, where the carbocyclic and the heterocyclic radical is unsubstituted or carries 1, 2, 3, 4 or 5 radicals R^{C3} ;

10 R^{C3} is selected from hydrogen, halogen, OH, CN, C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, hydroxy- C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, cyano- C_1 - C_4 -alkyl, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, C_2 - C_6 -alkenyl, $C(O)R^a$, benzyl, $Z-C(O)OR^b$, $Z-C(O)NR^cR^d$, $S(O)_2NR^eR^f$ and $Z-NR^eR^f$, where, Z, R^a , R^b , R^c , R^d , R^e and R^f are as defined above or two radicals R^{C3} which are bound at the same atom may form an oxygen atom;

15

provided that for X^3 being O or S, at least one of the radicals R^1 and R^7 is a moiety Y^1 -Cyc¹ or Y^2 -Cyc², respectively;

20 further provided that for X^3 being $X^4=C(R^8)$, one or two of the radicals R^1 , R^7 and R^9 are a moiety Y^1 -Cyc¹, Y^2 -Cyc² or Y^3 -Cyc³, respectively;

further provided that for X^3 being $X^5=C(R^9)$, one or two of the radicals R^1 , R^7 and R^9 are a moiety Y^1 -Cyc¹, Y^2 -Cyc² or Y^3 -Cyc³, respectively;

25

and the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

The present invention therefore relates to the compounds of the general formula I, their tautomers, the hydrates thereof, the pharmaceutically suitable salts of the compounds of formula I, the prodrugs of the compounds of formula I and the

30

pharmaceutically suitable salts of said prodrugs, tautomers or hydrates of the compounds of formula I.

The compounds of the formula I, their salts, their prodrugs, their hydrates and their tautomers effectively inhibit PDE10A even at low concentrations. They are additionally distinguished by a high selectivity in relation to the inhibition of the PDE10A vis-à-vis inhibition of other phosphodiesterase, such as PDE3 or PDE4. The compounds of the invention may additionally have one or more of the properties ii. to viii. mentioned above.

The compounds of the formula I, their salts, their prodrugs, their hydrates and their tautomers are therefore particularly suitable for treating disorders and conditions in creatures, especially human creatures, which can be treated or controlled by inhibition of phosphodiesterase type 10A.

The invention therefore also relates to the use of carboxamide compounds of the formula I, their tautomers, their hydrates and their pharmaceutically suitable salts for the manufacture of a medicament, in particular of a medicament which is suitable for the treatment of a disorder or a condition which can be treated by inhibition of phosphodiesterase type 10A.

The invention further relates to a medicament, in particular a medicament which is suitable for the treatment of a disorder or a condition which can be treated by inhibition of phosphodiesterase type 10A. The medicament comprises at least one compound of the formula I, as described herein, or a tautomer, or a hydrate or a prodrug of said compound I, or a pharmaceutically suitable salt of the compound of the formula I or a pharmaceutically suitable salt of the tautomer, the hydrate or the prodrug of compound of the formula I.

Detailed Description of the Invention

The terms "compound of the formula I" and "compounds I" are used as synonyms.

The term "prodrugs" means compounds which are metabolized in vivo to the compounds I of the invention. Typical examples of prodrugs are described in C.G. Wermuth (editor): The Practice of Medicinal Chemistry, Academic Press, San Diego, 1996, pages 671-715. These include for example phosphates, carbamates, amino acids,

esters, amides, peptides, ureas and the like. Suitable prodrugs in the present case may be for example derivatives of those compounds I carrying an OH or NH₂-group, where the OH or NH₂-group forms an ester/amide/peptide linkage, i.e. where one of the hydrogen atoms of the OH or NH₂-group is substituted by a C₁-C₄-alkylcarbonyl group, e.g. by
5 acetyl, propionyl, n-propylcarbonyl, isopropylcarbonyl, n-butylcarbonyl or tert-butylcarbonyl (pivaloyl), by benzoyl, or by an acyl group derived from an amino acid, e.g. glycine, alanine, serine, phenylalanine and the like, which is linked to the oxygen or nitrogen of the OH or NH₂-group via the carbonyl group of the amino acid. Further suitable prodrugs are alkylcarbonyloxyalkyl carbonates or carbamates of compounds I
10 carrying an OH- or NH₂-group in which one of the hydrogen atoms of the OH- or NH₂-group has been replaced by a group of the formula -C(=O)-O-CHR^p-O-C(=O)-R^q in which R^p and R^q are independently of one another C₁-C₄-alkyl. Such carbonates and carbamates are described for example in J. Alexander, R. Cargill, S. R. Michelson, H. Schwam, J. Medicinal Chem. 1988, 31(2), 318-322. These groups can then be
15 eliminated under metabolic conditions and result in compounds I. Therefore, said prodrugs and their pharmaceutically acceptable salts are also part of the invention.

The term "pharmaceutically acceptable salts" refers to cationic or anionic salts compounds, wherein the counter ion is derived from pharmaceutically acceptable non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids.

20 When the compound of formula I or its prodrug or N-oxide is acidic, salts may be prepared from pharmaceutically acceptable non-toxic bases, including inorganic and organic bases. Salts derived from inorganic bases include salts, wherein the counter ion is aluminium, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic, manganous, potassium, sodium, zinc ion and the like. Particularly preferred
25 are the ammonium, calcium, magnesium, potassium, and sodium ions. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, dibenzylethylene-diamine, diethylamine, 2-diethylamino-ethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethyl-morpholine,
30 N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins,

procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, and the like.

When the compound of formula I or its prodrug or N-oxide is basic, salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include acetic, trifluoroacetic acid, benzenesulfonic, benzoic, 5 camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric, p-toluenesulfonic acid, and the like. Particularly preferred are citric, hydrobromic, hydrochloric, maleic, 10 phosphoric, sulfuric, fumaric, and tartaric acids. It will be understood that, as used herein, references to the compounds of formula I are meant to also include the pharmaceutically acceptable salts.

The compounds of the invention may be in the form of a mixture of diastereomers, or of a mixture of diastereomers in which one of the two diastereomers is 15 enriched, or of essentially diastereomerically pure compounds (diastereomeric excess $de > 90\%$). The compounds are preferably in the form of essentially diastereomerically pure compounds (diastereomeric excess $de > 90\%$). The compounds I of the invention may furthermore be in the form of a mixture of enantiomers (for example as racemate), of a mixture of enantiomers in which one of the two enantiomers is enriched, or 20 essentially in enantiomerically pure compounds (enantiomeric excess $ee > 90\%$). It is preferred to employ the compounds enantiomerically pure or diastereomerically pure.

The present invention moreover relates to compounds as defined herein, wherein one or more of the atoms depicted in formula I have been replaced by its stable, preferably non-radioactive isotope (e.g., hydrogen by deuterium, ^{12}C by ^{13}C , ^{14}N by ^{15}N , 25 ^{16}O by ^{18}O) and preferably wherein at least one hydrogen atom has been replaced by a deuterium atom. Of course, the compounds according to the invention contain more of the respective isotope than this naturally occurs and thus is anyway present in the compounds I.

The compounds of the formula I and their salts in the solid form may exist in 30 more than one crystal structure (polymorphism), and may also be in the form of hydrates or other solvates. The present invention includes any polymorph of the compound I or its salt as well as any hydrate or other solvate.

In the context of the present description, unless stated otherwise, the terms "alkyl", "alkenyl", "alkoxy", "alkenyloxy", "fluoroalkyl", "fluoroalkoxy", "cycloalkyl", "fluorinated cycloalkyl", "alkylene", "alkandiyl", "hetaryl" and radicals derived
5 therefrom, such as "alkylcarbonyl", "alkylsulfanyl", "alkylsulfonyl", "fluoroalkylsulfonyl", "hydroxylalkyl", "cyanoalkyl", "alkoxylalkyl", "alkoxyalkoxy", "alkylsulfanylalkyl", "alkylsulfanylalkoxy" and "hetarylmethyl" represent groups of individual radicals. The groups of noncyclic radicals "alkyl", "alkenyl", "alkoxy", "alkenyloxy", "fluoroalkyl", "fluoroalkoxy", "alkylene", "alkandiyl", and the groups of
10 radicals derived therefrom always include both unbranched and branched "alkyl", "alkenyl", "alkoxy", "alkenyloxy", "fluoroalkyl", "fluoroalkoxy", "alkylene" and "alkandiyl", respectively.

The prefix C_n-C_m- indicates the respective number of carbons in the hydrocarbon unit. Unless indicated otherwise, fluorinated substituents preferably have one to five
15 identical or different fluorine atoms.

The term "halogen" designates in each case, fluorine, bromine, chlorine or iodine, specifically fluorine, chlorine or bromine.

Examples of other meanings are:

Alkyl, and the alkyl moieties for example in alkylcarbonyl, alkylsulfanyl,
20 alkylsulfonyl, alkylsulfanylalkyl and alkylsulfanylalkoxy: saturated, straight-chain or branched hydrocarbon radicals having one or more C atoms, e.g. 1 to 4 carbon atoms, e.g. C₁-C₄-alkyl such as methyl, ethyl, propyl, 1-methylethyl, n-butyl, 1-methylpropyl, 2-methylpropyl and 1,1-dimethylethyl.

Fluoroalkyl and the fluoroalkyl moieties for example in fluoroalkylsulfonyl: an
25 alkyl radical having ordinarily 1 to 4 C atoms, in particular 1 or 2 C-atoms (C₁-C₂-fluoroalkyl) as mentioned above, whose hydrogen atoms are partly or completely replaced by fluorine atoms such as fluoromethyl, difluoromethyl, trifluoromethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 2-fluoro-1-methylethyl, 2,2-difluoro-1-methylethyl, 2,2-trifluoro-1-methylethyl, 2-fluoropropyl, 3-
30 fluoropropyl, 2,2-difluoropropyl, 2,3-difluoropropyl, 3,3,3-trifluoropropyl, 2,3,3,3-pentafluoropropyl, heptafluoropropyl, 1-(fluoromethyl)-2-fluoroethyl, 4-fluorobutyl, and nonafluorobutyl.

Cycloalkyl, and the cycloalkyl moieties for example in cycloalkoxy or cycloalkyl-C₁-C₄-alkyl: monocyclic, saturated hydrocarbon groups having three or more C atoms, e.g. 3, 4, 5, 6 or 7 carbon ring members, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

- 5 Fluorinated cycloalkyl: monocyclic, saturated hydrocarbon groups having three or more C atoms, e.g. 3, 4, 5, 6 or 7 carbon ring members, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, wherein at least one, e.g. 1, 2, 3, 4, 5 or 6 of the hydrogen atoms are replaced by fluorine atoms, examples including 1-fluorocyclopropyl, 2-fluorocyclopropyl, 2,2-difluorocyclopropyl, 1,2-difluorocyclopropyl, 2,3-difluorocyclopropyl, etc..
- 10

Cycloalkoxy: a cycloalkyl radical as defined above which is linked via an oxygen atom, e.g. cyclopropyloxy, cyclobutyloxy, cyclopentyloxy or cyclohexyloxy.

- Cycloalkylalkyl: a cycloalkyl radical as defined above which is linked via an alkylene group, in particular via a methylene, 1,1-ethylene or 1,2-ethylene group, e.g. cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl or cyclohexylmethyl.
- 15

- Alkenyl, and alkenyl moieties for example in alkenyloxy: monounsaturated, straight-chain or branched hydrocarbon radicals having two or more C atoms, e.g. 2 to 4 carbon atoms and one C=C-double bond in any position, e.g. C₂-C₄-alkenyl such as ethenyl, 1-propenyl, 2-propenyl, 1-methylethenyl, 1-butenyl, 2-butenyl, 3-butenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 1-methyl-2-propenyl and 2-methyl-2-propenyl.
- 20

- Alkoxy or alkoxy moieties for example in alkoxyalkyl and alkoxyalkoxy: an alkyl radical as defined above having preferably 1 to 4 C atoms, which is connected to the remainder of the molecule via an O atom: e.g. methoxy, ethoxy, n-propoxy, 1-methylethoxy, butoxy, 1-methylpropoxy, 2-methylpropoxy or 1,1-dimethylethoxy.
- 25

- Fluoroalkoxy: alkoxy as described above, in which the hydrogen atoms of these groups are partly or completely replaced by fluorine atoms, i.e. for example C₁-C₄-fluoroalkoxy, in particular C₁-C₂-fluoroalkoxy, such as fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2-fluoroethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy, pentafluoroethoxy, 2-fluoropropoxy, 3-fluoropropoxy, 2,2-difluoropropoxy, 2,3-difluoropropoxy, 3,3,3-trifluoropropoxy, 2,2,3,3,3-
- 30

pentafluoropropoxy, heptafluoropropoxy, 1-(fluoromethyl)-2-fluoroethoxy, specifically fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2-fluoroethoxy, or 2,2,2-trifluoroethoxy.

- Hydroxyalkyl: an alkyl radical ordinarily having 1 to 4 C atoms, in which one hydrogen atom is replaced by an OH radical. Examples thereof are CH₂-OH, 1-hydroxyethyl, 2-hydroxyethyl, 1-hydroxypropyl, 2-hydroxypropyl, 1-methyl-1-hydroxyethyl, 1-methyl-2-hydroxyethyl, 3-hydroxypropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 1-methyl-2-hydroxypropyl, 1,1-dimethyl-2-hydroxyethyl, 1-methyl-1-hydroxypropyl etc.
- Cyanoalkyl: an alkyl radical ordinarily having 1 to 4 C atoms, in which one hydrogen atom is replaced by a CN radical. Examples thereof are CH₂-CN, 1-cyanoethyl, 2-cyanoethyl, 1-cyanopropyl, 2-cyanopropyl, 1-methyl-1-cyanoethyl, 1-methyl-2-cyanoethyl, 3-cyanopropyl, 2-cyanobutyl, 3-cyanobutyl, 4-cyanobutyl, 1-methyl-2-cyanopropyl, 1,1-dimethyl-2-cyanoethyl, 1-methyl-1-cyanopropyl etc.
- Alkoxyalkyl: an alkyl radical ordinarily having 1 to 4 C atoms, in which one hydrogen atom is replaced by an alkoxy radical ordinarily having 1 to 4 C atoms. Examples thereof are CH₂-OCH₃, CH₂-OC₂H₅, n-propoxymethyl, CH₂-OCH(CH₃)₂, n-butoxymethyl, (1-methylpropoxy)methyl, (2-methylpropoxy)methyl, CH₂-OC(CH₃)₃, 2-(methoxy)ethyl, 2-(ethoxy)ethyl, 2-(n-propoxy)ethyl, 2-(1-methylethoxy)ethyl, 2-(n-butoxy)ethyl, 2-(1-methylpropoxy)ethyl, 2-(2-methylpropoxy)ethyl, 2-(1,1-dimethylethoxy)ethyl, 2-(methoxy)propyl, 2-(ethoxy)propyl, 2-(n-propoxy)propyl, 2-(1-methylethoxy)propyl, 2-(n-butoxy)propyl, 2-(1-methylpropoxy)propyl, 2-(2-methylpropoxy)propyl, 2-(1,1-dimethylethoxy)propyl, 3-(methoxy)propyl, 3-(ethoxy)propyl, 3-(n-propoxy)propyl, 3-(1-methylethoxy)propyl, 3-(n-butoxy)propyl, 3-(1-methylpropoxy)propyl, 3-(2-methylpropoxy)propyl, 3-(1,1-dimethylethoxy)propyl, 2-(methoxy)butyl, 2-(ethoxy)butyl, 2-(n-propoxy)butyl, 2-(1-methylethoxy)butyl, 2-(n-butoxy)butyl, 2-(1-methylpropoxy)butyl, 2-(2-methylpropoxy)butyl, 2-(1,1-dimethylethoxy)butyl, 3-(methoxy)butyl, 3-(ethoxy)butyl, 3-(n-propoxy)butyl, 3-(1-methylethoxy)butyl, 3-(n-butoxy)butyl, 3-(1-methylpropoxy)butyl, 3-(2-methylpropoxy)butyl, 3-(1,1-dimethylethoxy)butyl, 4-(methoxy)butyl, 4-(ethoxy)butyl, 4-(n-propoxy)butyl, 4-(1-methylethoxy)butyl, 4-(n-

butoxy)butyl, 4-(1-methylpropoxy)butyl, 4-(2-methylpropoxy)butyl, 4-(1,1-dimethylethoxy)butyl, etc.

Alkoxyalkoxy: an alkoxyalkyl radical as defined above ordinarily having 1 to 4 C atoms both in the alkoxy and the alkyl moiety which is connected to the remainder of the molecule via an O atom: Examples thereof are OCH₂-OCH₃, OCH₂-OC₂H₅, n-propoxymethoxy, OCH₂-OCH(CH₃)₂, n-butoxymethoxy, (1-methylpropoxy)methoxy, (2-methylpropoxy)methoxy, OCH₂-OC(CH₃)₃, 2-(methoxy)ethoxy, 2-(ethoxy)ethoxy, 2-(n-propoxy)ethoxy, 2-(1-methylethoxy)ethoxy, 2-(n-butoxy)ethoxy, 2-(1-methylpropoxy)ethoxy, 2-(2-methylpropoxy)ethoxy, 2-(1,1-dimethylethoxy)ethoxy, etc.

Alkylcarbonyl: alkyl as defined above preferably having 1 to 4 C atoms, which is connected via a carbonyl group to the remainder of the molecule, e.g. acetyl, propionyl, butyryl, isobutyryl, pentanoyl, pivaloyl and the like.

Alkylsulfanyl and the alkylsulfanyl radicals in alkylsulfanylalkyl and alkylsulfanylalkoxy: alkyl as defined above preferably having 1 to 4 C atoms, which is connected via an S atom to the remainder of the molecule, e.g. methylsulfanyl, ethylsulfanyl, n-propylsulfanyl and the like.

Alkylsulfonyl: alkyl as defined above preferably having 1 to 4 C atoms, which is connected via an SO₂ group to the remainder of the molecule, e.g. methylsulfonyl, ethylsulfonyl, n-propylsulfonyl and the like.

Fluoroalkylsulfanyl: fluoroalkyl as defined above preferably having 1 to 4 C atoms, which is connected via an S atom to the remainder of the molecule, e.g. fluoromethylsulfanyl, difluoromethylsulfanyl, trifluoromethylsulfanyl, 2-fluoroethylsulfanyl, 2,2-difluoroethylsulfanyl, 2,2,2-trifluoroethylsulfanyl, pentafluoroethylsulfanyl, 2-fluoropropylsulfanyl, 3-fluoropropylsulfanyl, 2,2-difluoropropylsulfanyl, 2,3-difluoropropylsulfanyl, and heptafluoropropylsulfanyl.

Fluoroalkylsulfonyl: fluoroalkyl as defined above preferably having 1 to 4 C atoms, which is connected via an SO₂ group to the remainder of the molecule, e.g. fluoromethylsulfonyl, difluoromethylsulfonyl, trifluoromethylsulfonyl, 2-fluoroethylsulfonyl, 2,2-difluoroethylsulfonyl, 2,2,2-trifluoroethylsulfonyl, pentafluoroethylsulfonyl, 2-fluoropropylsulfonyl, 3-fluoropropylsulfonyl, 2,2-difluoropropylsulfonyl, 2,3-difluoropropylsulfonyl, and heptafluoropropylsulfonyl.

Alkylsulfanylalkyl: an alkyl radical ordinarily having 1 to 4 C atoms, in which one hydrogen atom is replaced by an alkylsulfanyl radical ordinarily having 1 to 4 C atoms. Examples thereof are CH₂-SCH₃, CH₂-SC₂H₅, n-propylsulfanylmethyl, CH₂-SCH(CH₃)₂, n-butylsulfanylmethyl, (1-methylpropylsulfanyl)methyl, (2-methylpropylsulfanyl)methyl, CH₂-OC(CH₃)₃, 2-(methylsulfanyl)ethyl, 2-(ethylsulfanyl)ethyl, 2-(n-propylsulfanyl)ethyl, 2-(1-methylethylsulfanyl)ethyl, 2-(n-butylsulfanyl)ethyl, 2-(1-methylpropylsulfanyl)ethyl, 2-(2-methylpropylsulfanyl)ethyl, 2-(1,1-dimethylethylsulfanyl)ethyl, 2-(methylsulfanyl)propyl, 2-(ethylsulfanyl)propyl, 2-(n-propylsulfanyl)propyl, 2-(1-methylethylsulfanyl)propyl, 2-(n-butylsulfanyl)propyl, 2-(1-methylpropylsulfanyl)propyl, 2-(2-methylpropylsulfanyl)propyl, 2-(1,1-dimethylethylsulfanyl)propyl, 3-(methylsulfanyl)propyl, 3-(ethylsulfanyl)propyl, 3-(n-propylsulfanyl)propyl, 3-(1-methylethylsulfanyl)propyl, 3-(n-butylsulfanyl)propyl, 3-(1-methylpropylsulfanyl)propyl, 3-(2-methylpropylsulfanyl)propyl, 3-(1,1-dimethylethylsulfanyl)propyl, 2-(methylsulfanyl)butyl, 2-(ethylsulfanyl)butyl, 2-(n-propylsulfanyl)butyl, 2-(1-methylethylsulfanyl)butyl, 2-(n-butylsulfanyl)butyl, 2-(1-methylpropylsulfanyl)butyl, 2-(2-methylpropylsulfanyl)butyl, 2-(1,1-dimethylethylsulfanyl)butyl, 3-(methylsulfanyl)butyl, 3-(ethylsulfanyl)butyl, 3-(n-propylsulfanyl)butyl, 3-(1-methylethylsulfanyl)butyl, 3-(n-butylsulfanyl)butyl, 3-(1-methylpropylsulfanyl)butyl, 3-(2-methylpropylsulfanyl)butyl, 3-(1,1-dimethylethylsulfanyl)butyl, 4-(methylsulfanyl)butyl, 4-(ethylsulfanyl)butyl, 4-(n-propylsulfanyl)butyl, 4-(1-methylethylsulfanyl)butyl, 4-(n-butylsulfanyl)butyl, 4-(1-methylpropylsulfanyl)butyl, 4-(2-methylpropylsulfanyl)butyl, 4-(1,1-dimethylethylsulfanyl)butyl, etc.

"Alkylen" or "Alkandiyl": a saturated hydrocarbon chain having ordinarily from 1 to 4 carbon atoms, such as methylen (-CH₂-), 1,2-ethylen (-CH₂CH₂-), 1,1-ethandiyl (-CH(CH₃)-), 1,2-propandiyl, 1,3-propandiyl, 1,4-butandiyl, 1,2-butandiyl, 1,3-butandiyl, 1-methyl-1,2-propandiyl, 2-methyl-1,3-propandiyl, 1-methyl-1,1-ethandiyl, 1-methyl-1,2-propandiyl etc.

Saturated or partially unsaturated 4 to 7-membered monocarbocyclic radicals include cycloalkyl as defined above and cycloalkenyl having ordinarily from 4 to 7 carbon atoms as ring members, e.g. 1-cyclobuten-1-yl, 2-cyclobutenyl, 1-cyclopentenyl,

2-cyclopentenyl, 1-cyclohexenyl, 2-cyclohexenyl, 3-cyclohexenyl, 1-cycloheptenyl, 2-cycloheptenyl, 3-cycloheptenyl.

Saturated or partially unsaturated 7 to 10-membered bicarbocyclic radicals include bicyclic carbocyclic radicals which ordinarily have from 7 to 10 carbon atoms as ring members and which are saturated or which have one or more, e.g. one or two C=C double bonds, or which include a monounsaturated carbocycle where the double bond is part of a fused benzene ring, e.g. bicyclo[2,2,1]-1-heptyl, bicyclo[2,2,1]-2-heptyl, bicyclo[2,2,1]-7-heptyl, bicyclo[3,3,0]-1-octyl, bicyclo[3,3,0]-2-octyl, bicyclo[3,3,0]-3-octyl, bicyclo[2,2,2]-1-octyl, bicyclo[2,2,2]-2-octyl, bicyclo[3,2,1]-1-octyl, bicyclo[3,2,1]-2-octyl, bicyclo[3,2,1]-6-octyl, bicyclo[3,2,1]-8-octyl, bicyclo[4,3,0]-1-nonyl, bicyclo[4,3,0]-2-nonyl, bicyclo[4,3,0]-3-nonyl, bicyclo[4,3,0]-7-nonyl, bicyclo[4,3,0]-8-nonyl, bicyclo[4,4,0]-1-decyl, bicyclo[4,4,0]-2-decyl, bicyclo[4,4,0]-3-decyl, bicyclo[2,2,1]-hept-2-en-1-yl, bicyclo[2,2,1]-hept-2-en-2-yl, bicyclo[2,2,1]-hept-2-en-5-yl, bicyclo[2,2,1]-hept-2-en-7-yl, bicyclo[2,2,2]-oct-2-en-1-yl, bicyclo[2,2,2]-oct-2-en-2-yl, bicyclo[2,2,2]-oct-2-en-5-yl, bicyclo[2,2,2]-oct-2-en-7-yl, bicyclo[3,3,0]-2-octen-1-yl, bicyclo[3,3,0]-2-octen-2-yl, bicyclo[3,3,0]-2-octen-3-yl, bicyclo[3,3,0]-2-octen-4-yl, bicyclo[3,3,0]-2-octen-5-yl, bicyclo[3,3,0]-2-octen-6-yl, bicyclo[3,3,0]-2-octen-7-yl, bicyclo[3,3,0]-2-octen-8-yl, inden-1-yl, inden-2-yl, inden-4-yl, inden-6-yl, tetrahydro-1-naphthyl, tetrahydro-2-naphthyl, tetrahydro-5-naphthyl, tetrahydro-6-naphthyl, etc..

Heterocyclyl: a heterocyclic radical which may be saturated or partly unsaturated and which may be a monocyclic heterocyclic radical ordinarily having 3, 4, 5, 6, 7 or 8 ring atoms or a heterobicyclic radical ordinarily having 7, 8, 9 or 10 ring atoms, where ordinarily 1, 2, 3 or 4, in particular 1, 2 or 3, of the ring atoms are heteroatoms such as N, S or O, or heteroatom groups such as S(=O) or S(=O)₂ besides carbon atoms as ring members.

Examples of saturated heteromonocycles are in particular:

- Saturated heteromonocyclic radical which ordinarily has 3, 4, 5, 6 or 7 ring atoms, where ordinarily 1, 2 or 3 of the ring atoms are heteroatoms such as N, S or O, besides carbon atoms as ring members. These include for example:
C-bonded, 3- or 4-membered saturated rings such as

2-oxiranyl, 2-oxetanyl, 3-oxetanyl, 2-aziridinyl, 3-thiethanyl, 1-azetidiny, 2-azetidiny.

C-bonded, 5-membered saturated rings such as

5 tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, tetrahydropyrrol-2-yl, tetrahydropyrrol-3-yl, tetrahydropyrazol-3-yl, tetrahydropyrazol-4-yl, tetrahydroisoxazol-3-yl, tetrahydroisoxazol-4-yl, tetrahydroisoxazol-5-yl, 1,2-oxathiolan-3-yl, 1,2-oxathiolan-4-yl, 1,2-oxathiolan-5-yl, tetrahydroisothiazol-3-yl, tetrahydroisothiazol-4-yl, tetrahydroisothiazol-5-yl, 1,2-dithiolan-3-yl, 1,2-dithiolan-4-yl, tetrahydroimidazol-2-yl, tetrahydroimidazol-4-yl, tetrahydrooxazol-2-yl, tetrahydrooxazol-4-yl, tetrahydrooxazol-5-yl, tetrahydrothiazol-2-yl, tetrahydrothiazol-4-yl, tetrahydrothiazol-5-yl, 1,3-dioxolan-2-yl, 1,3-dioxolan-4-yl, 1,3-oxathiolan-2-yl, 1,3-oxathiolan-4-yl, 1,3-oxathiolan-5-yl, 1,3-dithiolan-2-yl, 1,3-dithiolan-4-yl, 1,3,2-dioxathiolan-4-yl.

10

15

C-bonded, 6-membered saturated rings such as:

tetrahydropyran-2-yl, tetrahydropyran-3-yl, tetrahydropyran-4-yl, piperidin-2-yl, piperidin-3-yl, piperidin-4-yl, tetrahydrothiopyran-2-yl, tetrahydrothiopyran-3-yl, tetrahydrothiopyran-4-yl, 1,3-dioxan-2-yl, 1,3-dioxan-4-yl, 1,3-dioxan-5-yl, 1,4-dioxan-2-yl, 1,3-dithian-2-yl, 1,3-dithian-4-yl, 1,3-dithian-5-yl, 1,4-dithian-2-yl, 1,3-oxathian-2-yl, 1,3-oxathian-4-yl, 1,3-oxathian-5-yl, 1,3-oxathian-6-yl, 1,4-oxathian-2-yl, 1,4-oxathian-3-yl, 1,2-dithian-3-yl, 1,2-dithian-4-yl, hexahydropyrimidin-2-yl, hexahydropyrimidin-4-yl, hexahydropyrimidin-5-yl, hexahydropyrazin-2-yl, hexahydropyridazin-3-yl, hexahydropyridazin-4-yl, tetrahydro-1,3-oxazin-2-yl, tetrahydro-1,3-oxazin-4-yl, tetrahydro-1,3-oxazin-5-yl, tetrahydro-1,3-oxazin-6-yl, tetrahydro-1,3-thiazin-2-yl, tetrahydro-1,3-thiazin-4-yl, tetrahydro-1,3-thiazin-5-yl, tetrahydro-1,3-thiazin-6-yl, tetrahydro-1,4-thiazin-2-yl, tetrahydro-1,4-thiazin-3-yl, tetrahydro-1,4-oxazin-2-yl, tetrahydro-1,4-oxazin-3-yl, tetrahydro-1,2-oxazin-3-yl, tetrahydro-1,2-oxazin-4-yl, tetrahydro-1,2-oxazin-5-yl, tetrahydro-1,2-oxazin-6-yl.

20

25

30

N-bonded, 5-membered saturated rings such as:

23

tetrahydropyrrol-1-yl, tetrahydropyrazol-1-yl, tetrahydroisoxazol-2-yl, tetrahydroisothiazol-2-yl, tetrahydroimidazol-1-yl, tetrahydrooxazol-3-yl, tetrahydrothiazol-3-yl.

N-bonded, 6-membered saturated rings such as:

5 piperidin-1-yl, hexahydropyrimidin-1-yl, hexahydropyrazin-1-yl, hexahydro-pyridazin-1-yl, tetrahydro-1,3-oxazin-3-yl, tetrahydro-1,3-thiazin-3-yl, tetrahydro-1,4-thiazin-4-yl, tetrahydro-1,4-oxazin-4-yl, tetrahydro-1,2-oxazin-2-yl.

10 - Unsaturated heteromonocyclic radicals which ordinarily have 4, 5, 6 or 7 ring atoms, where ordinarily 1, 2 or 3 of the ring atoms are heteroatoms such as N, S or O, besides carbon atoms as ring members. These include for example:

C-bonded, 5-membered, partially unsaturated rings such as:

15 2,3-dihydrofuran-2-yl, 2,3-dihydrofuran-3-yl, 2,5-dihydrofuran-2-yl, 2,5-dihydrofuran-3-yl, 4,5-dihydrofuran-2-yl, 4,5-dihydrofuran-3-yl, 2,3-dihydrothien-2-yl, 2,3-dihydrothien-3-yl, 2,5-dihydrothien-2-yl, 2,5-dihydrothien-3-yl, 4,5-dihydrothien-2-yl, 4,5-dihydrothien-3-yl, 2,3-dihydro-1H-pyrrol-2-yl, 2,3-dihydro-1H-pyrrol-3-yl, 2,5-dihydro-1H-pyrrol-2-yl, 2,5-dihydro-1H-pyrrol-3-yl, 4,5-dihydro-1H-pyrrol-2-yl, 4,5-dihydro-1H-pyrrol-3-yl, 3,4-dihydro-2H-pyrrol-2-yl, 3,4-dihydro-2H-pyrrol-3-yl, 3,4-dihydro-5H-pyrrol-2-yl, 3,4-dihydro-5H-pyrrol-3-yl, 4,5-dihydro-1H-pyrazol-3-yl, 4,5-dihydro-1H-pyrazol-4-yl, 4,5-dihydro-1H-pyrazol-5-yl, 2,5-dihydro-1H-pyrazol-3-yl, 2,5-dihydro-1H-pyrazol-4-yl, 2,5-dihydro-1H-pyrazol-5-yl, 4,5-dihydroisoxazol-3-yl, 4,5-dihydroisoxazol-4-yl, 4,5-dihydroisoxazol-5-yl, 2,5-dihydroisoxazol-3-yl, 2,5-dihydroisoxazol-4-yl, 2,5-dihydroisoxazol-5-yl, 2,3-dihydroisoxazol-3-yl, 2,3-dihydroisoxazol-4-yl, 2,3-dihydroisoxazol-5-yl, 4,5-dihydroisothiazol-3-yl, 4,5-dihydroisothiazol-4-yl, 4,5-dihydroisothiazol-5-yl, 2,5-dihydroisothiazol-3-yl, 2,5-dihydroisothiazol-4-yl, 2,5-dihydroisothiazol-5-yl, 2,3-dihydroisothiazol-3-yl, 2,3-dihydroisothiazol-4-yl, 2,3-dihydroisothiazol-5-yl, 4,5-dihydro-1H-imidazol-2-yl, 4,5-dihydro-1H-imidazol-4-yl, 4,5-dihydro-1H-imidazol-5-yl, 2,5-dihydro-1H-imidazol-

20

25

30

- 2-yl, 2,5-dihydro-1H-imidazol-4-yl, 2,5-dihydro-1H-imidazol-5-yl, 2,3-dihydro-1H-imidazol-2-yl, 2,3-dihydro-1H-imidazol-4-yl, 4,5-dihydrooxazol-2-yl, 4,5-dihydrooxazol-4-yl, 4,5-dihydrooxazol-5-yl, 2,5-dihydrooxazol-2-yl, 2,5-dihydrooxazol-4-yl, 2,5-dihydrooxazol-5-yl, 2,3-dihydrooxazol-2-yl, 2,3-dihydrooxazol-4-yl, 2,3-dihydrooxazol-5-yl, 4,5-dihydrothiazol-2-yl, 4,5-dihydrothiazol-4-yl, 4,5-dihydrothiazol-5-yl, 2,5-dihydrothiazol-2-yl, 2,5-dihydrothiazol-4-yl, 2,5-dihydrothiazol-5-yl, 2,3-dihydrothiazol-2-yl, 2,3-dihydrothiazol-4-yl, 2,3-dihydrothiazol-5-yl, 1,3-dioxol-2-yl, 1,3-dioxol-4-yl, 1,3-dithiol-2-yl, 1,3-dithiol-4-yl, 1,3-oxathiol-2-yl, 1,3-oxathiol-4-yl, 1,3-oxathiol-5-yl.
- C-bonded, 6-membered, partially unsaturated rings such as:
- 2H-3,4-dihydropyran-6-yl, 2H-3,4-dihydropyran-5-yl, 2H-3,4-dihydropyran-4-yl, 2H-3,4-dihydropyran-3-yl, 2H-3,4-dihydropyran-2-yl, 2H-3,4-dihydrothiopyran-6-yl, 2H-3,4-dihydrothiopyran-5-yl, 2H-3,4-dihydrothiopyran-4-yl, 2H-3,4-dihydrothiopyran-3-yl, 2H-3,4-dihydrothiopyran-2-yl, 1,2,3,4-tetrahydropyridin-6-yl, 1,2,3,4-tetrahydropyridin-5-yl, 1,2,3,4-tetrahydropyridin-4-yl, 1,2,3,4-tetrahydropyridin-3-yl, 1,2,3,4-tetrahydropyridin-2-yl, 2H-5,6-dihydropyran-2-yl, 2H-5,6-dihydropyran-3-yl, 2H-5,6-dihydropyran-4-yl, 2H-5,6-dihydropyran-5-yl, 2H-5,6-dihydropyran-6-yl, 2H-5,6-dihydrothiopyran-2-yl, 2H-5,6-dihydrothiopyran-3-yl, 2H-5,6-dihydrothiopyran-4-yl, 2H-5,6-dihydrothiopyran-5-yl, 2H-5,6-dihydrothiopyran-6-yl, 1,2,5,6-tetrahydropyridin-2-yl, 1,2,5,6-tetrahydropyridin-3-yl, 1,2,5,6-tetrahydropyridin-4-yl, 1,2,5,6-tetrahydropyridin-5-yl, 1,2,5,6-tetrahydropyridin-6-yl, 2,3,4,5-tetrahydropyridin-2-yl, 2,3,4,5-tetrahydropyridin-3-yl, 2,3,4,5-tetrahydropyridin-4-yl, 2,3,4,5-tetrahydropyridin-5-yl, 2,3,4,5-tetrahydropyridin-6-yl, 4H-pyran-2-yl, 4H-pyran-3-yl, 4H-pyran-4-yl, 4H-thiopyran-2-yl, 4H-thiopyran-3-yl, 4H-thiopyran-4-yl, 1,4-dihydropyridin-2-yl, 1,4-dihydropyridin-3-yl, 1,4-dihydropyridin-4-yl, 2H-pyran-2-yl, 2H-pyran-3-yl, 2H-pyran-4-yl, 2H-pyran-5-yl, 2H-pyran-6-yl, 2H-thiopyran-2-yl, 2H-thiopyran-3-yl, 2H-thiopyran-4-yl, 2H-thiopyran-5-yl, 2H-thiopyran-6-yl, 1,2-dihydropyridin-2-yl, 1,2-dihydropyridin-3-yl, 1,2-dihydropyridin-

25

- 4-yl, 1,2-dihydropyridin-5-yl, 1,2-dihydropyridin-6-yl, 3,4-dihydropyridin-2-yl, 3,4-dihydropyridin-3-yl, 3,4-dihydropyridin-4-yl, 3,4-dihydropyridin-5-yl, 3,4-dihydropyridin-6-yl, 2,5-dihydropyridin-2-yl, 2,5-dihydropyridin-3-yl, 2,5-dihydropyridin-4-yl, 2,5-dihydropyridin-5-yl, 2,5-dihydropyridin-6-yl, 2,3-dihydropyridin-2-yl, 2,3-dihydropyridin-3-yl, 2,3-dihydropyridin-4-yl, 2,3-dihydropyridin-5-yl, 2,3-dihydropyridin-6-yl, 2H-5,6-dihydro-1,2-oxazin-3-yl, 2H-5,6-dihydro-1,2-oxazin-4-yl, 2H-5,6-dihydro-1,2-oxazin-5-yl, 2H-5,6-dihydro-1,2-oxazin-6-yl, 2H-5,6-dihydro-1,2-thiazin-3-yl, 2H-5,6-dihydro-1,2-thiazin-4-yl, 2H-5,6-dihydro-1,2-thiazin-5-yl, 2H-5,6-dihydro-1,2-thiazin-6-yl, 4H-5,6-dihydro-1,2-oxazin-3-yl, 4H-5,6-dihydro-1,2-oxazin-4-yl, 4H-5,6-dihydro-1,2-oxazin-5-yl, 4H-5,6-dihydro-1,2-oxazin-6-yl, 4H-5,6-dihydro-1,2-thiazin-3-yl, 4H-5,6-dihydro-1,2-thiazin-4-yl, 4H-5,6-dihydro-1,2-thiazin-5-yl, 4H-5,6-dihydro-1,2-thiazin-6-yl, 2H-3,6-dihydro-1,2-oxazin-3-yl, 2H-3,6-dihydro-1,2-oxazin-4-yl, 2H-3,6-dihydro-1,2-oxazin-5-yl, 2H-3,6-dihydro-1,2-oxazin-6-yl, 2H-3,6-dihydro-1,2-thiazin-3-yl, 2H-3,6-dihydro-1,2-thiazin-4-yl, 2H-3,6-dihydro-1,2-thiazin-5-yl, 2H-3,6-dihydro-1,2-thiazin-6-yl, 2H-3,4-dihydro-1,2-oxazin-3-yl, 2H-3,4-dihydro-1,2-oxazin-4-yl, 2H-3,4-dihydro-1,2-oxazin-5-yl, 2H-3,4-dihydro-1,2-oxazin-6-yl, 2H-3,4-dihydro-1,2-thiazin-3-yl, 2H-3,4-dihydro-1,2-thiazin-4-yl, 2H-3,4-dihydro-1,2-thiazin-5-yl, 2H-3,4-dihydro-1,2-thiazin-6-yl, 2,3,4,5-tetrahydropyridazin-3-yl, 2,3,4,5-tetrahydropyridazin-4-yl, 2,3,4,5-tetrahydropyridazin-5-yl, 2,3,4,5-tetrahydropyridazin-6-yl, 3,4,5,6-tetrahydropyridazin-3-yl, 3,4,5,6-tetrahydropyridazin-4-yl, 1,2,5,6-tetrahydropyridazin-3-yl, 1,2,5,6-tetrahydropyridazin-4-yl, 1,2,5,6-tetrahydropyridazin-5-yl, 1,2,5,6-tetrahydropyridazin-6-yl, 1,2,3,6-tetrahydropyridazin-3-yl, 1,2,3,6-tetrahydropyridazin-4-yl, 4H-5,6-dihydro-1,3-oxazin-2-yl, 4H-5,6-dihydro-1,3-oxazin-4-yl, 4H-5,6-dihydro-1,3-oxazin-5-yl, 4H-5,6-dihydro-1,3-oxazin-6-yl, 4H-5,6-dihydro-1,3-thiazin-2-yl, 4H-5,6-dihydro-1,3-thiazin-4-yl, 4H-5,6-dihydro-1,3-thiazin-5-yl, 4H-5,6-dihydro-1,3-thiazin-6-yl, 3,4,5,6-tetrahydropyrimidin-2-yl, 3,4,5,6-tetrahydropyrimidin-4-yl, 3,4,5,6-tetrahydropyrimidin-5-yl, 3,4,5,6-tetrahydropyrimidin-6-yl, 1,2,3,4-

- 5 tetrahydropyrazin-2-yl, 1,2,3,4-tetrahydropyrazin-5-yl, 1,2,3,4-tetrahydropyrimidin-2-yl, 1,2,3,4-tetrahydropyrimidin-4-yl, 1,2,3,4-tetrahydropyrimidin-5-yl, 1,2,3,4-tetrahydropyrimidin-6-yl, 2,3-dihydro-1,4-thiazin-2-yl, 2,3-dihydro-1,4-thiazin-3-yl, 2,3-dihydro-1,4-thiazin-5-yl, 2,3-dihydro-1,4-thiazin-6-yl, 2H-1,3-oxazin-2-yl, 2H-1,3-oxazin-4-yl, 2H-1,3-oxazin-5-yl, 2H-1,3-oxazin-6-yl, 2H-1,3-thiazin-2-yl, 2H-1,3-thiazin-4-yl, 2H-1,3-thiazin-5-yl, 2H-1,3-thiazin-6-yl, 4H-1,3-oxazin-2-yl, 4H-1,3-oxazin-4-yl, 4H-1,3-oxazin-5-yl, 4H-1,3-oxazin-6-yl, 4H-1,3-thiazin-2-yl, 4H-1,3-thiazin-4-yl, 4H-1,3-thiazin-5-yl, 4H-1,3-thiazin-6-yl, 6H-1,3-oxazin-2-yl, 6H-1,3-oxazin-4-yl, 6H-1,3-oxazin-5-yl, 6H-1,3-oxazin-6-yl, 6H-1,3-thiazin-2-yl, 6H-1,3-oxazin-4-yl, 6H-1,3-oxazin-5-yl, 6H-1,3-thiazin-6-yl, 2H-1,4-oxazin-2-yl, 2H-1,4-oxazin-3-yl, 2H-1,4-oxazin-5-yl, 2H-1,4-oxazin-6-yl, 2H-1,4-thiazin-2-yl, 2H-1,4-thiazin-3-yl, 2H-1,4-thiazin-5-yl, 2H-1,4-thiazin-6-yl, 4H-1,4-oxazin-2-yl, 4H-1,4-oxazin-3-yl, 4H-1,4-thiazin-2-yl, 4H-1,4-thiazin-3-yl, 1,4-dihydropyridazin-3-yl, 1,4-dihydropyridazin-4-yl, 1,4-dihydropyridazin-5-yl, 1,4-dihydropyridazin-6-yl, 1,4-dihydropyrazin-2-yl, 1,2-dihydropyrazin-2-yl, 1,2-dihydropyrazin-3-yl, 1,2-dihydropyrazin-5-yl, 1,2-dihydropyrazin-6-yl, 1,4-dihydropyrimidin-2-yl, 1,4-dihydropyrimidin-4-yl, 1,4-dihydropyrimidin-5-yl, 1,4-dihydropyrimidin-6-yl, 3,4-dihydropyrimidin-2-yl, 3,4-dihydropyrimidin-4-yl, 3,4-dihydropyrimidin-5-yl or 3,4-dihydropyrimidin-6-yl.
- 10 N-bonded, 5-membered, partially unsaturated rings such as:
 2,3-dihydro-1H-pyrrol-1-yl, 2,5-dihydro-1H-pyrrol-1-yl, 4,5-dihydro-1H-pyrazol-1-yl, 2,5-dihydro-1H-pyrazol-1-yl, 2,3-dihydro-1H-pyrazol-1-yl, 2,5-dihydroisoxazol-2-yl, 2,3-dihydroisoxazol-2-yl, 2,5-dihydroisothiazol-2-yl, 2,3-dihydroisoxazol-2-yl, 4,5-dihydro-1H-imidazol-1-yl, 2,5-dihydro-1H-imidazol-1-yl, 2,3-dihydro-1H-imidazol-1-yl, 2,3-dihydrooxazol-3-yl, 2,3-dihydrothiazol-3-yl.
- 15 2,5-dihydroisoxazol-2-yl, 2,3-dihydroisoxazol-2-yl, 2,5-dihydroisothiazol-2-yl, 2,3-dihydroisoxazol-2-yl, 4,5-dihydro-1H-imidazol-1-yl, 2,5-dihydro-1H-imidazol-1-yl, 2,3-dihydro-1H-imidazol-1-yl, 2,3-dihydrooxazol-3-yl, 2,3-dihydrothiazol-3-yl.
- 20 N-bonded, 6-membered, partially unsaturated rings such as:
 1,2,3,4-tetrahydropyridin-1-yl, 1,2,5,6-tetrahydropyridin-1-yl, 1,4-dihydropyridin-1-yl, 1,2-dihydropyridin-1-yl, 2H-5,6-dihydro-1,2-oxazin-2-yl, 2H-5,6-dihydro-1,2-thiazin-2-yl, 2H-3,6-dihydro-1,2-oxazin-2-yl, 2H-
- 25 1,2,3,4-tetrahydropyridin-1-yl, 1,2,5,6-tetrahydropyridin-1-yl, 1,4-dihydropyridin-1-yl, 1,2-dihydropyridin-1-yl, 2H-5,6-dihydro-1,2-oxazin-2-yl, 2H-5,6-dihydro-1,2-thiazin-2-yl, 2H-3,6-dihydro-1,2-oxazin-2-yl, 2H-
- 30 1,2,3,4-tetrahydropyridin-1-yl, 1,2,5,6-tetrahydropyridin-1-yl, 1,4-dihydropyridin-1-yl, 1,2-dihydropyridin-1-yl, 2H-5,6-dihydro-1,2-oxazin-2-yl, 2H-5,6-dihydro-1,2-thiazin-2-yl, 2H-3,6-dihydro-1,2-oxazin-2-yl, 2H-

3,6-dihydro-1,2-thiazin-2-yl, 2H-3,4-dihydro-1,2-oxazin-2-yl, 2H-3,4-dihydro-1,2-thiazin-2-yl, 2,3,4,5-tetrahydropyridazin-2-yl, 1,2,5,6-tetrahydropyridazin-1-yl, 1,2,5,6-tetrahydropyridazin-2-yl, 1,2,3,6-tetrahydropyridazin-1-yl, 3,4,5,6-tetrahydropyrimidin-3-yl, 1,2,3,4-tetrahydropyrazin-1-yl, 1,2,3,4-tetrahydropyrimidin-1-yl, 1,2,3,4-tetrahydropyrimidin-3-yl, 2,3-dihydro-1,4-thiazin-4-yl, 2H-1,2-oxazin-2-yl, 2H-1,2-thiazin-2-yl, 4H-1,4-oxazin-4-yl, 4H-1,4-thiazin-4-yl, 1,4-dihydropyridazin-1-yl, 1,4-dihydropyrazin-1-yl, 1,2-dihydropyrazin-1-yl, 1,4-dihydropyrimidin-1-yl or 3,4-dihydropyrimidin-3-yl.

10 Examples of saturated or partially unsaturated heterobicycles are in particular radicals corresponding to saturated or partially unsaturated bicarbocyclic radicals, wherein 1, 2 or 3 CH or CH₂ moieties have been replaced by N, NH, O, S, S(=O) or S(=O)₂, such as 2-oxa-6-azaspiro-[3,4]octyl, 2-azabicyclo[2.2.1]heptyl, 5-azabicyclo[2.2.1]heptyl, 2,5-diazabicyclo[2.2.1]heptyl, 3-azabicyclo[3.2.1]octyl, 8-azabicyclo[3.2.1]octyl, 3,8-diazabicyclo[3.2.1]octyl, dihydroindolyl, dihydroindolizynyl, dihydroisoindolyl, dihydroquinolynyl, dihydroisoquinolynyl, chromenyl and chromanyl.

Hetaryl: a 5- or 6-membered aromatic heteromonocyclic radical (also termed 5- or 6-membered monocyclic hetaryl) which ordinarily has 1, 2, 3 or 4 heteroatoms as ring members, which are selected from O, S and N, and which has in particular 1, 2, 3 or 4 nitrogen atoms or a heteroatom selected from oxygen and sulfur and, if appropriate, 1 or 2 nitrogen atoms as ring members besides carbon atoms as ring members and a 8- to 10-membered aromatic heterobicyclic radical (also termed 8- to 10-membered bicyclic hetaryl) which ordinarily has 1, 2, 3 or 4 heteroatoms as ring members, which are selected from O, S and N, and which has in particular 1, 2, 3 or 4 nitrogen atoms or a heteroatom selected from oxygen and sulfur and, if appropriate, 1 or 2 nitrogen atoms as ring members besides carbon atoms as ring members: for example

C-bonded, 5-membered monocyclic hetaryl having 1, 2 or 3 or 4 nitrogen atoms or a heteroatom selected from oxygen and sulfur and, if appropriate, having 1, 2 or 3 nitrogen atoms as ring members, such as:

2-furyl, 3-furyl, 2-thienyl, 3-thienyl, pyrrol-2-yl, pyrrol-3-yl, pyrazol-3-yl, pyrazol-4-yl, isoxazol-3-yl, isoxazol-4-yl, isoxazol-5-yl, isothiazol-3-yl,

isothiazol-4-yl, isothiazol-5-yl, imidazol-2-yl, imidazol-4-yl, oxazol-2-yl, oxazol-4-yl, oxazol-5-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, 1,2,3-oxadiazol-4-yl, 1,2,3-oxadiazol-5-yl, 1,2,4-oxadiazol-3-yl, 1,2,4-oxadiazol-5-yl, 1,3,4-oxadiazol-2-yl, 1,2,3-thiadiazol-4-yl, 1,2,3-thiadiazol-5-yl, 1,2,4-thiadiazol-3-yl, 1,2,4-thiadiazol-5-yl, 1,3,4-thiadiazolyl-2-yl, 1,2,3-triazol-4-yl, 1,2,4-triazol-3-yl, tetrazol-5-yl.

C-bonded, 6-membered monocyclic hetaryl having 1, 2 or 3 nitrogen atoms as ring members, such as:

pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridazin-3-yl, pyridazin-4-yl, pyrimidin-2-yl, pyrimidin-4-yl, pyrimidin-5-yl, pyrazin-2-yl, 1,3,5-triazin-2-yl, 1,2,4-triazin-3-yl, 1,2,4-triazin-5-yl, 1,2,4-triazin-6-yl, 1,2,4,5-tetrazin-3-yl.

N-bonded, 5-membered heteroaromatic radicals having 1, 2, 3 or 4 nitrogen atoms as ring members, such as:

pyrrol-1-yl, pyrazol-1-yl, imidazol-1-yl, 1,2,3-triazol-1-yl, 1,2,4-triazol-1-yl, tetrazol-1-yl.

bicyclic 8 to 10-membered hetaryl, hetaryl which has one of the aforementioned 5- or 6-membered heteroaromatic rings and a further aromatic carbocycle or 5- or 6-membered heterocycle fused thereto, for example a fused benzene, thiophene, furane, pyrrole, pyrazole, imidazole, pyridine or pyrimidine ring. These bicyclic hetaryl include for example quinolinyl, isoquinolinyl, cinnolinyl, indolyl, indolizynyl, isoindolyl, indazolyl, benzofuryl, benzothienyl, benzo[b]thiazolyl, benzoxazolyl, benzthiazolyl, benzimidazolyl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, imidazo-[2,1-b]-thiazol-6-yl and 1,2,4-triazolo[1,5-a]pyridine-2-yl.

Hetarylalkyl: a hetaryl radical as defined above which is linked via an alkylene group, in particular via a methylene, 1,1-ethylene or 1,2-ethylene group, to the remainder of the molecule.

The expression "optionally substituted" in the context of the present invention means that the respective moiety is unsubstituted or has 1, 2 or 3, in particular 1, substituents which are selected from halogen, C₁-C₄-alkyl, C₁-C₄-haloalkyl, OH, SH, CN, CF₃, O-CF₃, COOH, O-CH₂-COOH, C₁-C₆-alkoxy, C₁-C₄-haloalkoxy, C₁-C₆-alkylthio, C₃-C₇-cycloalkyl, COO-C₁-C₆-alkyl, CONH₂, CONH-C₁-C₆-alkyl, SO₂NH-

C₁-C₆-alkyl, CON-(C₁-C₆-alkyl)₂, SO₂N-(C₁-C₆-alkyl)₂, NH-SO₂-C₁-C₆-alkyl, NH-CO-C₁-C₆-alkyl, SO₂-C₁-C₆-alkyl, O-phenyl, O-CH₂-phenyl, CONH-phenyl, SO₂NH-phenyl, CONH-hetaryl, SO₂NH-hetaryl, SO₂-phenyl, NH-SO₂-phenyl, NH-CO-phenyl, NH-SO₂-hetaryl and NH-CO-hetaryl, where phenyl and hetaryl in the last 11 radicals
 5 mentioned are unsubstituted or may have 1, 2 or 3 substituents which are selected from halogen, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₁-C₄-alkoxy and C₁-C₄-haloalkoxy.

In relation to their use as inhibitors of PDE10A, the variables Het, A, A', Q, X¹, X², X³, Y¹, Y², Y³, R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, Cyc¹, Cyc² and Cyc³ preferably have the following meanings, where these represent, both considered on their own and
 10 in combination with at least one other or all, special configurations of the compounds of the formula I:

In a particular embodiment, Het is unsubstituted or may carry 1, 2, 3 or 4 identical or different substituents R^x. In this regard, R^x is selected from the group consisting of H, halogen, C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, C₃-C₆-
 15 cycloalkyl, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkyl, OH, hydroxy-C₁-C₄-alkyl, O-C₃-C₆-cycloalkyl, benzyloxy, C(O)O-(C₁-C₄-alkyl), O-(C₁-C₄-alkyl)-CO₂H, N(R^{x1})(R^{x2}), C(O)N(R^{x1})(R^{x2}), C₁-C₄-alkyl-N(R^{x1})(R^{x2}), -NR^{x3}-C(O)-N(R^{x1})(R^{x2}), NR^{x3}-C(O)O-(C₁-C₄-alkyl), -N(R^{x3})-SO₂-R^{x4}, phenyl, CN, -SF₅, -OSF₅, -SO₂R^{x4}, -SR^{x4} and trimethylsilyl, where R^{x1}, R^{x2}, R^{x3} and R^{x4}, independently of each other are selected
 20 from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-fluoroalkyl and C₃-C₆-cycloalkyl or R^{x1} and R^{x2} form together with the N atom to which they are attached a 3- to 7-membered, nitrogen heterocycle which may have 1, 2 or 3 further different or identical heteroatoms or heteroatom containing groups selected from the group of O, N, S, SO and SO₂ as ring members and which may carry 1, 2, 3, 4, 5 or 6 substituents
 25 selected from C₁-C₄-alkyl.

Het is preferably selected from the group consisting of C-bound 6-membered monocyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members, and C-bound, fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member, where monocyclic
 30 hetaryl and bicyclic hetaryl may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x, in particular 0, 1 or 2 substituents R^x. In this regard, R^x is preferably selected from halogen, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, phenyl, C₃-

C₆-cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C₃-C₆-cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, phenyl, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In a particular embodiment of the invention, Het is selected from fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member and which may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x, in particular 0, 1 or 2 substituents R^x. In this regard, R^x is preferably selected from halogen, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, C₃-C₆-cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C₃-C₆-cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In another particular embodiment of the invention, Het is selected from 6-membered monocyclic hetaryl, which may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x, in particular 0, 1 or 2 substituents R^x. In this regard, R^x is preferably selected from halogen, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, phenyl, C₃-C₆-cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C₃-C₆-cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl or one R^x may also be phenyl.

Particular preference is given to those Het radicals, which have at least one imino-nitrogen as ring member, which is located in the position adjacent to the carbon atom which is bound to A. Particular preference is given to those Het radicals, which have at least one imino-nitrogen as ring member, which is located in the position adjacent to the carbon atom which is bound to tA and which are selected from the group consisting of C-bound 6-membered monocyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members, benzofuryl and C-bound, fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as

ring member, where monocyclic hetaryl, benzofuryl and bicyclic hetaryl may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x , in particular 0, 1 or 2 substituents R^x . In this regard, R^x is preferably selected from halogen, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, phenyl, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C_3 - C_6 -cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, phenyl, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

Particular examples of Het are selected from the group consisting of 2-benzofuryl, 2-pyridyl, 2-pyrimidinyl, 4-pyrimidinyl, 2-pyrazinyl, 3-pyridazinyl, 2-quinolinyl, 3-isoquinolinyl, 2-quinazolinyl, 2-quinoxaliny, 1,5-naphthyridin-2-yl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, imidazo-[2,1-b]-thiazol-6-yl and 1,2,4-triazolo[1,5-a]pyridine-2-yl, where the aforementioned radicals are unsubstituted or may carry 1, 2 or 3 radicals R^x as defined above, which are in particular selected from the group consisting of fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In a particular embodiment of the invention, Het has at least one imino-nitrogen as ring member, which is located in the position adjacent to the carbon atom which is bound to A and Het is selected from the group consisting of fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member, where bicyclic hetaryl may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x , in particular 0, 1 or 2 substituents R^x . In this regard, R^x is preferably selected from halogen, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C_3 - C_6 -cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl. Particular examples of Het of

this embodiment are 2-quinolinyl, 3-isoquinolinyl, 2-quinazolinyl, 2-quinoxaliny, 1,5-naphthyridin-2-yl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, imidazo-[2,1-b]-thiazol-6-yl and 1,2,4-triazolo[1,5-a]pyridine-2-yl, where the aforementioned radicals are unsubstituted or may carry 1, 2 or 3 radicals R^x as defined above, which are in particular selected from the group consisting of fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

Particular preference is given to compounds, where Het is 2-quinolinyl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, and in particular 2-quinolinyl or imidazo[1,2-a]pyridine-2-yl, where these radicals are unsubstituted or may carry 1, 2 or 3 radicals R^x as defined above, which are in particular selected from the group consisting of fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In particular embodiments of the invention, the variable X^1 is CH. In these particular embodiments, X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H or Y^2-Cyc^2 . In these particular embodiments, X^3 is preferably S or $C(R^9)=C(R^8)$.

In further particular embodiments of the invention, the variable X^1 is N. In these particular embodiments, X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H or Y^2-Cyc^2 . In these particular embodiments, X^3 is preferably S or $C(R^9)=C(R^8)$.

In particular embodiments of the invention, the variable X^2 is $C-R^7$. In these particular embodiments R^7 is as defined above and in particular H or Y^2-Cyc^2 . In these embodiments, X^1 is CH or preferably N. In these particular embodiments, X^3 is preferably S or $C(R^9)=C(R^8)$.

In further particular embodiments of the invention, the variable X^2 is N. In this embodiment, X^1 is preferably CH. In these particular embodiments, X^3 is preferably $C(R^9)=C(R^8)$.

In particular embodiments of the invention X^3 is O, S, $-X^4=C(R^8)-$, where $C(R^8)$ is
 5 bound to the carbon atom which carries R^2 .

In particular embodiments of the invention X^3 is S. In these embodiments, X^1 is CH or preferably N and X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H or Y^2-Cyc^2 .

In particular embodiments of the invention X^3 is O. In these embodiments, X^1 is N
 10 or preferably CH, X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H or Y^2-Cyc^2 and R^1 is as defined above and in particular H or Y^1-Cyc^1 .

In further particular embodiments of the invention, the variable X^3 is $C(R^9)=C(R^8)$. In these embodiments, X^1 is CH or preferably N and X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H or Y^2-Cyc^2 .

15 In further particular embodiments of the invention, the variable X^3 is $N=C(R^9)$. In these embodiments, X^1 is CH or preferably N and X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H and R^1 is as defined above and in particular Y^1-Cyc^1 .

In the embodiments of the invention, where X^3 is $N=C(R^9)$, R^9 is preferably H.

In further particular embodiments of the invention, the variable X^3 is $N=C(R^8)$. In
 20 these embodiments, X^1 is preferably CH and X^2 is preferably $C-R^7$, where R^7 is as defined above and in particular H or Y^2-Cyc^2 .

In the embodiments of the invention, where X^2 is $C-R^7$, R^7 is preferably H or Y^2-Cyc^2 .

In the embodiments of the invention, where X^3 is $C(R^9)=C(R^8)$, R^9 is preferably H
 25 or Y^3-Cyc^3 , while R^8 is preferably hydrogen.

In the embodiments of the invention, where X^3 is $N=C(R^8)$, R^8 is preferably H.

In the embodiments of the invention, where X^2 is $C-R^7$, and where X^3 is $C(R^9)=C(R^8)$, R^7 is preferably H or Y^2-Cyc^2 , R^9 is preferably H or Y^3-Cyc^3 , while R^8 is preferably hydrogen, where preferably either R^7 is Y^2-Cyc^2 or R^9 is Y^3-Cyc^3 while one
 30 of R^7 and R^9 is different from Y^2-Cyc^2 or Y^3-Cyc^3 , respectively, or both R^7 and R^9 are different from Y^2-Cyc^2 or Y^3-Cyc^3 .

In this regard, those radicals R^1 , R^7 and R^9 , which are different from $Y^1\text{-Cyc}^1$, $Y^2\text{-Cyc}^2$, $Y^3\text{-Cyc}^3$, respectively, are in particular selected, independently of each other, from the group consisting of hydrogen, fluorine, $C_1\text{-C}_4\text{-alkyl}$, fluorinated $C_1\text{-C}_2\text{-alkyl}$, $C_1\text{-C}_4\text{-alkoxy}$, fluorinated $C_1\text{-C}_2\text{-alkoxy}$, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl. Those radicals R^1 , R^7 and R^9 , which are
 5 different from $Y^1\text{-Cyc}^1$, $Y^2\text{-Cyc}^2$, $Y^3\text{-Cyc}^3$, respectively, are most preferably hydrogen.

In particular preferred embodiments of the invention, R^1 is $Y^1\text{-Cyc}^1$. In these embodiments X^1 is CH or preferably N and X^2 is preferably $C\text{-R}^7$, where R^7 is as defined above and in particular H or $Y^2\text{-Cyc}^2$. In these embodiments, particular
 10 preference is given to compounds, where X^3 is S or X^3 is $C(R^9)=C(R^8)$, where R^9 is preferably H or $Y^3\text{-Cyc}^3$, while R^8 is preferably hydrogen.
 $Y^3\text{-Cyc}^3$, while R^8 is preferably hydrogen.

In other particular preferred embodiments of the invention, R^1 is different from $Y^1\text{-Cyc}^1$ and in particular hydrogen. In these embodiments X^1 is CH or preferably N. In
 15 these embodiments X^2 is preferably $C\text{-R}^7$, where R^7 is as defined above and in particular $Y^2\text{-Cyc}^2$ and X^3 is S or X^3 is preferably $C\text{-R}^7$, where R^7 is as defined above and in particular H or $Y^2\text{-Cyc}^2$ and X^3 is X^3 is $C(R^9)=C(R^8)$, where R^9 is preferably H or $Y^3\text{-Cyc}^3$, while R^8 is preferably hydrogen.

In the moiety $Y^1\text{-Cyc}^1$, Y^1 is preferably selected from O, NH and a chemical
 20 bond. In particular Y^1 is a chemical bond.

In the moiety $Y^2\text{-Cyc}^2$, Y^2 is preferably selected from O, NH and a chemical bond. In particular Y^2 is a chemical bond.

In the moiety $Y^3\text{-Cyc}^3$, Y^3 is preferably selected from O, NH and a chemical bond. In particular Y^3 is a chemical bond.

25 Preferably, Cyc^1 is selected from the groups of

(i) saturated 4-, 5-, 6-, 7- or 8-membered heteromonocycles or a saturated 7-, 8-, 9- or 10-membered heterobicycle, where the heteromonocycle and the heterobicycle have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O,
 30 S, $S(=O)$, $S(=O)_2$ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y\text{-R}^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where

R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O; and

(ii) phenyl or a 5- or 6 membered monocyclic hetaryl, which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, 9- or 10-membered bicyclic hetaryl which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of indolyl, quinoliny, isoquinoliny, quinazoliny, benzimidazolyl, benzotriazolyl, benzopyrazolyl and benzofuryl, where phenyl and hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In this regard, R^{C1} is preferably selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if Cyc^1 is phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 5- or 6-indolyl, 5- or 6-benzimidazolyl, 5- or 6-benzopyrazolyl, 5- or 6-benzotriazolyl, 5- or 6-benzofuranyl, 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, 5- or 6-quinoliny, 5- or 6-isoquinoliny, 5- or 6-quinazoliny, 2-amino-5-quinazoliny, and 2-amino-6-quinazoliny.

In this regard, R^{C2} is preferably selected from the group consisting of phenyl, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2, or 3 methyl groups, fluorinated C_3 - C_6 -cycloalkyl, and 5- or 6-membered saturated heteromonocyclic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, where phenyl the saturated heteromonocyclic radical is unsubstituted or carries 1, 2 or 3 radicals R^{C3} , which are preferably selected from fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 .

In particular, Cyc^1 is selected from the groups of

(i) saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1}, where R^{C1} is as defined herein; and

(ii) phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical Y'-R^{C2} and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1}, where R^{C1}, R^{C2} and Y' are as defined herein and where Y', if present, is preferably a chemical bond or O.

In particular embodiments of the invention, Cyc¹ is selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles or a saturated 7-, 8-, 9- or 10-membered heterobicycle, where the heteromonocycle and the heterobicycle have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical Y'-R^{C2} and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1}, where R^{C1}, R^{C2} and Y' are as defined herein and where Y', if present, is preferably a chemical bond or O.

In special embodiments of the invention, Cyc¹ is selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1}, where R^{C1} is as defined herein.

In this particular and special embodiment, Y¹ is preferably selected from O, NH and a chemical bond, with particular preference given to Y¹ being a chemical bond.

In this particular and special embodiment Y^1 -Cyc¹ is e.g. selected from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, 2-oxa-6-azaspiro-[3,4]octyl, 2,5-diazabicyclo[2.2.1]heptan-2-yl, 3,8-diazabicyclo[3.2.1]octan-8-yl, 5 thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino and especially from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and 10 oxetan-3-ylamino.

In other particular embodiments of the invention, Cyc¹ is phenyl or a 5- or 6 membered heteroaromatic radical, which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of pyridyl, pyrimidinyl, furyl, 15 thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered heteroaromatic radical are unsubstituted or either carry, independently of each other, carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical Y' - R^{C2} and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

20 In special embodiments of the invention, Cyc¹ is selected from the group consisting of phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical Y' - R^{C2} and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals 25 R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In particular Cyc¹ is selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and 30 hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if Cyc¹ is phenyl, two radicals R^{C1} which are bound to adjacent

carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 5- or 6-indolyl, 5- or 6-benzimidazolyl, 5- or 6-benzopyrazolyl, 5- or 6-benzotriazolyl, 5- or 6-benzofuranyl, 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, 5- or 6-quinoliny, 5- or 6-isoquinoliny, 5- or 6-quinazoliny, 2-amino-5-quinazoliny, and 2-amino-6-quinazoliny. Amongst these, particular preference is given to compounds, where Y^1 is a chemical bond. Amongst these, particular preference is given to compounds, where Cyc^1 is selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 .

Preferably, Cyc^2 and Cyc^3 are, independently from each other, selected from the groups of

(i) saturated 4-, 5-, 6-, 7- or 8-membered heteromonocycles or a saturated 7-, 8-, 9- or 10-membered heterobicycle, where the heteromonocycle and the heterobicycle have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, $S(=O)$, $S(=O)_2$ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O; and

(ii) phenyl or a 5- or 6 membered monocyclic hetaryl, which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, 9- or 10-membered bicyclic hetaryl which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of indolyl, quinoliny, isoquinoliny, quinazoliny, benzimidazolyl, benzotriazolyl, benzopyrazolyl

and benzofuryl, where phenyl and hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

5 In this regard, R^{C1} is preferably selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if Cyc^2 or Cyc^3 are phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 5- or 6-indolyl, 5- or 6-benzimidazolyl, 5- or 6-benzopyrazolyl, 10 5- or 6-benzotriazolyl, 5- or 6-benzofuranyl, 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, 5- or 6-quinolinyl, 5- or 6-isoquinolinyl, 5- or 6-quinazolinyl, 2-amino-5-quinazolinyl, and 2-amino-6-quinazolinyl.

In this regard, R^{C2} is preferably selected from the group consisting of phenyl, C_3 -
15 C_6 -cycloalkyl, optionally substituted by 1, 2, or 3 methyl groups, fluorinated C_3 - C_6 -cycloalkyl, and 5- or 6-membered saturated heteromonocyclic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, where phenyl the saturated heteromonocyclic radical is unsubstituted or carries 1, 2 or 3 radicals R^{C3} , which are preferably selected from fluorine, chlorine, CN, methyl, difluoromethyl, 20 trifluoromethyl, methoxy and NH_2 .

In particular, Cyc^2 and Cyc^3 are, independently from each other, selected from the groups of

(i) saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one
25 further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, $S(=O)$, $S(=O)_2$ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1} , where R^{C1} is as defined herein; and

(ii) phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, 30 furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals

R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In particular embodiments of the invention, Cyc^2 and Cyc^3 are, independently from each other, selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles or a saturated 7-, 8-, 9- or 10-membered heterobicycle, where the heteromonocycle and the heterobicycle have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In special embodiments of the invention, Cyc^2 and Cyc^3 are, independently from each other, selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1} , where R^{C1} is as defined herein.

In this particular and special embodiments Y^2 and Y^3 are, independently from each other preferably selected from O, NH and a chemical bond, with particular preference given to Y^2 and Y^3 being a chemical bond.

In this particular and special embodiments Cyc^2 and Cyc^3 are, independently from each other, e.g. selected from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, 2-oxa-6-azaspiro-[3,4]octyl, 2,5-diazabicyclo[2.2.1]heptan-2-yl, 3,8-diazabicyclo[3.2.1]octan-8-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino and especially from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino.

In other particular embodiments of the invention, $Y^2\text{-Cyc}^2$ and $Y^3\text{-Cyc}^3$ are, independently of each other, phenyl or a 5- or 6 membered heteroaromatic radical, which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered heteroaromatic radical are unsubstituted or either carry, independently of each other, carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'\text{-}R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In special embodiments of the invention, $Y^2\text{-Cyc}^2$ and $Y^3\text{-Cyc}^3$ are, independently from each other, selected from the group consisting of phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'\text{-}R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In particular $Y^2\text{-Cyc}^2$ and $Y^3\text{-Cyc}^3$ are, independently from each other, selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if one or both of $Y^2\text{-Cyc}^2$ and $Y^3\text{-Cyc}^3$ are phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 5- or 6-indolyl, 5- or 6-benzimidazolyl, 5- or 6-benzopyrazolyl, 5- or 6-benzotriazolyl, 5- or 6-benzofuranyl, 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, 5- or 6-quinoliny, 5- or 6-isoquinoliny, 5- or 6-quinazoliny, 2-amino-5-quinazoliny, and 2-amino-6-quinazoliny. Amongst these, particular preference is given to compounds, where $Y^2\text{-Cyc}^2$ and $Y^3\text{-Cyc}^3$ are, independently from each other, selected from the group consisting of phenyl and 5- or 6-membered hetaryl

selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 .

With regard to Cyc^1 , Cyc^2 and Cyc^3 , and in particular with regard to the aforementioned particular or special embodiments of Cyc^1 , Cyc^2 and Cyc^3 , R^{C1} is preferably selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 .

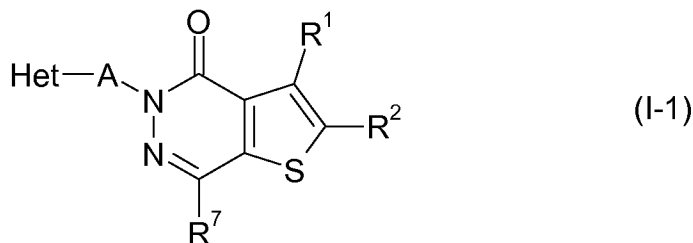
With regard to Cyc^1 , Cyc^2 and Cyc^3 , and in particular with regard to the aforementioned particular or special embodiments of Cyc^1 , Cyc^2 and Cyc^3 , R^{C2} is preferably selected from the group consisting of phenyl, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2, or 3 methyl groups, fluorinated C_3 - C_6 -cycloalkyl, and 5- or 6-membered saturated heteromonocyclic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, where phenyl the saturated heteromonocyclic radical is unsubstituted or carries 1, 2 or 3 radicals R^{C3} , which are preferably selected from fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 .

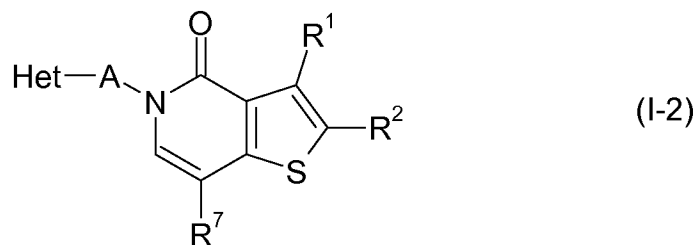
Irrespective from the aforementioned embodiments, R^2 is preferably selected from the group consisting of hydrogen, fluorine, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

Irrespective from the aforementioned embodiments, R^2 is in particular hydrogen.

Irrespective from the aforementioned embodiments, Q is in particular oxygen.

Particular embodiments of the invention relate to the compounds of the following formulae I-1 and I-2:

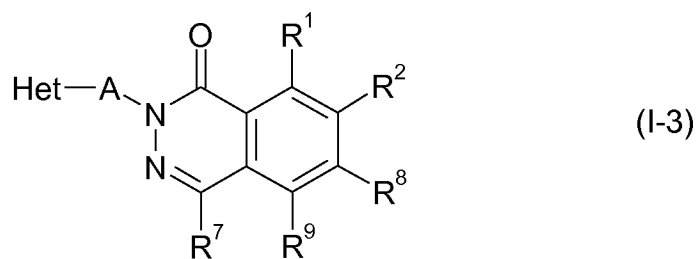
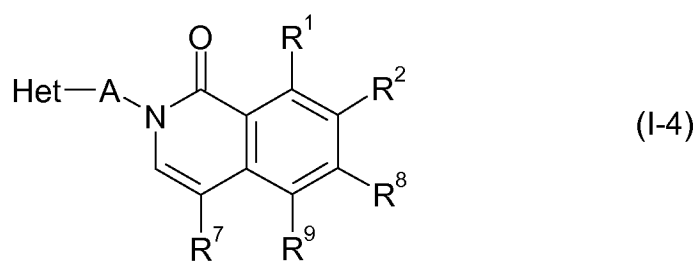




where Het, A, R¹, R² and R⁷ are as defined here and in the claims.

Other particular embodiments of the invention relate to the compounds of the following formulae I-3 and I-4:

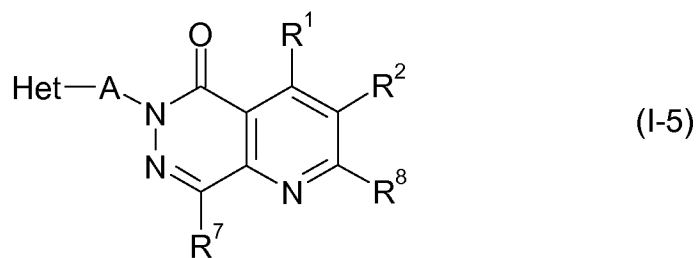
5

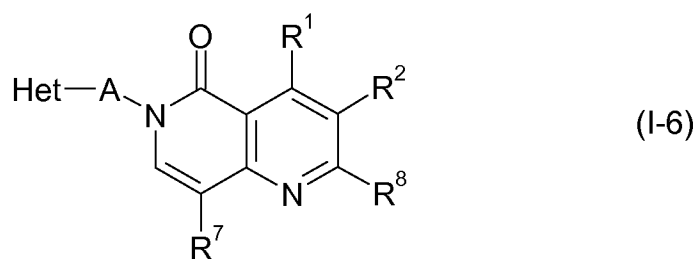


where Het, A, R¹, R², R⁷, R⁸ and R⁹ are as defined here and in the claims.

Further particular embodiments of the invention relate to the compounds of the following formulae I-5 and I-6:

10

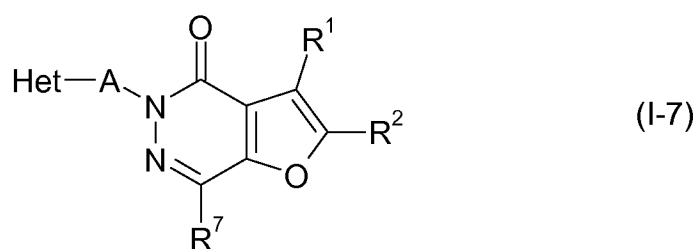
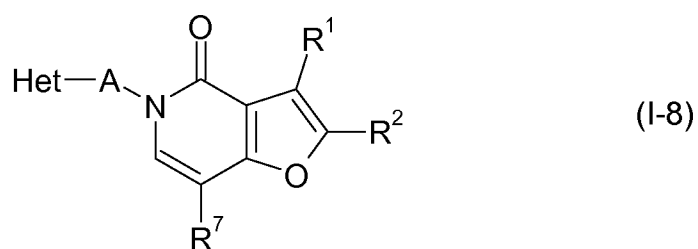




where Het, A, R¹, R², R⁷ and R⁸ are as defined here and in the claims.

Particular embodiments of the invention relate to the compounds of the following

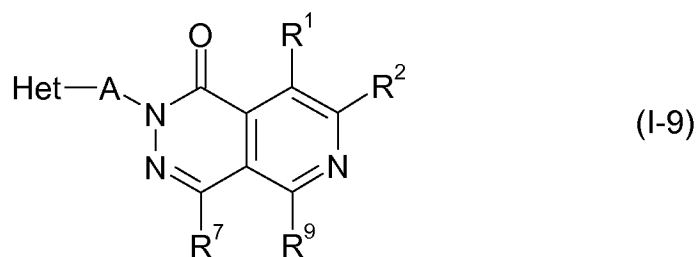
5 formulae I-7 and I-8:

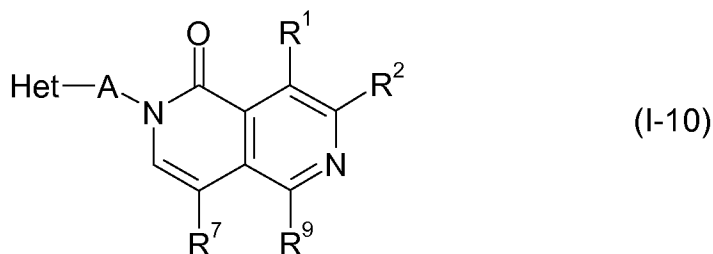


where Het, A, R¹, R² and R⁷ are as defined here and in the claims.

Further particular embodiments of the invention relate to the compounds of the

10 following formulae I-9 and I-10:





where Het, A, R¹, R², R⁷ and R⁹ are as defined here and in the claims.

In a particular embodiment of the invention, A in formula I is A¹, A², A³ or A⁴.

5 In a particular embodiment of the invention, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10 is a bivalent radical A¹.

Preference is given to compounds of the formula I, and likewise to compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, where R³, R⁴ are selected from hydrogen and fluorine and in particular to those compounds, where both R³ and R⁴ are hydrogen. Preference is given to compounds of the formula I, where R⁵ and R⁶ are, independently of each other, selected from the group consisting of hydrogen, fluorine and methyl, and in particular to those compounds, where both R⁵ and R⁶ are hydrogen.

In another particular embodiment of the invention, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, is a bivalent radical A².

15 In another particular embodiment of the invention, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, is a bivalent radical A³.

Preference is given to compounds of the formula I, and likewise to compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, where R⁴, R⁵ are selected from hydrogen and fluorine. In particular, both R⁴ and R⁵ are hydrogen.

20 In another particular embodiment of the invention, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, is a bivalent radical A⁴.

Preference is given to compounds of the formula I, and likewise to compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, where R⁴, R⁵ are selected from hydrogen and fluorine and in particular to those compounds, where both R⁴ and R⁵ are hydrogen. In the bivalent radical A⁴ the moiety A' is preferably CR^{3b}R^{3c}, where R^{3b} and R^{3c} are independently of each other selected from the group consisting of hydrogen, fluorine and methyl or together form CH₂CH₂ and where R^{3b} and R^{3b} are independently of each other in particular selected from the group consisting of hydrogen and fluorine.

Particular preference is given to compounds of the formula I, and likewise to compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, where A is a bivalent radical A^4 , where the moiety A' is $CR^{3b}R^{3c}$, where R^{3b} and R^{3c} are as defined herein and where R^{3b} and R^{3c} are in particular, independently of each other, selected from the group consisting of hydrogen, fluorine and methyl or together form CH_2CH_2 and especially where both R^{3b} and R^{3c} are hydrogen or fluorine.

In another particular embodiment of the invention, A in formula I and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10 is a bivalent radical A^4 , where A' is O.

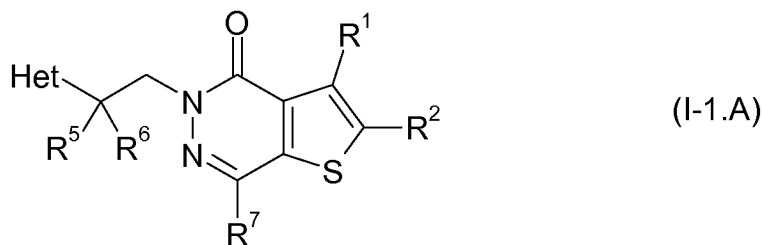
In another particular embodiment of the invention, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, is a bivalent radical A^4 , where A' is NR^{3a} with R^{3a} being as defined above in particular hydrogen or C_1 - C_4 -alkyl.

In another particular embodiment, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, is a bivalent radical A^4 , where A' is linear C_2 - C_3 -alkanediyl, where one of the CH_2 -moieties of C_2 - C_3 -alkandiyl may be replaced by oxygen or NR^{3a} , and where 1, 2, 3, or 4 of the hydrogen atoms of C_2 - C_3 -alkandiyl may be replaced by a radical R^{3d} . R^{3d} is preferably selected from halogen and C_1 - C_4 -alkyl.

In another particular embodiment of the invention, A in formula I, and likewise in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10 is a bivalent radical A^5 .

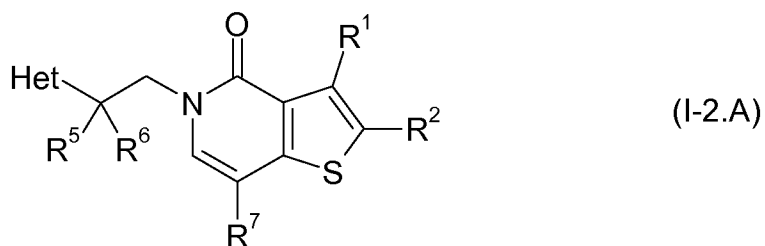
Preference is given to compounds of the formula I, and likewise to compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9 and I-10, where R^4 , R^5 are selected from hydrogen and methyl and in particular to those compounds, where both R^4 and R^5 are hydrogen. Preference is given to compounds of the formula I, where R^{3e} and R^{3f} are, independently of each other, selected from the group consisting of hydrogen and methyl, and in particular to those compounds, where both R^{3e} and R^{3f} are hydrogen.

A particular preferred embodiment of the invention relates to the compounds of formula I-1.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R¹, R², R⁵, R⁶ and R⁷ are as defined here and in the claims.

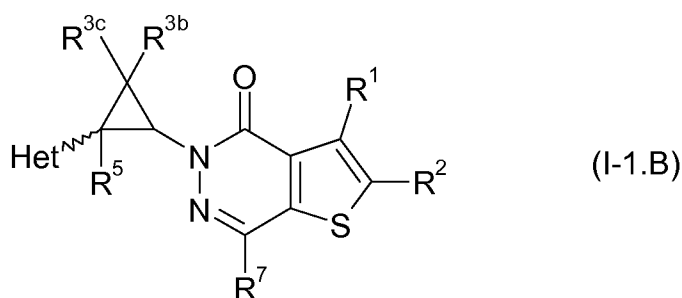
Another particular preferred embodiment of the invention relates to the compounds of formula I-2.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



5

where Het, R¹, R², R⁵, R⁶ and R⁷ are as defined here and in the claims.

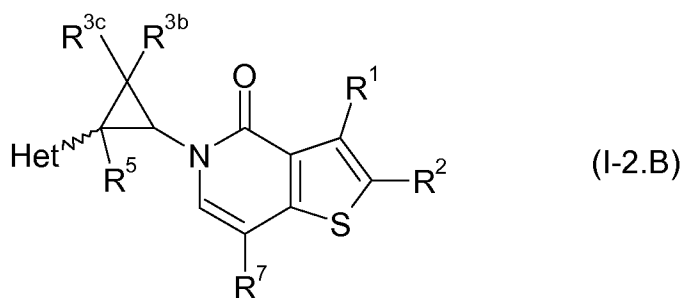
Another particular preferred embodiment of the invention relates to the compounds of formula I-1.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



10

where Het, R¹, R², R^{3b}, R^{3c}, R⁵ and R⁷ are as defined here and in the claims and where R⁵ is in particular hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-2.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:

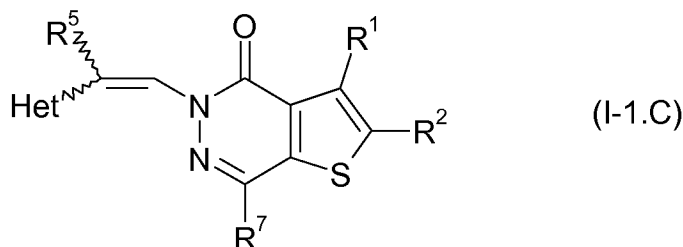


15

where Het, R¹, R², R^{3b}, R^{3c}, R⁵ and R⁷ are as defined here and in the claims and where R⁵ is in particular hydrogen. In formulae I-1.B and I-2.B, the variables R^{3b} and

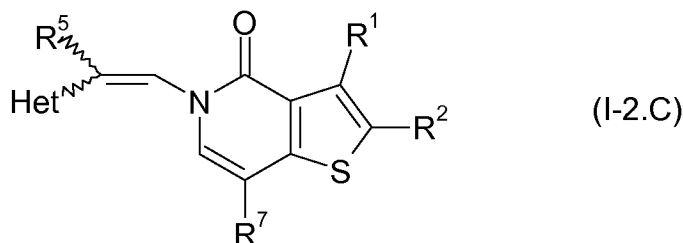
R^{3c} are independently of each other in particular selected from the group consisting of hydrogen, fluorine and methyl or together form CH_2CH_2 . Particular preference is given to compounds of the formulae I-1.B and I-2.B, where both R^{3b} and R^{3c} are hydrogen or fluorine.

- 5 Another particular preferred embodiment of the invention relates to the compounds of formula I-1.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



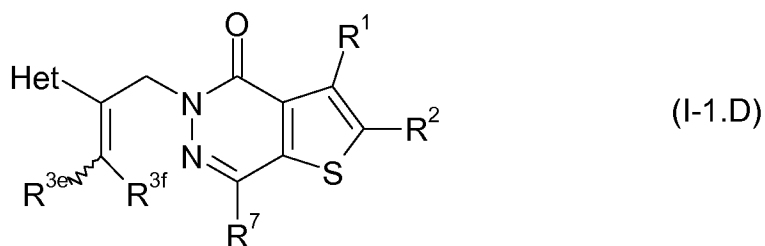
- 10 where Het, R^1 , R^2 , R^5 and R^7 are as defined here and in the claims and where R^5 is in particular hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-2.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



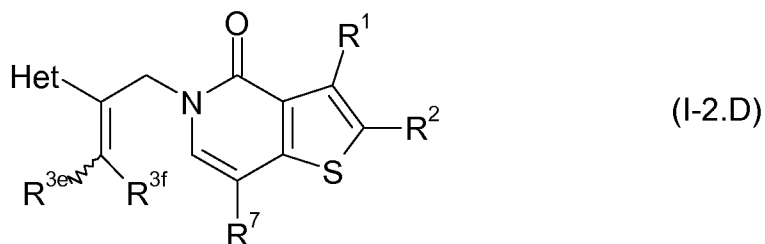
- 15 where Het, R^1 , R^2 , R^5 and R^7 are as defined here and in the claims and where R^5 is in particular hydrogen.

A particular preferred embodiment of the invention relates to the compounds of formula I-1.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R^1 , R^2 , R^{3e} , R^{3f} and R^7 are as defined here and in the claims and where R^{3e} and R^{3f} are in particular both hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-2.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:

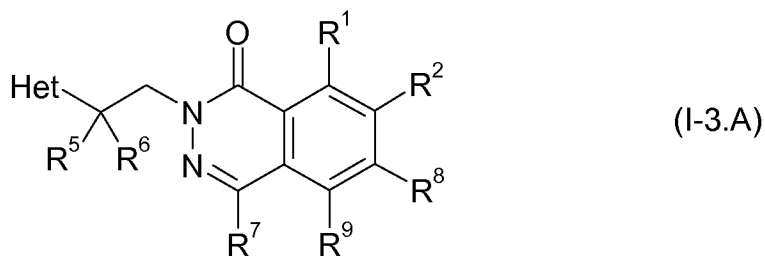


where Het, R^1 , R^2 , R^{3e} , R^{3f} and R^7 are as defined here and in the claims and where R^{3e} and R^{3f} are in particular both hydrogen.

Particular embodiments of the invention relate to compounds of the formulae I-1, I-2, I-1.A, I-2.A, I-1.B, I-2.B, I-1.C, I-2.C, I-1.D, and I-2.D described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R^1 is a radical Y^1 -Cyc¹ and R^7 is as defined above and in particular selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y^2 -Cyc², especially from the group consisting of hydrogen and Y^2 -Cyc².

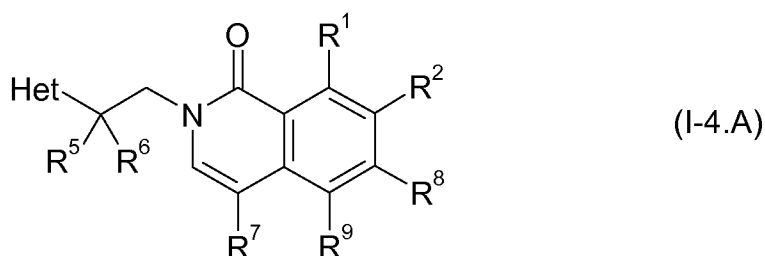
Further particular embodiments of the invention relate to compounds of the formulae I-1, I-2, I-1.A, I-2.A, I-1.B, I-2.B, I-1.C, I-2.C, I-1.D, and I-2.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R^1 is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and R^7 is a moiety Y^2 -Cyc². In these embodiments R^1 is in particular hydrogen.

A further particular preferred embodiment of the invention relates to the compounds of formula I-3.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



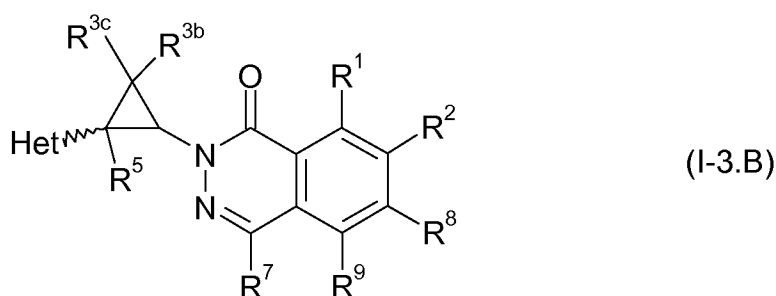
where Het, R¹, R², R⁵, R⁶, R⁷, R⁸ and R⁹ are as defined here and in the claims.

Another particular preferred embodiment of the invention relates to the compounds of formula I-4.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



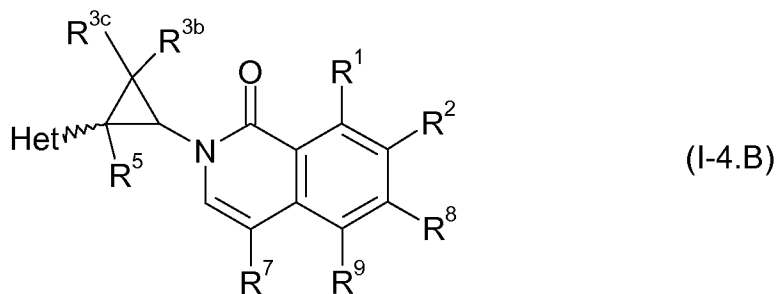
where Het, R¹, R², R⁵, R⁶, R⁷, R⁸ and R⁹ are as defined here and in the claims.

Another particular preferred embodiment of the invention relates to the compounds of formula I-3.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R¹, R², R^{3b}, R^{3c}, R⁷, R⁸ and R⁹ are as defined here and in the claims and where R⁵ is in particular hydrogen.

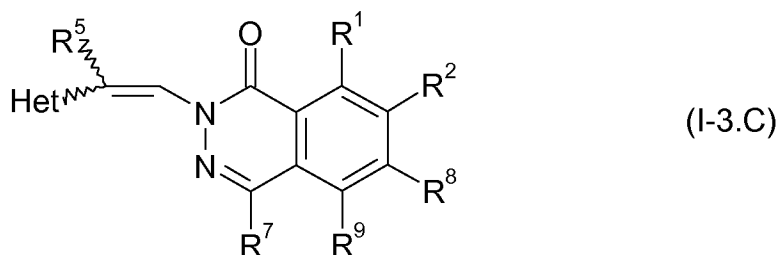
Another particular preferred embodiment of the invention relates to the compounds of formula I-4.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R^1 , R^2 , R^{3b} , R^{3c} , R^7 , R^8 and R^9 are as defined here and in the claims and where R^5 is in particular hydrogen.

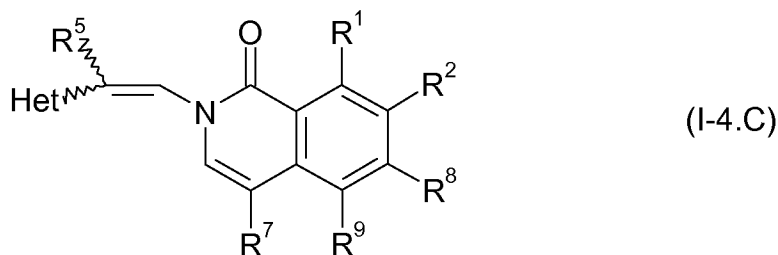
In formulae I-3.B and I-4.B, the variables R^{3b} and R^{3c} are independently of each other in particular selected from the group consisting of hydrogen, fluorine and methyl or together form CH_2CH_2 . Particular preference is given to compounds of the formulae I-3.B and I-4.B, where both R^{3b} and R^{3c} are hydrogen or fluorine.

Another particular preferred embodiment of the invention relates to the compounds of formula I-3.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



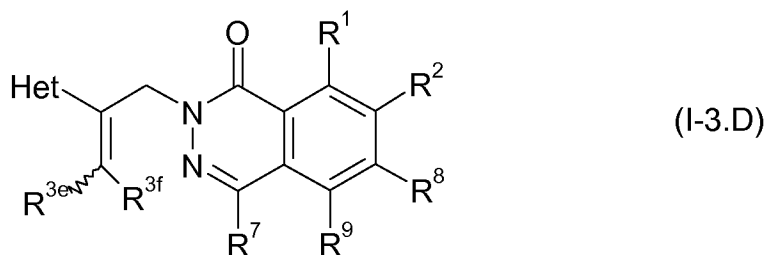
where Het, R^1 , R^2 , R^5 , R^7 , R^8 and R^9 are as defined here and in the claims and where R^5 is in particular hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-4.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



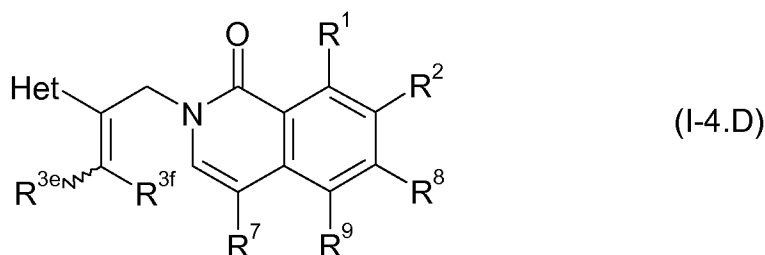
where Het, R^1 , R^2 , R^5 , R^7 , R^8 and R^9 are as defined here and in the claims and where R^5 is in particular hydrogen.

A further particular preferred embodiment of the invention relates to the compounds of formula I-3.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



- 5 where Het, R¹, R², R^{3e}, R^{3f}, R⁷, R⁸ and R⁹ are as defined here and in the claims and where R^{3e} and R^{3f} are in particular both hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-4.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



- 10 where Het, R¹, R², R^{3e}, R^{3f}, R⁷, R⁸ and R⁹ are as defined here and in the claims and where R^{3e} and R^{3f} are in particular both hydrogen.

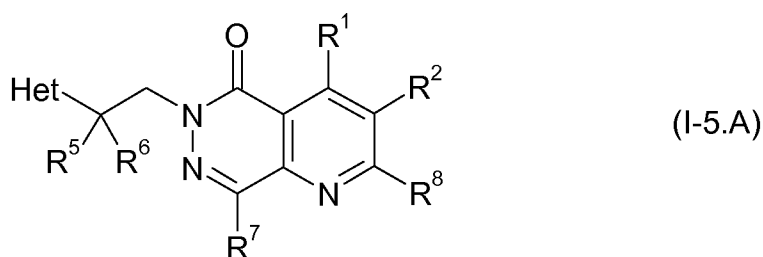
- Particular embodiments of the invention relate to compounds of the formulae I-3, I-4, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-3.D, I-4.C, and I-4.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is a radical Y¹-Cyc¹ and R⁷, R⁸ and R⁹ are as defined above and where R⁷ is in particular selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc², especially from the group consisting of hydrogen and Y²-Cyc² and where R⁹ is in particular selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y³-Cyc³, especially from the group consisting of hydrogen and Y³-Cyc³, provided that none or only one of

53

R^7 and R^9 is a moiety $Y^3\text{-Cyc}^3$, or $Y^3\text{-Cyc}^3$, respectively. R^7 and R^9 are in particular hydrogen.

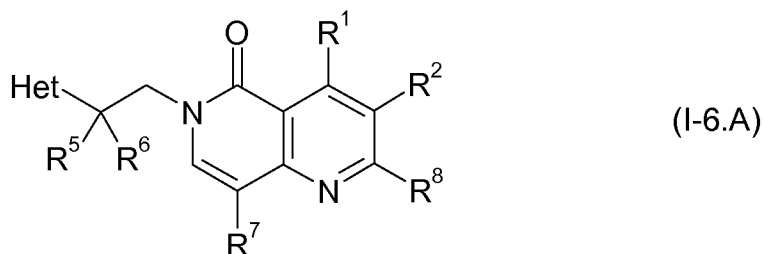
Further particular embodiments of the invention relate to compounds of the formulae I-3, I-4, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D and I-4.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R^1 is selected from the group consisting of hydrogen, fluorine, $C_1\text{-C}_4\text{-alkyl}$, $C_1\text{-C}_2\text{-fluoroalkyl}$, $C_1\text{-C}_4\text{-alkoxy}$, $C_1\text{-C}_2\text{-fluoroalkoxy}$, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and where R^7 and R^9 are selected, independently of each other, from the group consisting of hydrogen, fluorine, $C_1\text{-C}_4\text{-alkyl}$, $C_1\text{-C}_2\text{-fluoroalkyl}$, $C_1\text{-C}_4\text{-alkoxy}$, $C_1\text{-C}_2\text{-fluoroalkoxy}$, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and $Y^2\text{-Cyc}^2$ or $Y^3\text{-Cyc}^3$, respectively, provided that either R^7 is $Y^2\text{-Cyc}^2$ or R^9 is $Y^3\text{-Cyc}^3$. In these embodiments R^1 is in particular hydrogen. In these embodiments the radical R^7 or R^9 , which is different from $Y^2\text{-Cyc}^2$ or $Y^3\text{-Cyc}^3$, respectively, is in particular hydrogen.

A further particular preferred embodiment of the invention relates to the compounds of formula I-5.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



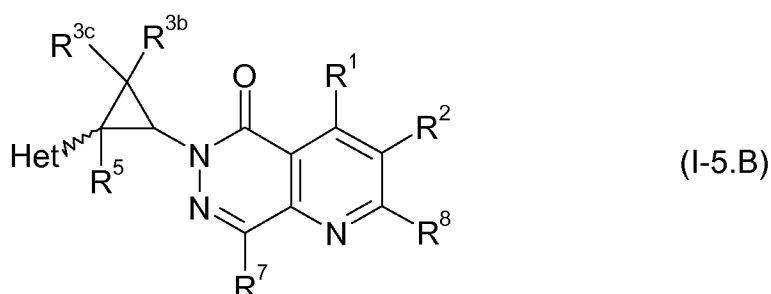
where Het, R^1 , R^2 , R^5 , R^6 , R^7 and R^8 are as defined here and in the claims.

Another particular preferred embodiment of the invention relates to the compounds of formula I-6.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



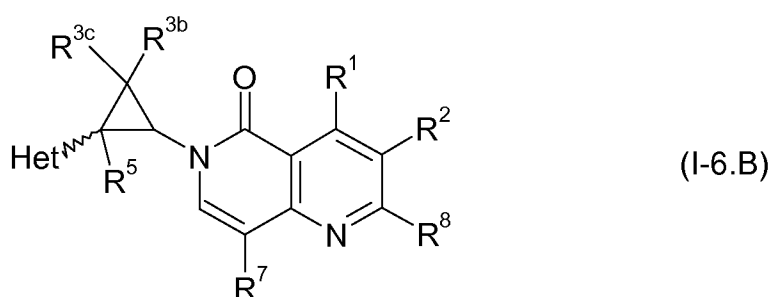
where Het, R^1 , R^2 , R^5 , R^6 , R^7 and R^8 are as defined here and in the claims.

A further particular preferred embodiment of the invention relates to the compounds of formula I-5.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



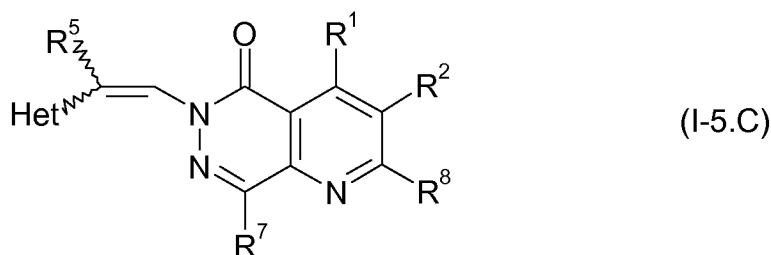
where Het, R^1 , R^2 , R^{3b} , R^{3c} , R^5 , R^7 and R^8 are as defined here and in the claims and where R^5 is in particular hydrogen.

A further particular preferred embodiment of the invention relates to the compounds of formula I-6.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R^1 , R^2 , R^{3a} , R^{3b} , R^5 , R^7 and R^8 are as defined here and in the claims and where R^5 is in particular hydrogen. In formulae I-5.B and I-6.B, the variables R^{3b} and R^{3c} are independently of each other in particular selected from the group consisting of hydrogen, fluorine and methyl or together form CH_2CH_2 . Particular preference is given to compounds of the formulae I-5.B and I-6.B, where both R^{3b} and R^{3c} are hydrogen or fluorine.

A further particular preferred embodiment of the invention relates to the compounds of formula I-5.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:

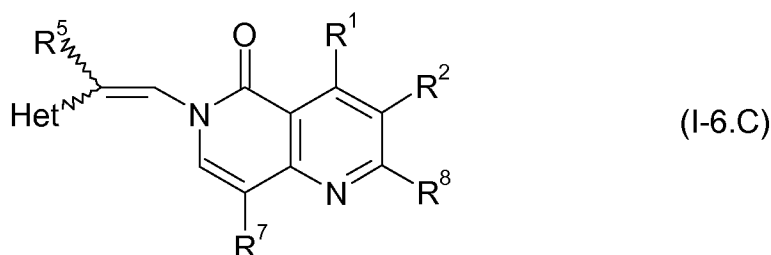


5

where Het, R¹, R², R⁵, R⁷ and R⁸ are as defined here and in the claims and where R⁵ is in particular hydrogen.

A further particular preferred embodiment of the invention relates to the compounds of formula I-6.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:

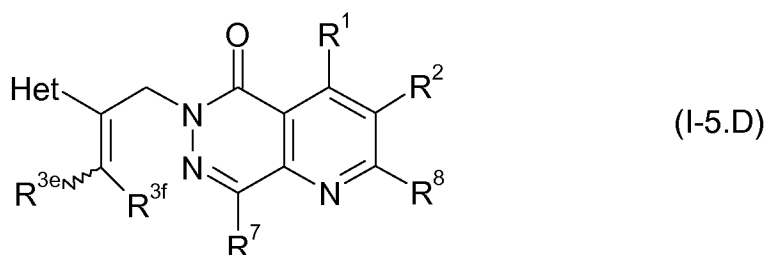
10



where Het, R¹, R², R⁵, R⁷ and R⁸ are as defined here and in the claims and where R⁵ is in particular hydrogen.

15

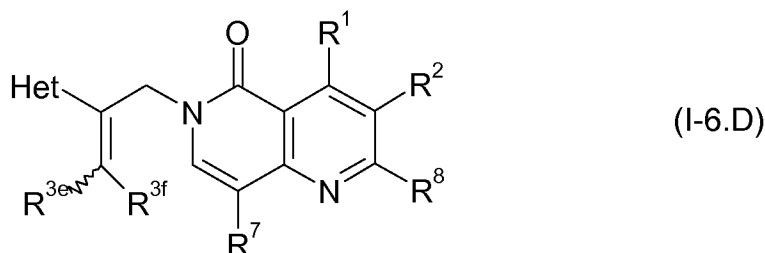
A further particular preferred embodiment of the invention relates to the compounds of formula I-5.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



20

where Het, R¹, R², R^{3e}, R^{3f}, R⁷, R⁸ and R⁹ are as defined here and in the claims and in particular, R^{3e} and R^{3f} are both hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-6.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:

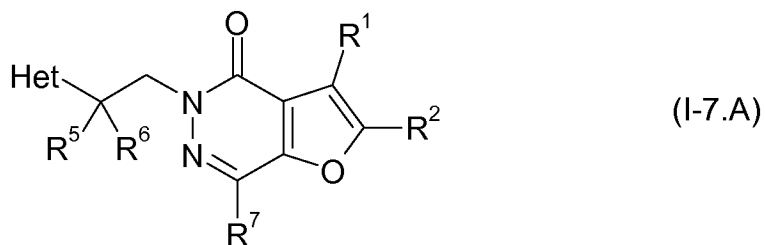


- 5 where Het, R¹, R², R^{3e}, R^{3f}, R⁷, R⁸ and R⁹ are as defined here and in the claims and in particular, R^{3e} and R^{3f} are both hydrogen.

- Particular embodiments of the invention relate to compounds of the formulae I-5, I-6, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D and I-6.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is a radical Y¹-Cyc¹ and R⁷ is as defined above and in particular selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc², especially from the group consisting of hydrogen and Y²-Cyc².

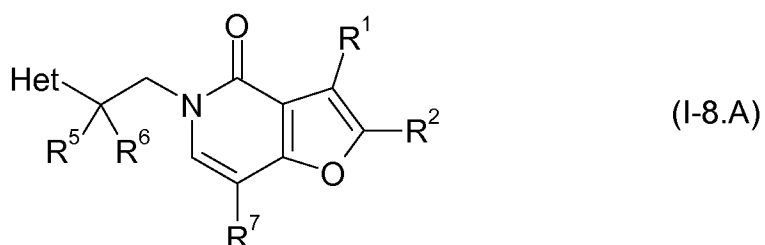
- 15 Further particular embodiments of the invention relate to compounds of the formulae I-5, I-6, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, and I-6.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and R⁷ is a moiety Y²-Cyc². In these embodiments R¹ is in particular hydrogen.

- A particular preferred embodiment of the invention relates to the compounds of formula I-7.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



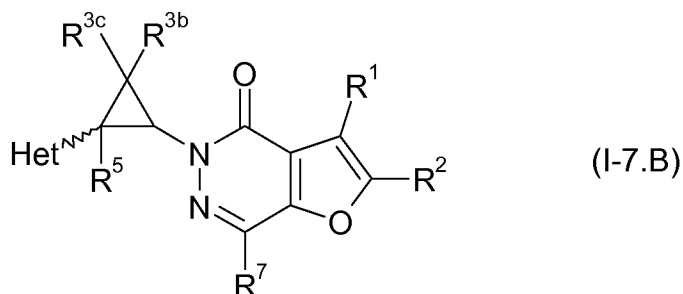
where Het, R¹, R², R⁵, R⁶ and R⁷ are as defined here and in the claims.

Another particular preferred embodiment of the invention relates to the compounds of formula I-8.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



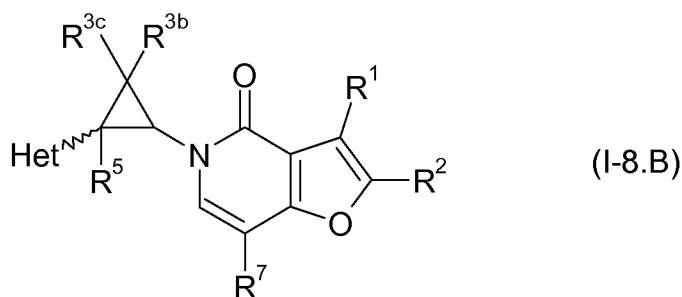
where Het, R¹, R², R⁵, R⁶ and R⁷ are as defined here and in the claims.

Another particular preferred embodiment of the invention relates to the compounds of formula I-7.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R¹, R², R^{3b}, R^{3c}, R⁵ and R⁷ are as defined here and in the claims and where R⁵ is in particular hydrogen.

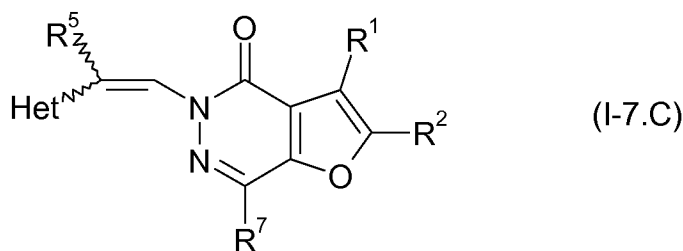
Another particular preferred embodiment of the invention relates to the compounds of formula I-8.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R^1 , R^2 , R^{3b} , R^{3c} , R^5 and R^7 are as defined here and in the claims and where R^5 is in particular hydrogen.

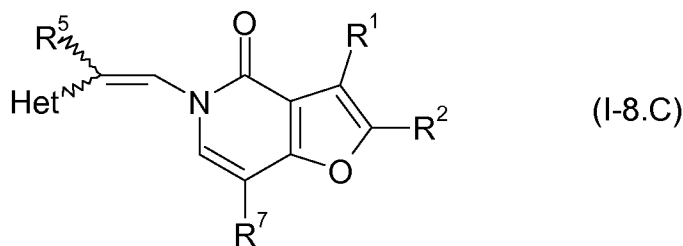
In formulae I-7.B and I-8.B, the variables R^{3b} and R^{3c} are independently of each other in particular selected from the group consisting of hydrogen, fluorine and methyl or together form CH_2CH_2 . Particular preference is given to compounds of the formulae I-7.B and I-8.B, where both R^{3b} and R^{3c} are hydrogen or fluorine.

Another particular preferred embodiment of the invention relates to the compounds of formula I-7.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



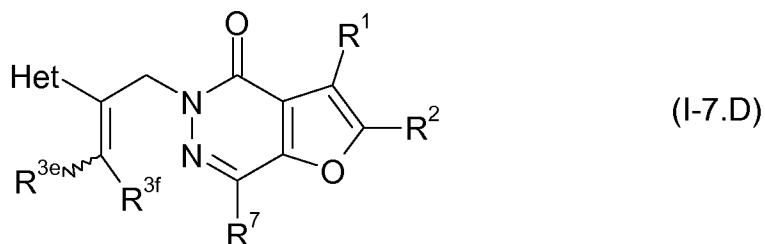
where Het, R^1 , R^2 , R^5 and R^7 are as defined here and in the claims and where R^5 is in particular hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-8.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R^1 , R^2 , R^5 and R^7 are as defined here and in the claims and where R^5 is in particular hydrogen.

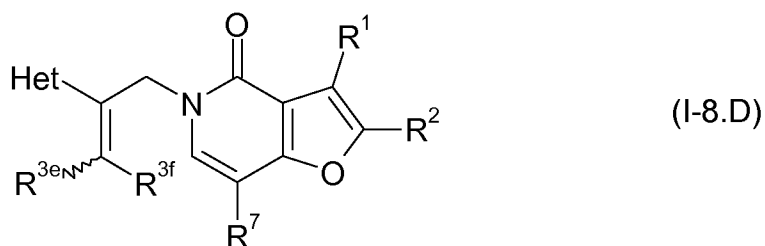
A particular preferred embodiment of the invention relates to the compounds of formula I-7.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



- 5 where Het, R¹, R², R^{3f}, R^{3e} and R⁷ are as defined here and in the claims where R^{3e} and R^{3f} are both in particular hydrogen.

Another particular preferred embodiment of the invention relates to the compounds of formula I-8.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:

10



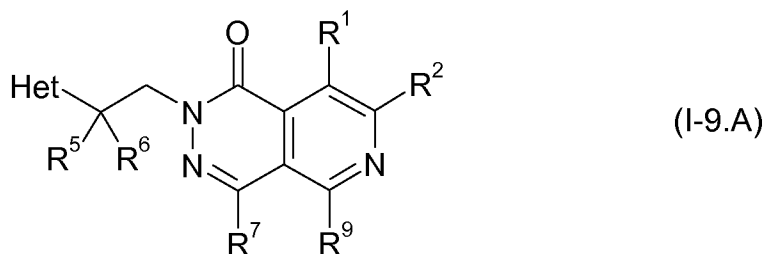
where Het, R¹, R², R^{3f}, R^{3e} and R⁷ are as defined here and in the claims where R^{3e} and R^{3f} are both in particular hydrogen.

- Particular embodiments of the invention relate to compounds of the formulae I-7, I-8, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, and I-8.D described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is a radical Y¹-Cyc¹ and R⁷ is as defined above and in particular selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc², especially from the group consisting of hydrogen and Y²-Cyc².

- Further particular embodiments of the invention relate to compounds of the formulae I-7, I-8, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D and I-8.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is selected from the group consisting

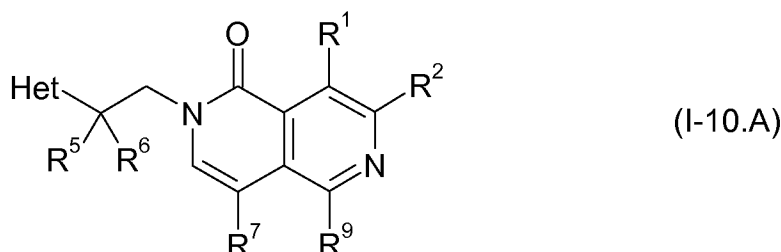
of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and R⁷ is a moiety Y²-Cyc². In these embodiments R¹ is in particular hydrogen.

- 5 A further particular preferred embodiment of the invention relates to the compounds of formula I-9.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



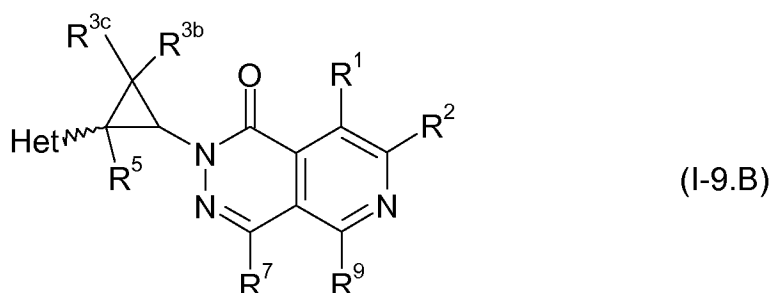
where Het, R¹, R², R⁵, R⁶, R⁷ and R⁹ are as defined here and in the claims.

- 10 Another particular preferred embodiment of the invention relates to the compounds of formula I-10.A, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



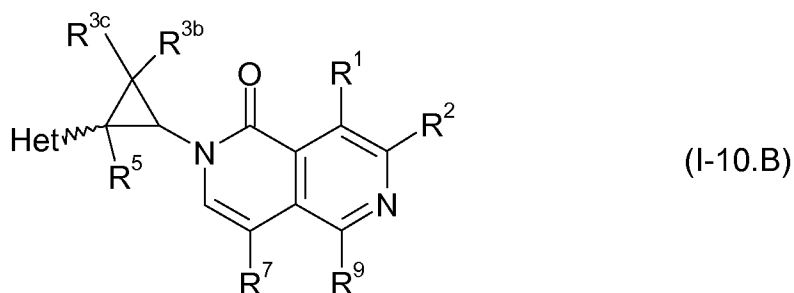
where Het, R¹, R², R⁵, R⁶, R⁷, and R⁹ are as defined here and in the claims.

- 15 Another particular preferred embodiment of the invention relates to the compounds of formula I-9.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R¹, R², R^{3b}, R^{3c}, R⁷, and R⁹ are as defined here and in the claims and where R⁵ is in particular hydrogen.

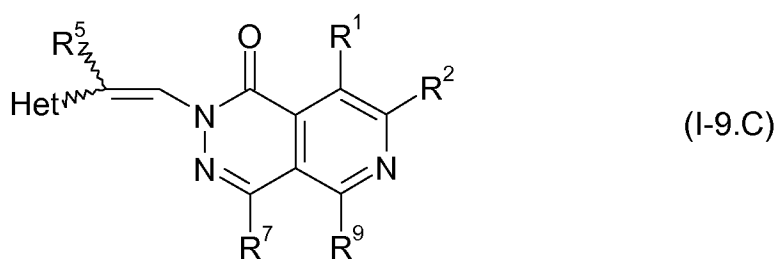
Another particular preferred embodiment of the invention relates to the
 5 compounds of formula I-10.B, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R¹, R², R^{3b}, R^{3c}, R⁷, and R⁹ are as defined here and in the claims and where R⁵ is in particular hydrogen.

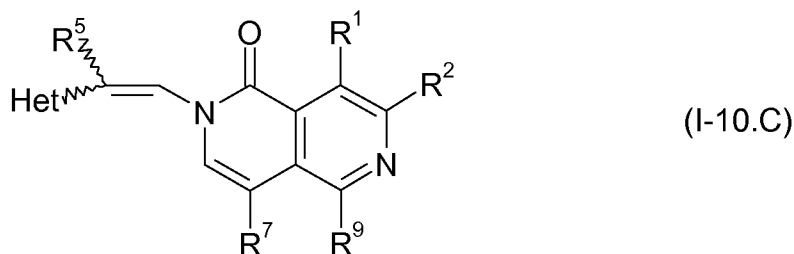
10 In formulae I-9.B and I-10.B, the variables R^{3b} and R^{3c} are independently of each other in particular selected from the group consisting of hydrogen, fluorine and methyl or together form CH₂CH₂. Particular preference is given to compounds of the formulae I-3.B and I-4.B, where both R^{3b} and R^{3c} are hydrogen or fluorine.

Another particular preferred embodiment of the invention relates to the
 15 compounds of formula I-9.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



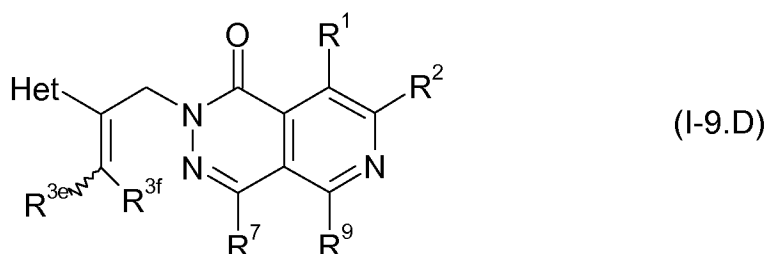
where Het, R¹, R², R⁵, R⁷, and R⁹ are as defined here and in the claims and where R⁵ is in particular hydrogen.

20 Another particular preferred embodiment of the invention relates to the compounds of formula I-10.C, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



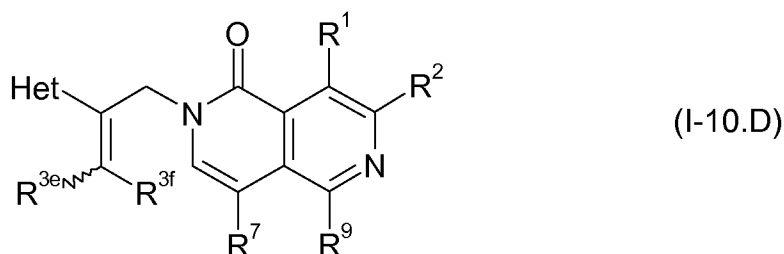
where Het, R¹, R², R⁵, R⁷, and R⁹ are as defined here and in the claims and where R⁵ is in particular hydrogen.

A further particular preferred embodiment of the invention relates to the
 5 compounds of formula I-9.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



where Het, R¹, R², R^{3ᵉ}, R^{3ᶠ}, R⁷, and R⁹ are as defined here and in the claims and where R^{3ᵉ} and R^{3ᶠ} are in particular both hydrogen.

10 Another particular preferred embodiment of the invention relates to the compounds of formula I-10.D, described below, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof:



15 where Het, R¹, R², R^{3ᵉ}, R^{3ᶠ}, R⁷, and R⁹ are as defined here and in the claims and where R^{3ᵉ} and R^{3ᶠ} are in particular both hydrogen.

Particular embodiments of the invention relate to compounds of the formulae I-9, I-10, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is a radical Y¹-Cyc¹ and R⁷, and R⁹ are
 20 as defined above and where R⁷ is in particular selected from the group consisting of

hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc², especially from the group consisting of hydrogen and Y²-Cyc² and where R⁹ is in particular selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y³-Cyc³, especially from the group consisting of hydrogen and Y³-Cyc³, provided that none or only one of R⁷ and R⁹ is a moiety Y³-Cyc³, or Y³-Cyc³, respectively. R⁷ and R⁹ are in particular hydrogen.

Further particular embodiments of the invention relate to compounds of the formulae I-9, I-10, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, described above, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where R¹ is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and where R⁷ and R⁹ are selected, independently of each other, from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc² or Y³-Cyc³, respectively, provided that either R⁷ is Y²-Cyc² or R⁹ is Y³-Cyc³. In these embodiments R¹ is in particular hydrogen. In these embodiments the radical R⁷ or R⁹, which is different from Y²-Cyc² or Y³-Cyc³, respectively, is in particular hydrogen.

In formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, R² is preferably selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl. R² is in particular hydrogen.

Preference is given to compounds of the formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-

9.A, I-10.A, I-9.B, I-10.B, I-9.C and I-10.C, where R^{3b} , R^{3c} , R^5 and R^6 , if present, are, independently of each other, selected from the group consisting of hydrogen, fluorine and methyl, and in particular to those compounds, where both R^5 and R^6 are hydrogen.

In formulae I-3, I-4, I-5, I-6, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D,
5 I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, R^8 is in particular hydrogen.

With regard to formulae I-1, I-2, I-3, I-5, I-4, I-6, I-7, I-8, I-9, I-10; I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, the
10 variable Het is as defined above and preferably selected from the group consisting of C-bound 6-membered monocyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members, and C-bound, fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member, where monocyclic hetaryl and bicyclic hetaryl may be unsubstituted or may carry 1, 2, 3
15 or 4 substituents R^x , in particular 0, 1 or 2 substituents R^x . In this regard, R^x is preferably selected from halogen, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, phenyl, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C_3 - C_6 -cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy,
20 fluoromethoxy, difluoromethoxy, trifluoromethoxy, phenyl, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.B, I-9.A, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Het is in
25 particular selected from the group consisting of fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member and which may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x , in particular 0, 1 or 2 substituents R^x . In this regard, R^x is preferably
30 selected from halogen, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C_3 - C_6 -cycloalkyl. In this regard, R^x is in particular selected from fluorine,

chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In another particular embodiments of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D Het is selected from 6-membered monocyclic hetaryl, which may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x , in particular 0, 1 or 2 substituents R^x . In this regard, R^x is preferably selected from halogen, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, phenyl, C_3 - C_6 -cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C_3 - C_6 -cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl or one R^x may also be phenyl.

Particular preference is given to those compounds of I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where the Het radical has at least one imino-nitrogen as ring member, which is located in the position adjacent to the carbon atom which is bound to the group CR^5 . Amongst these, particular preference is given to those, where the Het radical has at least one imino-nitrogen as ring member, which is located in the position adjacent to carbon atom bound to the group CR^5 and which is selected from the group consisting of C-bound 6-membered monocyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members, and C-bound, fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member, where monocyclic hetaryl and bicyclic hetaryl may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x , in particular 0, 1 or 2 substituents R^x . In this regard, R^x is preferably selected from

halogen, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, phenyl, C₃-C₆-cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C₃-C₆-cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy,

5 difluoromethoxy, trifluoromethoxy, phenyl, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

Particular examples of Het in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D are selected from the group consisting of 2-benzofuryl, 2-pyridyl, 2-pyrimidinyl, 4-pyrimidinyl, 2-pyrazinyl, 3-pyridazinyl, 2-quinolinyl, 3-isoquinolinyl, 2-quinazolinyl, 2-quinoxaliny, 1,5-naphthyridin-2-yl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, 15 imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, imidazo-[2,1-b]-thiazol-6-yl and 1,2,4-triazolo[1,5-a]pyridine-2-yl, where the aforementioned radicals are unsubstituted or may carry 1, 2 or 3 radicals R_x as defined above, which are in particular selected from the group consisting of fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, 20 trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

In a particular embodiment of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D Het has at least one imino-nitrogen as ring member, which is located in the position adjacent to carbon atom bound to the group CR⁵ and Het is selected from the group consisting of fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as 30 ring member, where bicyclic hetaryl may be unsubstituted or may carry 1, 2, 3 or 4 substituents R^x, in particular 0, 1 or 2 substituents R^x. In this regard, R^x is preferably selected from halogen, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-

fluoralkoxy, C₃-C₆-cycloalkyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated C₃-C₆-cycloalkyl. In this regard, R^x is in particular selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted
 5 by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl. Particular examples of Het of this embodiment are 2-quinolinyl, 3-isoquinolinyl, 2-quinazolinyl, 2-quinoxaliny, 1,5-naphthyridin-2-yl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, imidazo-[2,1-b]-thiazol-6-yl and 1,2,4-triazolo[1,5-a]pyridine-2-yl,
 10 where the aforementioned radicals are unsubstituted or may carry 1, 2 or 3 radicals R^x as defined above, which are in particular selected from the group consisting of fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

15 Particular preference is given to compounds, where Het in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D is selected from the group consisting of 2-quinolinyl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl, 1-methylbenzimidazol-2-yl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl,
 20 and in particular 2-quinolinyl or imidazo[1,2-a]pyridine-2-yl, where these radicals are unsubstituted or may carry 1, 2 or 3 radicals R^x as defined above, which are in particular selected from the group consisting of fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.
 25

With regard to formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, the
 30

variables Y^1 , Y^2 , Cyc^1 and Cyc^2 are as defined above and in particular have the preferred meanings.

In particular, Cyc^1 , if present in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D is selected from the groups of

(i) saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1} , where R^{C1} is as defined herein; and

(ii) phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In particular embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Cyc^1 , if present, is selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles or a saturated 7-, 8-, 9- or 10-membered heterobicycle, where the heteromonocycle and the heterobicycle have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where

R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Cyc^1 , if present, is selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicyclic are unsubstituted or carry 1, 2, or 3 radicals R^{C1} , where R^{C1} is as defined herein.

In these particular and special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^1 , if present, is preferably selected from O, NH and a chemical bond, with particular preference given to Y^1 being a chemical bond.

In these particular and special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^1-Cyc^1 , if present, is e.g. selected from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, 2-oxa-6-azaspiro-[3,4]octyl, 2,5-diazabicyclo[2.2.1]heptan-2-yl, 3,8-diazabicyclo[3.2.1]octan-8-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino and especially from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, thiomorpholin-4-yl,

1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino.

In other particular embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Cyc¹, if present, is phenyl or a 5- or 6 membered heteroaromatic radical, which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered heteroaromatic radical are unsubstituted or either carry, independently of each other, carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical Y'-R^{C2} and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1}, where R^{C1}, R^{C2} and Y' are as defined herein and where Y', if present, is preferably a chemical bond or O.

In other special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Cyc¹, if present, is selected from the group consisting of phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical Y'-R^{C2} and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1}, where R^{C1}, R^{C2} and Y' are as defined herein and where Y', if present, is preferably a chemical bond or O.

More particularly, Cyc¹, if present in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, is selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl,

pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if Cyc^1 is phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 5- or 6-indolyl, 5- or 6-benzimidazolyl, 5- or 6-benzopyrazolyl, 5- or 6-benzotriazolyl, 5- or 6-benzofuranyl, 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, 5- or 6-quinoliny, 5- or 6-isoquinoliny, 5- or 6-quinazoliny, 2-amino-5-quinazoliny, and 2-amino-6-quinazoliny. Amongst these, particular preference is given to compounds, where Y^1 is a chemical bond. Amongst these, particular preference is given to compounds, where Cyc^1 in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, is selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 .

In particular, Cyc^2 and Cyc^3 , if present in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, are, independently from each other, selected from the groups of

(i) saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, $S(=O)$, $S(=O)_2$ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1} , where R^{C1} is as defined herein; and

(ii) phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In particular embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-7, I-8, I-9, I-10I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y²-Cyc² and Y³-Cyc³, if present, are, independently from each other, selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles or a saturated 7-, 8-, 9- or 10-membered heterobicycle, where the heteromonocycle and the heterobicycle have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y²-Cyc² and Y³-Cyc³, if present, are, independently from each other, selected from the group consisting of saturated 4-, 5-, 6- or 7-membered heteromonocycles, where the heteromonocycle has one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, or 3 radicals R^{C1} , where R^{C1} is as defined herein.

In this particular and special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^2 -Cyc² and Y^3 -Cyc³, if present, are,
 5 independently from each other preferably selected from O, NH and a chemical bond, with particular preference given to Y^2 and Y^3 being a chemical bond.

In this particular and special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^2 -Cyc² and Y^3 -Cyc³, if present, are,
 10 independently from each other, e.g. selected from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, 2-oxa-6-azaspiro-[3,4]octyl, 2,5-diazabicyclo[2.2.1]heptan-2-yl, 3,8-diazabicyclo[3.2.1]octan-8-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino and especially from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl, 4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl, morpholin-4-yl, thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-dioxothiomorpholin-4-yl and oxetan-3-ylamino.
 20

In other particular embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^2 -Cyc² and Y^3 -Cyc³, if present, are,
 25 independently of each other, phenyl or a 5- or 6 membered heteroaromatic radical, which has one heteroatom, selected from O, S and N as ring member and optionally one or two further heteroatoms as ring members, and which is in particular selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered heteroaromatic radical are unsubstituted or either carry, independently of each other, carry 1, 2, 3, 4 or 5, in
 30

particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In special embodiments of the compounds of formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^2-Cyc^2 and Y^3-Cyc^3 , if present, are, independently from each other, selected from the group consisting of phenyl or a 5- or 6 membered hetaryl, selected from pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and the 5- or 6 membered hetaryl are unsubstituted or carry 1, 2, 3, 4 or 5, in particular 1, 2, or 3 radicals R^{C1} or one radical $Y'-R^{C2}$ and 0, 1, 2, 3 or 4, in particular 0, 1 or 2 radicals R^{C1} , where R^{C1} , R^{C2} and Y' are as defined herein and where Y' , if present, is preferably a chemical bond or O.

In particular, Y^2-Cyc^2 and Y^3-Cyc^3 , if present in formulae I-1, I-2, I-3, I-4, I-5, I-6, I-7, I-8, I-9, I-10, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D and I-10.D, Y^2-Cyc^2 and Y^3-Cyc^3 , are, independently from each other, selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if one or both of Y^2-Cyc^2 and Y^3-Cyc^3 are phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 5- or 6-indolyl, 5- or 6-benzimidazolyl, 5- or 6-benzopyrazolyl, 5- or 6-benzotriazolyl, 5- or 6-benzofuranyl, 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, 5- or 6-quinolinyl, 5- or 6-isoquinolinyl, 5- or 6-quinazolinyl, 2-amino-5-quinazolinyl, and 2-amino-6-quinazolinyl. Amongst these, particular preference is given to compounds, where Y^2-Cyc^2 and Y^3-Cyc^3 are,

independently from each other, selected from the group consisting of phenyl and 5- or 6-membered hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the
5 group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH₂.

Particular embodiment of the invention relates to the compounds of formula I, to the N-oxides, the prodrugs, the hydrates and the tautomers thereof and to the pharmaceutically suitable salts thereof, where the compounds of the formula I are
10 selected from the group consisting of:

- 3,7-di(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 7-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 15 3,7-di(pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(quinolin-2-yl)ethyl]-3-[4-(trifluoromethyl)phenyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-[4-(propan-2-yl)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 3-(4-ethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}benzonitrile;
- 3-(4-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 3-(4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-[4-(dimethylamino)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- (4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}phenyl)acetonitrile;
- 30 3-(4-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-chlorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;

- 3-(2-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-ethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5 3-(2-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(quinolin-2-yl)ethyl]-3-[2-(trifluoromethyl)phenyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-[3-(methoxymethyl)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-10 4(5H)-one;
3-(3-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(3-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-[3-(dimethylamino)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
15 3-[4-Oxo-5-(2-quinolin-2-yl-ethyl)-4,5-dihydro-thieno[2,3-d]pyridazin-3-yl}-benzonitrile;
3-(3-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(3-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
N,N-dimethyl-3-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-20 d]pyridazin-3-yl}benzamide;
3-(3-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(quinolin-2-yl)ethyl]-3-(thiophen-2-yl)thieno[2,3-d]pyridazin-4(5H)-one;
3-(1-methyl-1H-indol-5-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one;
25 3-(1H-indol-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
30 3-(4-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(furan-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;

- 3-(quinolin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(isoquinolin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(isoquinolin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(1H-indol-4-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one;
5 3-(2,3-dihydrobenzofuran-5-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one;
3-(quinolin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(3,5-dimethyl-1,2-oxazol-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
10 3-(6-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-methylpyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
15 one;
3-(5-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-[6-(morpholin-4-yl)pyridin-3-yl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
20 3-(1,3-benzodioxol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(quinolin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(1-methyl-1H-pyrazol-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
25 3-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
tert-butyl 2-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}-1H-pyrrole-1-carboxylate;
3-(2-methoxypyrimidin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
30 5-[2-(quinolin-2-yl)ethyl]-3-(2,3,4-trifluorophenyl)thieno[2,3-d]pyridazin-4(5H)-one;

- 3-(4-fluoro-3-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4-fluoro-2-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5 3-(3-chloro-4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-chloro-4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 10 3-(3,4-dimethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,4-dimethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,4-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 15 3-(2,4-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,5-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,3-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 3-(3,4-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,4-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 3-(5-fluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4-fluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,5-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 30 3-(2,5-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;

- 3-(2,3-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3-fluoro-4-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5 3-(2-fluoro-3-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,5-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 10 3-(3-fluoro-5-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-methoxy-5-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,5-dichlorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 15 3-(naphthalen-2-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-phenyl-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(1-benzofuran-2-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(1H-indazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 3-(1-methyl-1H-pyrazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4,5-difluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 3-(2-fluoro-4-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-fluoro-5-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-methyl-4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}benzonitrile;
- 30 5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;

- 5-[2,2-difluoro-2-(quinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5 [5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
8-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
10 2-[2-(quinolin-2-yl)ethyl]-8-[4-(trifluoromethyl)phenyl]phthalazin-1(2H)-one;
8-(4-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-[4-(propan-2-yl)phenyl]-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(4-ethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
4-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophtalazin-5-yl} benzonitrile;
15 8-(4-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
(4-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophtalazin-5-yl}phenyl)acetonitrile;
8-(4-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
20 8-(2-chlorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-ethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
25 8-(3-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
3-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophtalazin-5-yl} benzonitrile;
8-(3-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
N,N-dimethyl-3-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophtalazin-5-yl} benzamide;
30 8-(3-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
2-[2-(quinolin-2-yl)ethyl]-8-(thiophen-2-yl)phthalazin-1(2H)-one;

- 8-(1-methyl-1H-indol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,5-dimethyl-1H-pyrazol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1H-indol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1H-indol-6-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
5 8-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(furan-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(quinolin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
10 8-(1H-indol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,3-dihydro-1-benzofuran-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-dihydro-2H-1,5-benzodioxepin-7-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
15 8-(1-benzofuran-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(6-methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methylpyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
20 8-(5-methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(5-fluoropyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1,3-benzodioxol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1-methyl-1H-pyrazol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
25 tert-butyl 2-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophtalazin-5-yl}-1H-pyrrole-1-carboxylate;
8-(3-chloro-4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-chloro-4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
30 8-(3,4-dimethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,4-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,5-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;

- 8-(2,3-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(5-fluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
5 8-(4-fluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,5-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,5-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-fluoro-4-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-fluoro-3-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
10 8-(3,5-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-fluoro-5-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(naphthalen-2-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-phenyl-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1-benzofuran-2-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
15 8-(1-methyl-1H-pyrazol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(4,5-difluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
one;
8-(2-fluoro-4-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-fluoro-5-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(3-methoxypyridin-4-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyrimidin-5-yl)phthalazin-1(2H)-one;
25 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-methyl-1H-pyrazol-3-yl)phthalazin-1(2H)-one;
8-(furan-3-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxo-2,3-dihydro-1H-indol-6-yl)phthalazin-1(2H)-one;
30 8-(3,4-dihydro-2H-chromen-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;

- 8-(1,1-dioxidothiomorpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(morpholin-4-yl)phthalazin-1(2H)-one;
- 8-(1,1-dioxidothiomorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)phthalazin-1(2H)-one;
- 8-(5,5-difluorohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperazin-1-yl)phthalazin-1(2H)-one;
- 8-(4,4-difluoropiperidin-1-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[4-(chloromethyl)-4-(hydroxymethyl)piperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-1-yl)phthalazin-1(2H)-one;
- 8-(2,3-dihydro-4H-1,4-benzoxazin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[4-(trifluoromethyl)piperidin-1-yl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(4-methylpiperazin-1-yl)phthalazin-1(2H)-one;
- 8-(1,3-dihydro-2H-isoindol-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(7-benzyl-2,7-diazaspiro[4.4]non-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-({[(3aR,4S,6aS)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]methyl} amino)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- tert-butyl (3R)-3-({3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl} amino)pyrrolidine-1-carboxylate;
- 8-(2,6-dimethylmorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;

- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,4-oxazepan-4-yl)phthalazin-1(2H)-one;
- tert-butyl 4-{3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl}-3,6-dihydropyridine-1(2H)-carboxylate;
- 5 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(1-methyl-1H-pyrazol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(1,1-dioxidothiomorpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-3-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyrimidin-5-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(morpholin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)phthalazin-1(2H)-one;
- 15 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(pyrimidin-5-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(morpholin-4-yl)phthalazin-1(2H)-one;
- 3-(3-methoxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 3-(3-hydroxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 20 3-(1-methyl-1H-pyrazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 3-(pyrimidin-5-yl)-5-(2-quinolin-2-yl)ethylthieno[3,2-c]pyridin-4(5H)-one;
- 25 3-(2-oxoindolin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 3-(3-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 5-[2-(5-ethylpyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 30 3-(morpholin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- tert-butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-5,6-dihydropyridine-1(2H) carboxylate;

- 5-(2-(quinolin-2-yl)ethyl)-3-(1,2,3,6-tetrahydropyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
tert-butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-piperidine-1 carboxylate;
- 5 3-(piperidin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
3-methyl-7-(pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)thieno[3,2-c]pyridin-4(5H)-one;
3-(pyridin-4-yl)-5-[2-(5,6,7,8-tetrahydroquinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 10 (R)-tert-butyl 3-(3-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)-4-oxo-3,4-dihydrophthalazin-5-ylamino)pyrrolidine-1-carboxylate;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3R)-pyrrolidin-3-ylamino]phthalazin-1(2H)-one;
5-(3-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 15 (E)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)vinyl)isoquinolin-1(2H)-one;
anti (rac) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti (+)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti (-)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
8-(pyridin-4-yl)-2-(2-quinolin-2-yl-ethyl)isoquinolin-1(2H)-one;
- 20 anti (rac) 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti (+) 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti (-) 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 25 (E)-8-pyridin-4-yl-2-(2-quinolin-2-yl-vinyl)-2H-phthalazin-1-one;
anti (rac) 8-pyridin-4-yl-2-(2-quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one;
anti (+) 8-pyridin-4-yl-2-(2-quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one;
anti (-) 8-pyridin-4-yl-2-(2-quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one;
- 30 and the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

Further particular embodiments of the invention relate to the compounds of formula I, where the compounds of the formula I are selected from the group consisting of:

- 7-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]furo[3,2-c]pyridin-4(5H)-one;
5 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one;
5-(2-(1H-benzo[d]imidazol-2-yl)ethyl)-3-(pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one;
5-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)-3-(pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one;
10 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one;
4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)allyl)pyrido[2,3-d]pyridazin-5(6H)-one;
syn 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
15 anti 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
syn 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
anti 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
20 syn 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
25 anti 8-(pyridazin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(pyridazin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-(6-fluoropyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(6-fluoropyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
30 anti 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;

- syn 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 anti 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(1-methyl-1H-pyrazol-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(1-methyl-1H-pyrazol-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 10 anti 8-(3-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- one;
- syn 8-(3-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- one;
- 15 anti 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- one;
- syn 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- one;
- anti 8-((3S)-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 20 syn 8-((3S)-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(3-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 25 syn 8-(3-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 1-(1-oxo-2-(2-(quinolin-2-yl)cyclopropyl)-1,2-dihydroisoquinolin-8-yl)piperidine-4-carbonitrile;
- 30 syn 1-(1-oxo-2-(2-(quinolin-2-yl)cyclopropyl)-1,2-dihydroisoquinolin-8-yl)piperidine-4-carbonitrile;

- anti 8-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 anti 8-((3S)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((3S)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 10 anti 8-((3R)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((3R)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 15 anti 8-(methyl(oxetan-3-yl)amino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(methyl(oxetan-3-yl)amino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(4-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 20 anti 8-(4-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(4-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 25 anti 8-(1-acetylpiperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(1-acetylpiperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 30 anti 8-(piperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(piperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;

- anti 2-(2-(quinolin-2-yl)cyclopropyl)-8-(tetrahydro-2H-pyran-4-yl)isoquinolin-1(2H)-one;
syn 2-(2-(quinolin-2-yl)cyclopropyl)-8-(tetrahydro-2H-pyran-4-yl)isoquinolin-1(2H)-one;
- 5 anti 2-(2-(quinolin-2-yl)cyclopropyl)-8-(2-oxa-6-azaspiro[3.4]octan-6-yl)isoquinolin-1(2H)-one;
syn 2-(2-(quinolin-2-yl)cyclopropyl)-8-(2-oxa-6-azaspiro[3.4]octan-6-yl)isoquinolin-1(2H)-one;
- 10 anti 8-(dihydro-1H-furo[3,4-c]pyrrol-5(3H,6H,6aH)-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(dihydro-1H-furo[3,4-c]pyrrol-5(3H,6H,6aH)-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4,4-difluoropiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 15 syn 8-(4,4-difluoropiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(3-(difluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 20 syn 8-(3-(difluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-((1R,5S)-3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 25 syn 8-((1R,5S)-3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4-methylpiperazin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(4-methylpiperazin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 30 anti 8-(3-(fluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;

- syn 8-(3-(fluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 syn 8-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4-fluorophenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(4-fluorophenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(furan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 10 syn 8-(furan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4,5-dihydrofuran-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(4,5-dihydrofuran-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 15 anti 8-(4-methoxyphenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(4-methoxyphenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-morpholinoisoquinolin-1(2H)-one;
- syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-morpholinoisoquinolin-1(2H)-one;
- 20 anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-3-yl)isoquinolin-1(2H)-one;
- syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-3-yl)isoquinolin-1(2H)-one;
- 25 anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyrimidin-5-yl)isoquinolin-1(2H)-one;
- syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyrimidin-5-yl)isoquinolin-1(2H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 30 one;
- syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)isoquinolin-1(2H)-one;

- anti 4-fluoro-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 4-fluoro-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 anti 4-chloro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 4-chloro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)cyclopropyl)pyrido[2,3-d]pyridazin-
- 10 5(6H)-one;
- syn 4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)cyclopropyl)pyrido[2,3-d]pyridazin-5(6H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)phthalazin-1(2H)-one;
- 15 syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)phthalazin-1(2H)-one;
- anti 7-fluoro-3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 7-fluoro-3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-
- 20 c]pyridin-4(5H)-one;
- anti 3-(2-fluoropyridin-4-yl)-5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(2-fluoropyridin-4-yl)-5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 25 anti 5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-
- 30 4(5H)-one;
- syn 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;

- anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 5 anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(6-fluoropyridin-3-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-
- 10 c]pyridin-4(5H)-one;
- syn 3-(6-fluoropyridin-3-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(2-methylpyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-
- c]pyridin-4(5H)-one;
- 15 syn 3-(2-methylpyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-
- 20 4(5H)-one;
- anti 3-(2-fluoropyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-
- c]pyridin-4(5H)-one;
- syn 3-(2-fluoropyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-
- 4(5H)-one;
- 25 anti 3-(morpholin-4-yl)-5[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(morpholin-4-yl)-5[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-
- 4(5H)-one;
- anti 3-(pyridin-3-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-
- 30 c]pyridin-4(5H)-one;
- syn 3-(pyridin-3-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-
- c]pyridin-4(5H)-one;

- anti 3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 5 anti 3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- syn 3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- anti 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 10 d]pyridazin-4(5H)-one;
- syn -(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- anti 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 15 syn 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 20 one;
- anti 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- syn 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 anti 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- anti 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- anti 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- 30 syn 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- anti 5-(morpholin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 5-(morpholin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;

- anti 4-fluoro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 4-fluoro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 8-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]pyrido[3,4-d]pyridazin-1(2H)-one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(1-methyl-1H-imidazol-4-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(1-methyl-1H-pyrazol-4-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 10 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(pyridin-3-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(6-chloroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 5-[2-(3-methylquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 15 one;
- 5-[2-(8-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- one;
- 5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-3-yl)thieno[3,2-c]pyridin-4(5H)-one;
- one;
- 20 5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-3-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 3-(pyridin-4-yl)-5-[2-(quinoxalin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 5-[2-(1,5-naphthyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- one;
- 5-[2-(1H-indazol-1-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(1-methyl-1H-pyrazol-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 4(5H)-one;
- 30 3-(1H-pyrazol-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(1H-benzimidazol-1-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- one;

- 5-[2-(1H-benzimidazol-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(6-chloroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5 3-(pyridin-3-ylethynyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(pyridin-4-ylethynyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(3,5-dimethylpyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 10 5-[2-(7-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(pyrazin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 2-[2-(1,6-naphthyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 15 2-[2-(8-fluoroquinolin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 8-(pyridin-4-yl)-2-[1-(quinolin-2-yl)propan-2-yl]isoquinolin-1(2H)-one;
- 2-[2-(3-methylquinolin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1H-pyrazol-3-yl)phthalazin-1(2H)-one;
- 8-(morpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-oxa-4,9-diazaspiro[5.6]dodec-9-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-7-azaspiro[3.5]non-7-yl)phthalazin-1(2H)-one;
- 8-[(3R)-3-hydroxypiperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 25 8-[(3S)-3-hydroxypiperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-6-azaspiro[3.3]hept-6-yl)phthalazin-1(2H)-one;
- 30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,2-oxazolidin-2-yl)phthalazin-1(2H)-one;

- 8-(hexahydrocyclopenta[b][1,4]oxazin-4(4aH)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydrofuran-3-yl)phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-6-azaspiro[3.4]oct-6-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2,2,6,6-tetrafluoromorpholin-4-yl)phthalazin-1(2H)-one;
- 10 8-(4-hydroxypiperidin-1-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-methylpyrimidin-5-yl)phthalazin-1(2H)-one;
- 15 8-(2-cyclopropylpyrimidin-5-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridazin-4-yl)phthalazin-1(2H)-one;
- 8-(5-fluoropyridin-3-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 8-[2-(3-fluorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-methoxypyrimidin-5-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[2-(trifluoromethyl)pyridin-4-yl]phthalazin-1(2H)-one;
- 25 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[2-(trifluoromethyl)morpholin-4-yl]phthalazin-1(2H)-one;
- 30 8-(2,2-dimethylmorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;

- 8-[2-(4-chlorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[2-(3,4-difluorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-4-yl)phthalazin-1(2H)-one;
- 8-(2,6-diazabicyclo[3.2.1]oct-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 8-[(1S,5S)-3,6-diazabicyclo[3.2.0]hept-3-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(furan-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-methyl-1H-pyrazol-4-yl)phthalazin-1(2H)-one;
- 15 8-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(2,7-diazaspiro[4.4]non-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 8-(2,7-diazaspiro[3.5]non-7-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(2,6-diazaspiro[3.5]non-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 25 8-(piperidin-4-yl)-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[2-(aminomethyl)-4-chloropyrrolidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4,8-di(pyridin-4-yl)phthalazin-1(2H)-one;
- 30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aR,4S,7R,7aS)-octahydro-1H-4,7-epiminoisoindol-8-yl]phthalazin-1(2H)-one;

- 8-[5-(4-chlorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 4-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-yl)phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aS,8aS)-octahydropyrrolo[3,4-c]azepin-2(1H)-yl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aS,8aR)-octahydropyrrolo[3,4-c]azepin-2(1H)-yl]phthalazin-1(2H)-one;
- tert-butyl (3aR,4S,7R,7aS)-8-{3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl}octahydro-2H-4,7-epiminoisoindole-2-carboxylate;
- 10 8-(hexahydro-5H-furo[2,3-c]pyrrol-5-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,2,3,6-tetrahydropyridin-4-yl)phthalazin-1(2H)-one;
- 15 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3S)-tetrahydrofuran-3-ylamino]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3R)-tetrahydrofuran-3-ylamino]phthalazin-1(2H)-one;
- 8-{[5-(hydroxymethyl)-1,4-dioxan-2-yl]methoxy}-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(oxetan-3-yloxy)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-ylmethoxy)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(morpholin-4-ylmethyl)phthalazin-1(2H)-one;
- 25 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yloxy)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(oxetan-3-ylmethyl)amino]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-4-ylamino)phthalazin-1(2H)-one;
- 30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(1-methylazetidin-3-yl)amino]phthalazin-1(2H)-one;

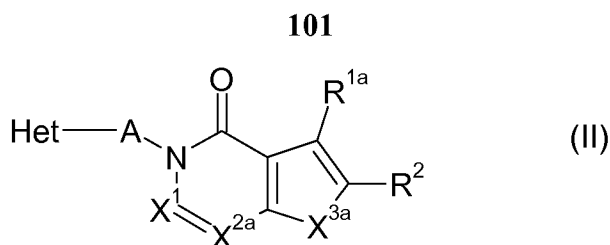
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,3-oxazol-2-ylamino)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[methyl(oxetan-3-yl)amino]phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-4-ylamino)phthalazin-1(2H)-one;
- 8-[(1-acetylpiperidin-3-yl)amino]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[(1-acetylpiperidin-4-yl)amino]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydrofuran-3-ylamino)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-3-ylamino)phthalazin-1(2H)-one;
- 15 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-3-ylamino)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-{methyl[(3-methyloxetan-3-yl)methyl]amino}phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(oxetan-3-ylamino)phthalazin-1(2H)-one;
- 20 one;
- 8-{[(3aS,4S,6aS)-octahydrocyclopenta[c]pyrrol-4-ylmethyl]amino}-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(morpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(1H-benzimidazol-2-yl)ethyl]-5-(pyridin-4-yl)phthalazin-1(2H)-one;
- 25 4-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(1,4-dihydropyrimidin-5-yl)-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-4-yl)phthalazin-1(2H)-one;
- 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-{[(3-methyloxetan-3-yl)methyl]amino}-phthalazin-1(2H)-one;
- 4-(pyridin-4-yl)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one;

4-(morpholin-4-yl)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one;
4-(oxetan-3-ylamino)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one;

- 2-[2-(6-methoxypyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
5 2-[2-(1,3-benzothiazol-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
2-[2-(5-methylpyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
5-[*E*]-2-(6-methoxyquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-*c*]pyridin-4(5H)-one;
8-(pyridin-4-yl)-2-[*E*]-2-(quinazolin-2-yl)ethenyl]isoquinolin-1(2H)-one;
10 5-[*E*]-2-(6-chloroquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-*c*]pyridin-4(5H)-one;
5-[*E*]-2-(3-methylquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-*c*]pyridin-4(5H)-one;
8-(pyridin-4-yl)-2-[*E*]-2-(quinolin-2-yl)ethenyl]isoquinolin-1(2H)-one;
15 5-[*E*]-2-(1,3-benzothiazol-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-*c*]pyridin-4(5H)-one;
3-(pyridin-4-yl)-5-[*E*]-2-(quinolin-2-yl)ethenyl]thieno[3,2-*c*]pyridin-4(5H)-one;
and the enantiomers, the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

- 20 The compounds of the invention of the general formula I and the starting materials used to prepare them can be prepared in analogy to known processes of organic chemistry as are described in standard works of organic chemistry, e.g. Houben-Weyl, "Methoden der Organischen Chemie", Thieme-Verlag, Stuttgart, Jerry March "Advanced Organic Chemistry", 5th edition, Wiley & Sons and the literature cited
25 therein, and R. Larock, "Comprehensive Organic Transformations", 2nd edition, Weinheim, 1999 and the literature cited therein. The compounds of the invention of the general formula I are advantageously prepared by the methods described below and/or in the experimental section.

- Compounds of the formula I, wherein Q is oxygen, can be prepared e.g. by
30 reacting a compound of the formula II



wherein

X^{2a} is N or C- R^{7a} ;

X^{3a} is S, O, N=C(R^8), C(R^{9a})=C(R^8) or N=C(R^9);

5 Het, A, X^1 , R^2 , R^6 and R^8 are as defined for formulae I, I-1.A, I-1.B, I-2.A, I-2.B, I-1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D or I-10.D;

10 R^{1a} , R^{7a} , R^{9a} independently of each other, are selected from the group consisting of hydrogen, halogen, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkylsulfanyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkylsulfanyl-C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, CN, $NR^{x1}R^{x2}$, $NR^{x1}R^{x2}$ -C₁-C₄-alkoxy;

15

provided that 1 or 2 of the radicals R^{1a} , R^{7a} and R^{9a} , in particular exactly one of these radicals is bromine or iodine, while the others are different from bromine or iodine;

with a compound of formula III,

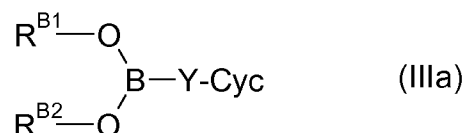
20

M-Y-Cyc (III)

where Y has one of the meanings given for Y^1 , Y^2 , and Y^3 and Cyc has one of the meanings given herein for Cyc¹, Cyc², and Cyc³ and wherein

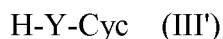
25 M is a Li, B(OR^{B1})(OR^{B2}) radical or an Sn(R^{Sn})₃ radical, where R^{B1} and R^{B2} are, independently of each other, hydrogen or C₁-C₄-alkyl or R^{B1} and R^{B2} together form a C₂-C₆-alkandiyl moiety, e.g. ethan-1,2-diyl, propan-1,3-diyl or 1,1,2,2-tetramethylethan-1,2-diyl, and wherein R^{Sn} is C₁-C₆-alkyl or C₃-C₆-cycloalkyl or phenyl.

Amongst the compounds of formula III, where Y is a chemical bond, particular preference is given to the compounds of formula IIIa and, if R^{B1} and R^{B2} are hydrogen, the trimers thereof.



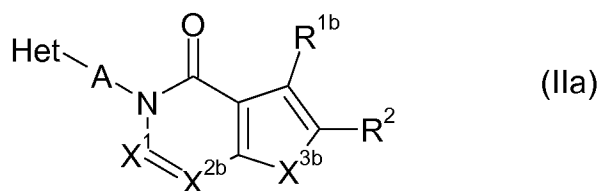
5 The reaction of the compound II with the compound III can be performed by analogy to known coupling reactions in the presence of suitable transition metal catalysts, in particular palladium catalysts. Typical reactions conditions are those of Stille coupling (see e.g. Stille et al. *Angew. Chem. Int. Ed. Engl.* 1986, 25,508; J. Eluguero et al.; *Synthesis* **1997**, 5, 563-566) or Suzuki coupling (see e.g. A. Suzuki et al, *Chem. Rev.* **1995**, 95, 2457-2483, N. Zhe et al.; *J. Med. Chem.* **2005**, 48 (5), 1569-1609; Young et al.; *J. Med. Chem.* **2004**, 47 (6), 1547-1552; C. Slee et al.; *Bioorg. Med. Chem. Lett.* **2001**, 9, 3243-3253).

15 In a similar manner, compounds of the formula I, where Y¹, Y² or Y³ is NH or were Cyc¹-Y¹, Cyc²-Y² or Cyc³-Y³ (Y¹, Y² or Y³ are single bonds) an N-bound heterocycle (Y¹, Y² or Y³ are single bonds) can be prepared by reacting a compound of the formula II, as defined above, with a compound of the formula III'



20 where Y and Cyc are as defined for formula III. The reaction of II with III' is preferably carried out in an aprotic solvent, such as dimethylsulfoxide, acetonitrile, N-methylpyrrolidone, dimethylformamide, dimethylacetamide, tetramethyl urea, or mixtures thereof or mixtures thereof with halogenated hydrocarbons such as dichloromethane. The reaction is preferably carried out in the presence of a suitable base, e.g. an alkalimetal carbonate such as lithium carbonate, sodium carbonate, potassium carbonate or caesium carbonate or an alkalimetal alkoxide.

25 Compounds of the formula I, where Q is O, can also be prepared e.g. by reacting a compound of the formula IIa



wherein

X^{2b} is N or C- R^{7b} ;

X^{3b} is S, O, N=C(R^8), C(R^{9b})=C(R^8) or N=C(R^9);

Het, A, X^1 , R^2 and R^8 are as defined for formulae I, I-1.A, I-1.B, I-2.A, I-2.B, I-

5 1.C, I-2.C, I-1.D, I-2.D, I-3.A, I-4.A, I-3.B, I-4.B, I-3.C, I-4.C, I-3.D, I-4.D, I-5.A, I-6.A, I-5.B, I-6.B, I-5.C, I-6.C, I-5.D, I-6.D, I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C, I-7.D, I-8.D, I-9.A, I-10.A, I-9.B, I-10.B, I-9.C, I-10.C, I-9.D or I-10.D;

10 R^{1b} , R^{7b} , R^{9b} independently of each other, are selected from the group consisting of hydrogen, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkylsulfanyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkylsulfanyl-C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, CN, $NR^{x1}R^{x2}$, $NR^{x1}R^{x2}$ -C₁-C₄-alkoxy or a moiety M;

15 provided that 1 or 2 of the radicals R^{1b} , R^{7b} and R^{9b} , in particular exactly one of these radicals is moiety M, while the others are different from M, where M is as defined for formula III and in particular a B(OR^{B1})(OR^{B2}) radical; with a compound of formula IIIb,

20 Hal-Y-Cyc (IIIb)

where Y and Cyc are as defined herein and wherein Hal is bromine or iodine.

The reaction of the compound IIa with the compound IIIb can be performed by analogy tot the reaction of compound II with compound III.

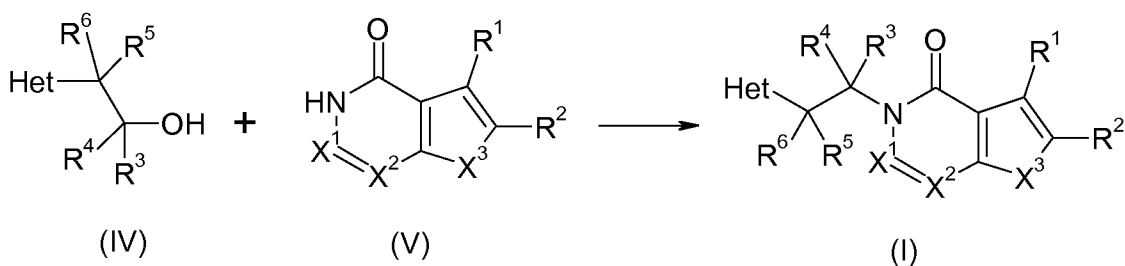
25 The compounds II, IIa, III, III', IIIa and IIIb are known or can be prepared by standard methods of organic chemistry.

Compounds of the formula I, where Y¹-Cyc¹, Y²-Cyc² or Y³-Cyc³ is a N-bound radical can be obtained by a coupling reaction between the compound II and the corresponding amine in the presence of a palladium catalyst in terms of a Buchwald-Hartwig reaction. Suitable palladium catalyst are for example tris-(dibenzylidene-
30 acetone)dipalladium(0) (Pd₂(dba)₃), [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (PdCl₂(dppf)) or palladium acetate (Pd(OAc)₂). The reaction is usually

carried out in the presence of a tri(substituted)phosphine, e.g. a triarylphosphine such as triphenylphosphine, tritolylphosphine or 2,2'-bis(diphenylphosphino)-1,1'-binaphthalene (BINAP), tri(cyclo)alkylphosphine such as tris-n-butylphosphine, tris(tert-butyl)phosphine or tris(cyclohexylphosphine), or dicyclohexyl-(2',4',6'-tri-iso-propyl-biphenyl-2-yl)-phosphane (X-Phos). Usually, the reaction is performed in the presence of a base such as an alkaline alkoxide, earth alkine alkoxide, alkaline carbonate or earth alkaline carbonate such as or sodium tert-butoxide or cesium carbonate.

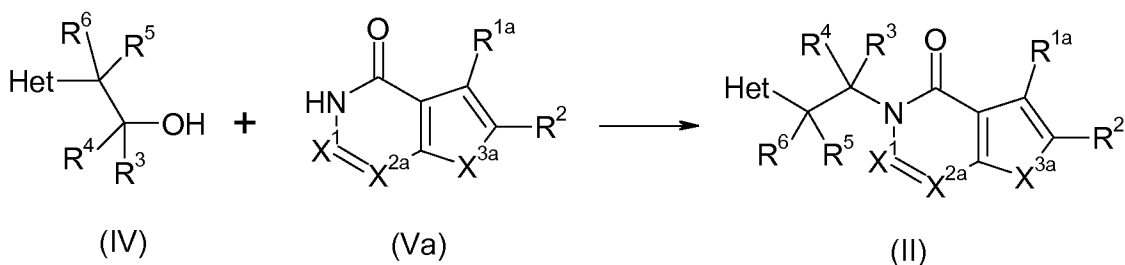
Compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A¹ can be prepared according to the following reaction schemes 1 and 2 by successively reacting compounds of the formulae V or Va, respectively with a suitable hydroxy compound IV, in terms of a Mitsunobu reaction.

Scheme 1:



15

Scheme 2:

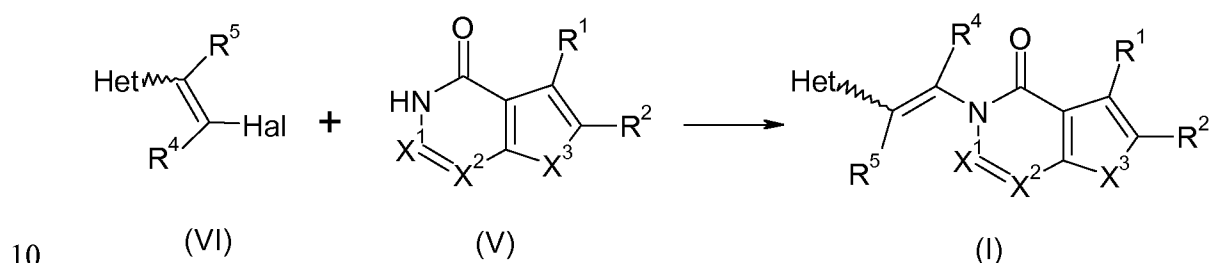


In schemes 1 and 2, X¹, X², X³, X^{2a}, X^{3a}, R¹, R^{1a}, R², R³, R⁴, R⁵, R⁶ and Het are as defined above. Compounds of the formulae V and Va, respectively, can be prepared in analogy to known methods, e.g. as described in Natl. Symposium Vacuum Technol., Chicago, (Trans.), 161-3; 1956, Journal of Organic Chemistry, 74(10), 3849-3855; 2009, or Journal of Heterocyclic Chemistry, 8(1), 57-60; 1971.

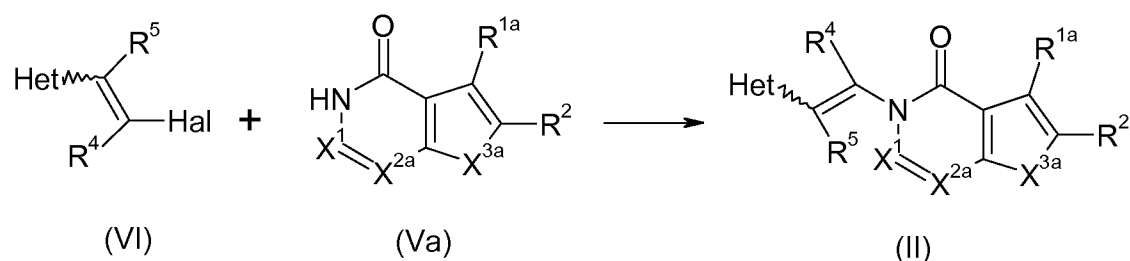
Alternatively, compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A¹ can be prepared by hydrogenation of compounds of the formula I (or likewise the compounds II), where A is A³.

Compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A³ can be prepared according to the following reaction schemes 3 and 4 by successively reacting compounds of the formulae V or Va, respectively with a suitable halocompound VI.

Scheme 3:



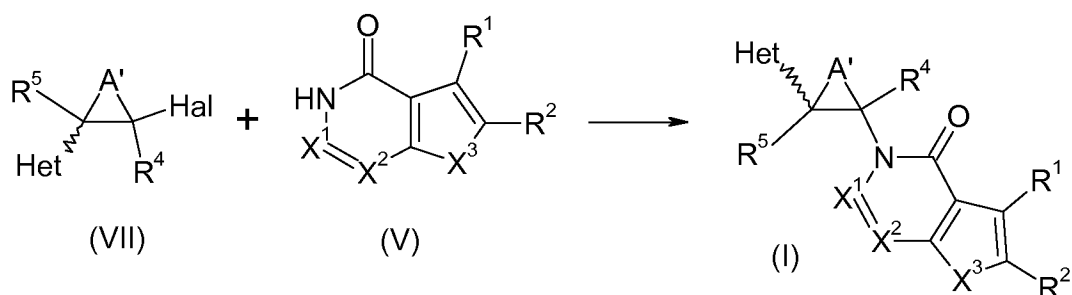
Scheme 4:



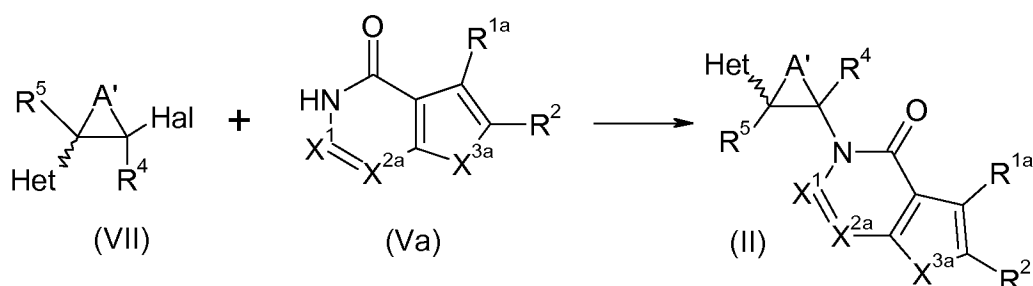
In schemes 3 and 4, X¹, X², X³, X^{2a}, X^{3a}, R¹, R^{1a}, R², R⁴, R⁵ and Het are as defined above. Hal is halogen, preferably bromine or iodine. The reaction is usually performed in the presence of a base. Suitable bases are alkali metal carbonates and hydrogen carbonates or earth metal carbonates and hydrogencarbonates such as cesium carbonate.

Compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A⁴ can be prepared according to the following reaction schemes 5 and 6 by successively reacting compounds of the formulae V or Va, respectively with a suitable halocompound VII.

Scheme 5:

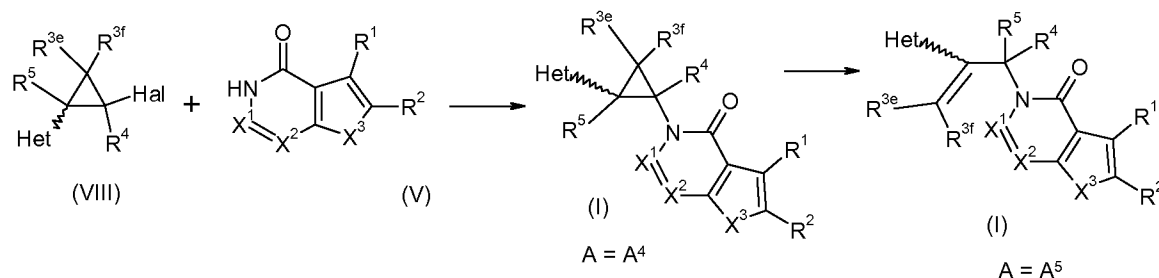


Scheme 6:



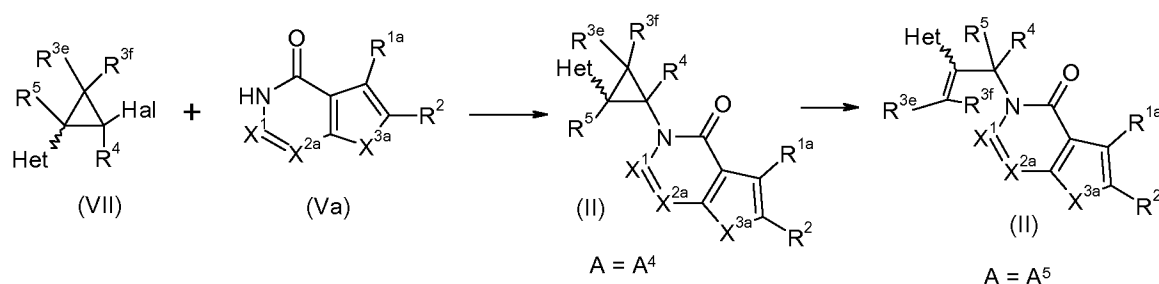
- 5 In schemes 5 and 6, X¹, X², X³, X^{2a}, X^{3a}, R¹, R^{1a}, R², R⁴, R⁵, A' and Het are as defined above. Hal is halogen, preferably bromine or iodine. The reaction is usually performed in the presence of a base. Suitable bases are alkali metal carbonates and hydrogen carbonates or earth metal carbonates and hydrogencarbonates such as cesium carbonate.
- 10 Alternatively, compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A⁴ with A' being a CR^{3b}R^{3c} (R^{3b} and R^{3c} are as defined above) can be prepared by cyclopropanation of compounds of the formula I (or likewise the compounds II), where A is A³, in terms of a Simmon-Smith reaction. Compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A⁴ with A'
- 15 being a O can be prepared by epoxidation of compounds of the formula I (or likewise the compounds II), where A is A³, using hydrogen peroxide.
- Compounds of the formula I (or likewise the compounds II), where A is a radical A⁴ can be obtained in the form of enantiomers, for example as racemate, in the form of a mixture of enantiomers, as pure enantiomers or in the form of diastereomers.
- 20 Compounds of the formula I (or likewise the compounds II), where Q is O and A is a radical A⁵ can be prepared according to the following reaction schemes 7 and 8 by reacting compounds of the formulae V or Va, respectively with a suitable halocompound VIII under basic conditions for a longer period.

Scheme 7:



Scheme 8:

5



In schemes 7 and 8, X^1 , X^2 , X^3 , X^{2a} , X^{3a} , R^1 , R^{1a} , R^2 , R^{3e} , R^{3f} , R^4 , R^5 , and Het are as defined above. Hal is halogen, preferably bromine or iodine. The reaction is usually performed in the presence of a base. Suitable bases are alkali metal carbonates and hydrogen carbonates or earth metal carbonates and hydrogencarbonates such as cesium carbonate. Apart from that, compounds of the formula I and likewise compounds of the formula II, where Q is S can be prepared by successively reacting compounds of the formulae I and II, where Q is O with a suitable sulfurizing agent, such as Lawenson's reagent or P_2S_5 .

The N-oxides of compound I may be prepared from the compounds of formula I according to conventional oxidation methods, for example by treating said compounds with an organic peracid; such as metachloroperbenzoic acid or 3-chloroperbenzoic acid [Journal of Medicinal Chemistry 38(11), 1892-1903 (1995), WO 03/64572]; or with inorganic oxidizing agents; such as hydrogen peroxide [cf. Journal of Heterocyclic Chemistry 18 (7), 1305-1308 (1981)] or oxone [cf. Journal of the American Chemical Society 123(25), 5962-5973 (2001)]. The oxidation may lead to pure mono-N-oxides or to a mixture of different N-oxides, which can be separated by conventional methods; such as chromatography.

Compounds of the formula IIa can be prepared from compounds of the formula II by suitable metal-halogen exchange reactions.

The compounds of the formulae III, IIIa, IV, V and Va are well known in the art or can be prepared by analogy to well established reactions of organic synthetic chemistry or by analogy to the methods as described in standard works of organic chemistry, e.g. Houben-Weyl, "Methoden der Organischen Chemie", Thieme-Verlag, Stuttgart, Jerry March "Advanced Organic Chemistry", 5th edition, Wiley & Sons and the literature cited therein, and R. Larock, "Comprehensive Organic Transformations", 2nd edition, Weinheim, 1999 and the literature cited therein. Compounds of the formula VI can be prepared in analogy to known methods, e.g. in terms of a Wittig reaction. Compounds of the formula VII can be prepared in analogy to known methods. E.g., compounds of the formula VII, where A' is CR^{3b}R^{3c} can be prepared by cyclopropanation of compounds VI in terms of a Simmon-Smith reaction.

The reactions are usually performed in an organic solvent, including aprotic organic solvent, e.g. substituted amides, lactames and ureas; such as dimethylformamide, dimethylacetamide, N-methylpyrrolidone, tetramethyl urea, cyclic ethers; such as dioxane, tetrahydrofuran, halogenated hydrocarbons; such as dichloromethane, and mixtures thereof as well as mixtures thereof with C₁-C₆-alkanols and/or water.

The reactions described above will be usually performed at temperatures ranging from -10°C to 100°C, depending on the reactivity of the used compounds.

The reaction mixtures are worked up in a conventional way, e.g. by mixing with water, separating the phases and, where appropriate, purifying the crude products by chromatography. The intermediates and final products in some cases result in the form of colorless or pale brownish, viscous oils which are freed of volatiles or purified under reduced pressure and at moderately elevated temperature. If the intermediates and final products are obtained as solids, the purification can also take place by recrystallization or digestion.

Due to their capability of inhibiting PDE10A at low concentrations, the compounds of the formula I, their N-oxides, their hydrates, their tautomers and their prodrugs and the pharmaceutically acceptable salts thereof, are particularly suitable for treating disorders or conditions, which can be treated by inhibition of phosphodiesterase

type 10A. The terms "treating" and "treatment" in terms of the present invention have to be understood to include both curative treatment of the cause of a disease or disorder, the treatment of the symptoms associated with a disease or disorder, i.e. controlling the disease or disorder or ameliorating the conditions or symptoms associated with a
5 disease or disorder, and prophylactic treatment, i.e. a treatment for reducing the risk of a disease or disorder.

Neurological and psychiatric disorders or conditions which can be treated by inhibition of PDE10A, including curative treatment, control or amelioration and prophylaxis, include CNS disorders, in particular schizophrenia, depression, bipolar
10 disorders, cognitive dysfunctions associated with schizophrenia, cognitive dysfunctions associated with Alzheimer's disease, Huntington's disease (Huntington chorea), anxiety and substance-related disorders, especially substance use disorder, substance tolerance conditions associated with substance withdrawal. Disorders or conditions which can be treated by inhibition of PDE10A, including curative treatment, control or amelioration
15 and prophylaxis, also include treatment of diet induced obesity.

Thus, the invention relates to the use of compounds of formula I, their N-oxides, their hydrates, their tautomers and their prodrugs and the pharmaceutically acceptable salts thereof, for treatment of disorders or conditions, which can be treated by inhibition of phosphodiesterase type 10A, i.e. the invention relates to the use of such compounds
20 for curative treatment of such a disease or disorder, controlling such a disease or disorder, ameliorating the symptoms associated with such a disease or disorder and reducing the risk for such a disease or disorder.

The present invention also relates to a method for the treatment of a medical disorder, selected from neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A, said method comprising administering an
25 effective amount of at least one compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically acceptable salts thereof, to a mammal in need thereof.

The present invention in particular relates to:

- 30 • a method for treating, controlling, ameliorating or reducing the risk of schizophrenia in a mammalian;

- a method for treating, controlling, ameliorating or reducing the risk of cognitive disturbances associated with schizophrenia in a mammalian;
- a method for treating, controlling, ameliorating or reducing the risk of depression in a mammalian;
- 5 • a method for treating, controlling, ameliorating or reducing the risk of bipolar disorders in a mammalian;
- a method for treating or ameliorating the symptoms associated with substance use disorders in a mammalian;
- a method for treating or ameliorating the symptoms associated with diet-
10 induced obesity in a mammalian;
- a method for treating, controlling, ameliorating or reducing the risk of cognitive disturbances associated with Alzheimer's disease in a mammalian;
- a method for treating, controlling, ameliorating or reducing the risk of behavioral symptoms in Alzheimer's disease;
- 15 • a method for treating, controlling, ameliorating or reducing the risk of anxiety in a mammalian;
- a method for treating, controlling, ameliorating or reducing the risk of Huntington's disease in a mammalian;

which methods comprising administering an effective amount of at least one
20 compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically acceptable salts thereof, to a mammal in need thereof.

The subject treated in the present methods is generally a mammal, preferably a human being, male or female, in whom inhibition of PDE10A is desired. The terms
25 "effective amount" and "therapeutically effective amount" mean the amount of the subject compound that will elicit the biological or medical response of a tissue, system, animal or human that is being sought by the researcher, veterinarian, medical doctor or other clinician. It is recognized that one skilled in the art may affect the neurological and psychiatric disorders by treating a patient presently afflicted with the disorders or
30 by prophylactically treating a patient afflicted with the disorders with an effective amount of the compound of the present invention. As used herein, the terms "treatment" and "treating" refer to all processes, wherein there may be a slowing, interrupting,

arresting, controlling, or stopping of the progression of the disorders described herein, but does not necessarily indicate a total elimination of all disorder symptoms, as well as the prophylactic therapy of the mentioned conditions, particularly in a patient who is predisposed to such disease or disorder. The term "composition" as used herein is
5 intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts. Such term in relation to pharmaceutical composition, is intended to encompass a product comprising the active ingredient(s), and the inert ingredient(s) that make up the carrier, as well as any product
10 which results, directly or indirectly, from combination, complexation or aggregation of any two or more of the ingredients, or from dissociation of one or more of the ingredients, or from other types of reactions or interactions of one or more of the ingredients. Accordingly, the pharmaceutical compositions of the present invention encompass any composition made by admixing a compound of the present invention
15 and a pharmaceutically acceptable carrier. By "pharmaceutically acceptable" it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

The terms "administration of and or "administering a" compound should be understood to mean providing a compound of the invention or a prodrug of a compound
20 of the invention to the individual in need of treatment.

A preferred embodiment of the present invention provides a method for treating schizophrenia, comprising: administering to a patient in need thereof an effective amount of at least one compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically
25 acceptable salts thereof.

In another preferred embodiment, the present invention provides a method for treating cognitive disturbances associated with schizophrenia, comprising:
administering to a patient in need thereof an effective amount of at least one compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their
30 tautomers, their prodrugs and the pharmaceutically acceptable salts thereof.

At present, the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (1994, American Psychiatric Association, Washington, D.C.),

provides a diagnostic tool including schizophrenia and other psychotic disorders. These include: disorders having psychotic symptoms as the defining feature. The term psychotic refers to delusions, prominent hallucinations, disorganized speech, disorganized or catatonic behavior. The disorder includes: paranoid, disorganized, 5 catatonic, undifferentiated, and residual schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, substance-induced psychotic disorder, and psychotic disorder not otherwise specified. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification 10 systems for neurological and psychiatric disorders, and particular schizophrenia, and that these systems evolve with medical scientific progress. Thus, the term "schizophrenia" is intended to include like disorders that are described in other diagnostic sources.

In another preferred embodiment, the present invention provides a method for 15 treating substance-related disorders, comprising: administering to a patient in need thereof an effective amount of at least one compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically acceptable salts thereof.

In another preferred embodiment, the present invention provides a method for 20 treating anxiety, comprising: administering to a patient in need thereof an effective amount of at least one compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically acceptable salts thereof. At present, the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (1994, American Psychiatric Association, 25 Washington, D.C.), provides a diagnostic tool including anxiety and related disorders. These include: panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, acute stress disorder, generalized anxiety disorder, anxiety disorder due to a general medical condition, substance-induced anxiety disorder and 30 anxiety disorder not otherwise specified. As used herein the term "anxiety" includes treatment of those anxiety disorders and related disorder as described in the DSM-IV. The skilled artisan will recognize that there are alternative nomenclatures, nosologies,

and classification systems for neurological and psychiatric disorders, and particular anxiety, and that these systems evolve with medical scientific progress. Thus, the term "anxiety" is intended to include like disorders that are described in other diagnostic sources.

5 In another preferred embodiment, the present invention provides a method for treating depression, comprising: administering to a patient in need thereof an effective amount of at least one compound, selected from the group of compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically acceptable salts thereof. At present, the fourth edition of the Diagnostic and Statistical
10 Manual of Mental Disorders (DSM-IV) (1994, American Psychiatric Association, Washington, D.C.), provides a diagnostic tool including depression and related disorders. Depressive disorders include, for example, single episodic or recurrent major depressive disorders, and dysthymic disorders, depressive neurosis, and neurotic depression; melancholic depression including anorexia, weight loss, insomnia and early
15 morning waking, and psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, anxiety and phobias; seasonal affective disorder; or bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder. As used herein the term "depression" includes treatment of those depression
20 disorders and related disorder as described in the DSM-IV.

 In another preferred embodiment, the present invention provides a method for treating substance-related disorders, especially substance dependence, substance abuse, substance tolerance, and substance withdrawal, comprising: administering to a patient in need thereof an effective amount at least one compound, selected from the group of
25 compounds of formula I, their N-oxides, their hydrates, their tautomers, their prodrugs and the pharmaceutically acceptable salts thereof. At present, the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (1994, American Psychiatric Association, Washington, D.C.), provides a diagnostic tool including disorders related to taking a drug of abuse (including alcohol), to the side effects of a
30 medication, and to toxin exposure. Substances include alcohol, amphetamine and similarly acting sympathomimetics, caffeine, cannabis, cocaine, hallucinogens, inhalants, nicotine, opioids, phencyclidine (PCP) or similarly acting

arylcyclohexylamines, and sedatives, hypnotics, or anxiolytics. Also, polysubstance dependence and other unknown substance-related disorders are included. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification systems for neurological and psychiatric disorders, and particular
5 substance-related disorders, and that these systems evolve with medical scientific progress. Thus, the term "substance-related disorder" is intended to include like disorders that are described in other diagnostic sources.

In the treatment, prevention, control, amelioration, or reduction of risk of conditions which require inhibition of PDE10A an appropriate dosage level will
10 generally be about 0.01 to 500 mg per kg patient body weight per day which can be administered in single or multiple doses. Preferably, the dosage level will be about 0.1 to about 250 mg/kg per day; more preferably about 0.5 to about 100 mg/kg per day. A suitable dosage level may be about 0.01 to 250 mg/kg per day, about 0.05 to 100 mg/kg per day, or about 0.1 to 50 mg/kg per day. Within this range the dosage may be 0.05 to
15 0.5, 0.5 to 5 or 5 to 50 mg/kg per day. For oral administration, the compositions are preferably provided in the form of tablets containing 1.0 to 1000 milligrams of the active ingredient, particularly 1.0, 5.0, 10.0, 15.0, 20.0, 25.0, 50.0, 75.0, 100.0, 150.0, 200.0, 250.0, 300.0, 400.0, 500.0, 600.0, 750.0, 800.0, 900.0, and 1000.0 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be
20 treated. The compounds may be administered on a regimen of 1 to 4 times per day, preferably once or twice per day. When treating, preventing, controlling, ameliorating, or reducing the risk of neurological and psychiatric disorders or other diseases for which compounds of the present invention are indicated, generally satisfactory results are obtained when the compounds of the present invention are administered at a daily
25 dosage of from about 0.1 milligram to about 100 milligram per kilogram of animal body weight, preferably given as a single daily dose or in divided doses two to six times a day, or in sustained release form. For most large mammals, the total daily dosage is from about 1.0 milligrams to about 1000 milligrams, preferably from about 1 milligram to about 50 milligrams, in the case of a 70 kg adult human, the total daily dose will
30 generally be from about 7 milligrams to about 350 milligrams. This dosage regimen may be adjusted to provide the optimal therapeutic response. It will be understood, however, that the specific dose level and frequency of dosage for any particular patient

may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular
5 condition, and the host undergoing therapy.

The compounds of the present invention may be administered by conventional routes of administration, including parenteral (e.g., intramuscular, intrapentoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, or implant), oral, by inhalation spray, nasal, vaginal, rectal, sublingual, or topical routes of
10 administration.

The compounds according to the present invention are further useful in a method for the prevention, treatment, control, amelioration, or reduction of risk of the aforementioned diseases, disorders and conditions in combination with other agents.

The compounds of the present invention may be used in combination with one or
15 more other drugs in the treatment, prevention, control, amelioration, or reduction of risk of diseases or conditions for which compounds of Formula I or the other drugs may have utility, where the combination of the drugs together are safer or more effective than either drug alone. Such other drug(s) may be administered, by a route and in an amount commonly used therefore, contemporaneously or sequentially with a compound
20 of Formula I. When a compound of formula I is used contemporaneously with one or more other drugs, a pharmaceutical composition in unit dosage form containing such other drugs and the compound of formula I is preferred. However, the combination therapy may also include therapies in which the compound of formula I and one or more other drugs are administered on different overlapping schedules. It is also contemplated
25 that when used in combination with one or more other active ingredients, the compounds of the present invention and the other active ingredients may be used in lower doses than when each is used singly. Accordingly, the pharmaceutical compositions of the present invention include those that contain one or more other active ingredients, in addition to a compound of formula I. The above combinations
30 include combinations of a compound of the present invention not only with one other active compound, but also with two or more other active compounds.

Likewise, compounds of the present invention may be used in combination with other drugs that are used in the prevention, treatment, control, amelioration, or reduction of risk of the diseases or conditions for which compounds of the present invention are useful. Such other drugs may be administered, by a route and in an amount commonly
5 used therefore, contemporaneously or sequentially with a compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition containing such other drugs in addition to the compound of the present invention is preferred. Accordingly, the pharmaceutical compositions of the present invention include those that also contain
10 one or more other active ingredients, in addition to a compound of the present invention.

The weight ratio of the compound of the compound of the present invention to the second active ingredient may be varied and will depend upon the effective dose of each ingredient. Generally, an effective dose of each will be used. Thus, for example, when a
15 compound of the present invention is combined with another agent, the weight ratio of the compound of the present invention to the other agent will generally range from about 1000: 1 to about 1:1000, preferably about 200:1 to about 1:200. Combinations of a compound of the present invention and other active ingredients will generally also be within the aforementioned range, but in each case, an effective dose of each active
20 ingredient should be used. In such combinations the compound of the present invention and other active agents may be administered separately or in conjunction. In addition, the administration of one element may be prior to, concurrent to, or subsequent to the administration of other agent(s).

The present invention also relates to pharmaceutical compositions (i.e.
25 medicaments) which comprise at least one compound of the present invention and, where appropriate, one or more suitable excipients.

These excipients/drug carriers are chosen according to the pharmaceutical form and the desired mode of administration.

The compounds of the present invention can be used to manufacture
30 pharmaceutical compositions for parenteral (e.g., intramuscular, intrapentoneal, intravenous, ICV, intracisternal injection or infusion, subcutaneous injection, or implant), oral, sublingual, intratracheal, intranasal, topical, transdermal, vaginal or

rectal administration, and be administered to animals or humans in unit dose forms, mixed with conventional pharmaceutical carriers, for the prophylaxis or treatment of the above impairments or diseases.

In the pharmaceutical compositions, the at least one compound of the present invention may be formulated alone or together with further active compounds, in suitable dosage unit formulations containing conventional excipients, which generally are non-toxic and/or pharmaceutically acceptable. Carriers or excipients can be solid, semisolid or liquid materials which serve as vehicles, carriers or medium for the active compound. Suitable excipients are listed in the specialist medicinal monographs. In addition, the formulations can comprise pharmaceutically acceptable carriers or customary auxiliary substances, such as glidants; wetting agents; emulsifying and suspending agents; preservatives; antioxidants; antiirritants; chelating agents; coating auxiliaries; emulsion stabilizers; film formers; gel formers; odor masking agents; taste corrigents; resin; hydrocolloids; solvents; solubilizers; neutralizing agents; diffusion accelerators; pigments; quaternary ammonium compounds; refatting and overfatting agents; raw materials for ointments, creams or oils; silicone derivatives; spreading auxiliaries; stabilizers; sterilants; suppository bases; tablet auxiliaries, such as binders, fillers, glidants, disintegrants or coatings; propellants; drying agents; opacifiers; thickeners; waxes; plasticizers and white mineral oils. A formulation in this regard is based on specialist knowledge as described, for example, in Fiedler, H. P., *Lexikon der Hilfsstoffe für Pharmazie, Kosmetik und angrenzende Gebiete* [Encyclopedia of auxiliary substances for pharmacy, cosmetics and related fields], 4th edition, Aulendorf: ECV-Editio-Kantor-Verlag, 1996.

Suitable unit dose forms include forms for oral administration, such as tablets, gelatin capsules, powders, granules and solutions or suspensions for oral intake, forms for sublingual, buccal, intratracheal or intranasal administration, aerosols, implants, forms of subcutaneous, intramuscular or intravenous administration and forms of rectal administration.

The compounds of the invention can be used in creams, ointments or lotions for topical administration.

If a solid composition is prepared in the form of tablets, the main ingredient is mixed with a pharmaceutical carrier such as gelatin, starch, lactose, magnesium stearate, talc, silicon dioxide or the like.

5 The tablets may be coated with sucrose, a cellulose derivative or another suitable substance or be treated otherwise in order to display a prolonged or delayed activity and in order to release a predetermined amount of the active basic ingredient continuously.

A preparation in the form of gelatin capsules is obtained by mixing the active ingredient with an extender and taking up the resulting mixture in soft or hard gelatin capsules.

10 A preparation in the form of a syrup or elixir or for administration in the form of drops may comprise active ingredients together with a sweetener, which is preferably calorie-free, methylparaben or propylparaben as antiseptics, a flavoring and a suitable coloring.

15 The water-dispersible powders or granules may comprise the active ingredients mixed with dispersants, wetting agents or suspending agents such as polyvinylpyrrolidones, and sweeteners or taste improvers.

Rectal administration is achieved by the use of suppositories which are prepared with binders which melt at the rectal temperature, for example cocobutter or polyethylene glycols. Parenteral administration is effected by using aqueous
20 suspensions, isotonic salt solutions or sterile and injectable solutions which comprise pharmacologically suitable dispersants and/or wetting agents, for example propylene glycol or polyethylene glycol.

The active basic ingredient may also be formulated as microcapsules or liposomes/centrosomes, if suitable with one or more carriers or additives.

25 In addition to the compounds of the general formula I, their prodrugs, their N-oxides, their tautomers, their hydrates or their pharmaceutically suitable salts, the compositions of the invention may comprise further active basic ingredients which may be beneficial for the treatment of the impairments or diseases indicated above.

30 The present invention thus further relates to pharmaceutical compositions in which a plurality of active basic ingredients are present together, where at least one thereof is a compound of the invention.

When producing the pharmaceutical compositions, the compounds according to the invention are optionally mixed or diluted with one or more carriers.

The compounds of the invention also include those compounds in which one or more atoms have been replaced by their stable, non-radioactive isotopes, for example, a
5 hydrogen atom by deuterium.

Stable isotopes (e.g., deuterium, ^{13}C , ^{15}N , ^{18}O) are nonradioactive isotopes which contain one additional neutron than the normally abundant isotope of the respective atom. Deuterated compounds have been used in pharmaceutical research to investigate the in vivo metabolic fate of the compounds by evaluation of the mechanism of action
10 and metabolic pathway of the non deuterated parent compound (Blake et al. *J. Pharm. Sci.* 64, 3, 367-391 (1975)). Such metabolic studies are important in the design of safe, effective therapeutic drugs, either because the in vivo active compound administered to the patient or because the metabolites produced from the parent compound prove to be toxic or carcinogenic (Foster et al., *Advances in Drug Research* Vol. 14, pp. 2-36,
15 Academic press, London, 1985; Kato et al., *J. Labelled Comp. Radiopharmaceut.*, 36(10):927-932 (1995); Kushner et al., *Can. J. Physiol. Pharmacol.*, 77, 79-88 (1999).

Incorporation of a heavy atom particularly substitution of deuterium for hydrogen, can give rise to an isotope effect that could alter the pharmacokinetics of the drug. This effect is usually insignificant if the label is placed at a metabolically inert position of the
20 molecule.

Stable isotope labeling of a drug can alter its physico-chemical properties such as pKa and lipid solubility. These changes may influence the fate of the drug at different steps along its passage through the body. Absorption, distribution, metabolism or excretion can be changed. Absorption and distribution are processes that depend
25 primarily on the molecular size and the lipophilicity of the substance. These effects and alterations can affect the pharmacodynamic response of the drug molecule if the isotopic substitution affects a region involved in a ligand-receptor interaction.

Drug metabolism can give rise to large isotopic effect if the breaking of a chemical bond to a deuterium atom is the rate limiting step in the process. While some
30 of the physical properties of a stable isotope-labeled molecule are different from those of the unlabeled one, the chemical and biological properties are the same, with one important exception: because of the increased mass of the heavy isotope, any bond

involving the heavy isotope and another atom will be stronger than the same bond between the light isotope and that atom. In any reaction in which the breaking of this bond is the rate limiting step, the reaction will proceed slower for the molecule with the heavy isotope due to "kinetic isotope effect". A reaction involving breaking a C--D
5 bond can be up to 700 percent slower than a similar reaction involving breaking a C--H bond. If the C--D bond is not involved in any of the steps leading to the metabolite, there may not be any effect to alter the behavior of the drug. If a deuterium is placed at a site involved in the metabolism of a drug, an isotope effect will be observed only if breaking of the C--D bond is the rate limiting step. There is evidence to suggest that
10 whenever cleavage of an aliphatic C--H bond occurs, usually by oxidation catalyzed by a mixed-function oxidase, replacement of the hydrogen by deuterium will lead to observable isotope effect. It is also important to understand that the incorporation of deuterium at the site of metabolism slows its rate to the point where another metabolite produced by attack at a carbon atom not substituted by deuterium becomes the major
15 pathway a process called "metabolic switching".

Deuterium tracers, such as deuterium-labeled drugs and doses, in some cases repeatedly, of thousands of milligrams of deuterated water, are also used in healthy humans of all ages, including neonates and pregnant women, without reported incident (e.g. Pons G and Rey E, *Pediatrics* 1999 104: 633; Coward W A et al., *Lancet* 1979 7:
20 13; Schwarcz H P, *Control. Clin. Trials* 1984 5(4 Suppl): 573; Rodewald L E et al., *J. Pediatr.* 1989 114: 885; Butte N F et al. *Br. J. Nutr.* 1991 65: 3; MacLennan A H et al. *Am. J. Obstet Gynecol.* 1981 139: 948). Thus, it is clear that any deuterium released, for instance, during the metabolism of compounds of this invention poses no health risk.

The weight percentage of hydrogen in a mammal (approximately 9%) and natural
25 abundance of deuterium (approximately 0.015%) indicates that a 70 kg human normally contains nearly a gram of deuterium. Furthermore, replacement of up to about 15% of normal hydrogen with deuterium has been effected and maintained for a period of days to weeks in mammals, including rodents and dogs, with minimal observed adverse effects (Czajka D M and Finkel A J, *Ann. N.Y. Acad. Sci.* 1960 84: 770; Thomson J F,
30 *Ann. New York Acad. Sci* 1960 84: 736; Czajka D M et al., *Am. J. Physiol.* 1961 201: 357). Higher deuterium concentrations, usually in excess of 20%, can be toxic in animals. However, acute replacement of as high as 15%-23% of the hydrogen in

humans' fluids with deuterium was found not to cause toxicity (Blagojevic N et al. in "Dosimetry & Treatment Planning for Neutron Capture Therapy", Zamenhof R, Solares G and Harling O Eds. 1994. Advanced Medical Publishing, Madison Wis. pp.125-134; Diabetes Metab. 23: 251 (1997)).

5 Increasing the amount of deuterium present in a compound above its natural abundance is called enrichment or deuterium-enrichment. Examples of the amount of enrichment include from about 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 16, 21, 25, 29, 33, 37, 42, 46, 50, 54, 58, 63, 67, 71, 75, 79, 84, 88, 92, 96, to about 100 mol %.

10 The hydrogens present on a particular organic compound have different capacities for exchange with deuterium. Certain hydrogen atoms are easily exchangeable under physiological conditions and, if replaced by deuterium atoms, it is expected that they will readily exchange for protons after administration to a patient. Certain hydrogen atoms may be exchanged for deuterium atoms by the action of a deuterio acid such as D₂SO₄/D₂O. Alternatively, deuterium atoms may be incorporated in various
15 combinations during the synthesis of compounds of the invention. Certain hydrogen atoms are not easily exchangeable for deuterium atoms. However, deuterium atoms at the remaining positions may be incorporated by the use of deuterated starting materials or intermediates during the construction of compounds of the invention.

20 Deuterated and deuterium-enriched compounds of the invention can be prepared by using known methods described in the literature. Such methods can be carried out utilizing corresponding deuterated and optionally, other isotope-containing reagents and/or intermediates to synthesize the compounds delineated herein, or invoking standard synthetic protocols known in the art for introducing isotopic atoms to a chemical structure. Relevant procedures and intermediates are disclosed, for instance in
25 Lizondo, J et al., *Drugs Fut*, 21(11), 1116 (1996); Brickner, S J et al., *J Med Chem*, 39(3), 673 (1996); Mallesham, B et al., *Org Lett*, 5(7), 963 (2003); PCT publications WO1997010223, WO2005099353, WO1995007271, WO2006008754; US Patent Nos. 7538189; 7534814; 7531685; 7528131; 7521421; 7514068; 7511013; and US Patent Application Publication Nos. 20090137457; 20090131485; 20090131363;
30 20090118238; 20090111840; 20090105338; 20090105307; 20090105147; 20090093422; 20090088416; 20090082471, the methods are hereby incorporated by reference.

The following examples are intended for further illustration of the present invention.

Abbreviations which have been used in the descriptions of the schemes and the Examples that follow are: BINAP for 2,2'-bis (diphenylphosphino)-1,1'-binaphthyl;
5 DCM for dichloromethane; DEAD for diethyl azodicarboxylate; DIAD for diisopropyl azodicarboxylate; DMF for dimethylformamide; EA for ethyl acetate; EDCI 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide; Et for ethyl; EX. for EXAMPLE; HMPA for hexamethylphosphoramide; HOBT for hydroxybenzotriazole; i-Pr for isopropyl; LDA for lithium diisopropylamide; MeOH for methanol; PE for petroleum ether; Pd₂(dba)₃
10 for tris (dibenzylideneacetone)dipalladium(0); PdCl₂(dppf) for 1,1'-bis (diphenylphosphino)ferrocene-palladium (II)-dichloride; R_t for retention time; TEA for triethylamine; THF for tetrahydrofuran; TMEDA for N,N,N',N'-tetramethyl 1,2-ethanediamine; TMSCl for trimethylsilyl chloride.

15 LC-MS measurements were run on Agilent 1200 HPLC/6100 SQ System.

The compounds I of the invention were purified in some cases by preparative HPLC. The compounds I then result as the salts.

Preparation Examples

20

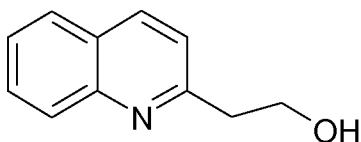
I. Preparation of intermediates

The starting materials used in the examples are either commercially available or can be synthesized by the average skilled person trained in organic chemistry following routine laboratory practice as outlined, for example in the examples below.

25

a) Preparation of compounds of the general formula Het-A¹-OH

a1) 2-Quinolin-2-yl-ethanol



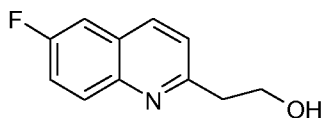
30 a1.1) Quinolin-2-yl-acetic acid ethyl ester

To a suspension of vacuum dried Zn dust (6.0 g, 93.8 mmol) in dry THF (100 mL) was added TMSCl (0.5 mL) dropwise over 5 min under N₂ atmosphere and under stirring. The mixture was stirred for 30 min and warmed to 45°C. Ethyl bromoacetate (5.2 mL, 46.9 mmol) was added dropwise via a syringe. After addition, the mixture was stirred at the same temperature for 1 h. After sedation at room temperature for 2 h, a clear orange solution was formed. The orange solution (50 mL) was carefully sucked into a syringe through a long needle and added to a mixture of 2-bromoquinoline (2.0 g, 9.6 mmol) and PdCl₂(dppf) (200 mg, 0.27 mmol) in a three-neck flask. The mixture was refluxed under N₂ for 3 h. The reaction was monitored with LC-MS. Ethyl acetate (200 mL) was added to dilute the mixture and water (50 mL) was added to quench the reaction. The mixture was filtered through a celite pad. The filtration was partitioned between brine and ethyl acetate. The organic layer was separated, washed with brine (100 mL), dried over sodium sulfate and concentrated. The residue was purified with silica column (PE/EA=3: 1) to give the title compound as orange oil (1.0 g, 48%). LC-MS (ESI+): m/e 216 (M+H)⁺, R_t: 0.62 min.

a1.2) 2-Quinolin-2-yl-ethanol

To a cold (0 °C) solution of the compound from Example a1.1a (10 g, 45 mmol) in THF (200 mL) was added LiAlH₄ (2.65 mg, 70 mmol) in small portions over a period of 5 min. The resulting mixture was stirred for 1h. Water was added dropwise very slowly. Then more water and EA were added. The organic phase was collected, dried and concentrated. The residue was purified by silica gel chromatography (PE/EA=2: 1) to give the title compound as a yellow solid (2.5 g, 30%). LC-MS (ESI+): m/e 174 (M+H)⁺, R_t: 0.75 min.

a2) 2-(6-Fluoroquinolin-2-yl)-ethanol

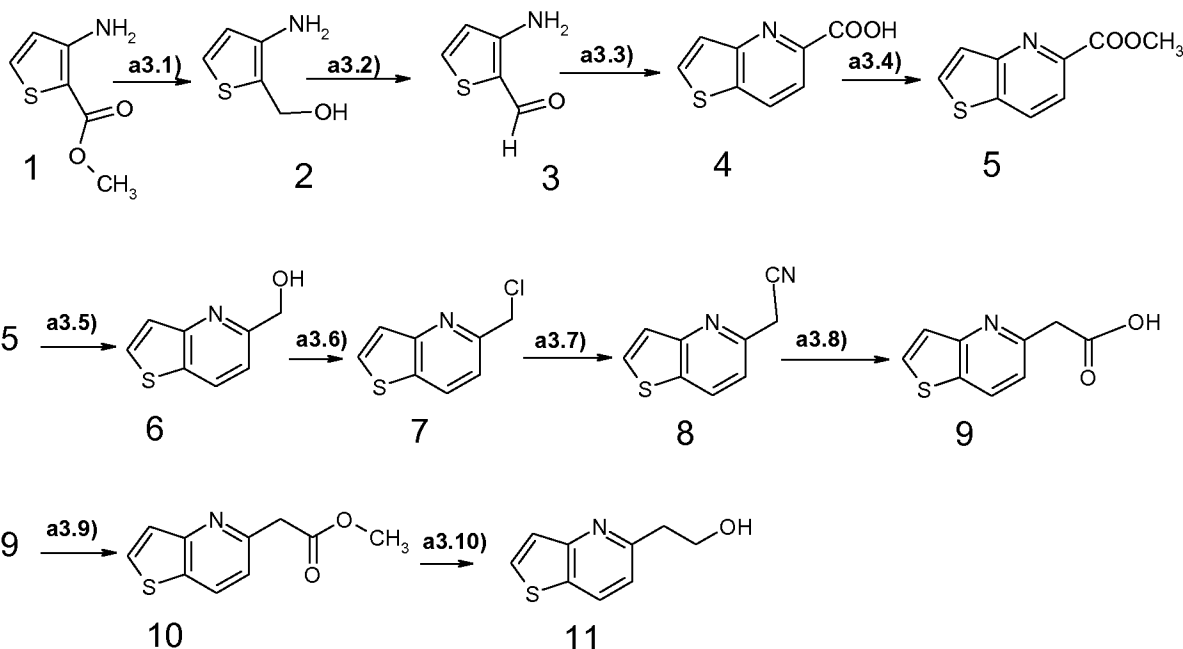


6-Fluoro-2-methylquinoline (1.00 g, 6.20 mmol) and sodium hydroxide were each added sequentially to the mixture of HCHO in water. Then 2 mL of EtOH were added to the mixture. The resulting solution was stirred at about 85 °C overnight. The organic layer was extracted with EA (3 x 10 mL), collected and dried with anhydrous Na₂SO₄,

filtered and concentrated to afford a pink oil. The crude material was purified by chromatography on silica-gel (eluent: PE/EA=6/1) and then further purified by combi-flash chromatography (NH₄HCO₃/H₂O, MeOH/H₂O=40%~60%) to give 360 mg of the title product (yield: 30.3%).

5 LC-MS: m/e (M+H): 192.7, R_t: 1.63 min.

a3) 2-Thieno[3,2-b]pyridin-5-yl-ethanol



a3.1) Compound (2)

15 To a suspension of LiAlH₄ (1.39 g, 36.58 mmol) in anhydrous THF (30 mL) was added a solution of methyl 3-aminothiophene 2-carboxylate (compound 1, 5.00 g, 31.81 mmol) dropwise at 0 °C. The reaction mixture was stirred at room temperature overnight. Water (4 mL) was added dropwise to quench the reaction. The mixture was stirred for 30 min. and then more water was added (10 mL). The solid was filtered off
20 and then washed with NaOH solution (50 mL, 5 N). The filtrate was concentrated *in vacuo* and the residue was dissolved in EtOAc (200 mL). The solution was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The crude solid was used in the next step without further purification (2.71 g, yield 66%). LC-MS (ESI⁺): m/e 130 (M+H)⁺, R_t: 1.57 min.

a3.2) Compound (3)

A mixture of compound **2** (8.14 g, 63.00 mmol) and MnO₂ (32.8 g, 0.378 mol) in EtOAc (100 mL) was stirred at 30°C for 48 h. The mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was used in the next step without further
5 purification (6.82 g, yield 85%). LC-MS (ESI⁺): m/e 128 (M+H)⁺, R_t: 1.55 min.

a1.3) Compound (4)

To a solution of compound **3** (6.82 g, 53.62 mmol) in EtOH (70 mL) was added a mixture of pyruvic acid (9.44 g, 0.107 mol) and NaOH (10.7 g, 0.268 mol) in H₂O (70
10 mL) in one portion. The mixture was heated at 60 °C for 2 h, then cooled and extracted with Et₂O/EtOAc (1: 1, 30 mL). The aqueous layer was acidified with HCl (2 N) to pH = 3 at 0°C and the water was removed under reduced pressure. The residue was co-evaporated with toluene (50 mL×3) and then used in the next step without further purification. LC-MS (ESI⁺): m/e 180 (M+H)⁺, R_t: 1.50 min.

15

a3.4) Compound (5)

To a mixture of crude compound **4** (7 g, 39 mmol) in methanol (60 mL) was added thionyl chloride (10 mL) dropwise at 0°C. The reaction mixture was then heated at 65 °C for 3 h. The excess of solvent was removed under reduced pressure. The
20 residue was diluted with EtOAc (100 mL) and washed with saturated NaHCO₃ aqueous solution (30 mL×4) and brine (30 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was purified on a silica column (PE/EtOAc = 5: 1, v/v) to afford the title product as an off-white solid (715 mg, total yield 9.5%). LC-MS (ESI⁺): m/e 194 (M+H)⁺, R_t: 1.78 min.

25

a3.5) Compound (6)

To a solution of compound **5** (100 mg, 0.52 mmol) in THF (2 mL) was added LiBH₄ (11 mg) in one portion. The mixture was allowed to stir at room temperature overnight. The reaction was quenched with saturated NH₄Cl solution, and then extracted
30 with EtOAc (20 mL). The organic layer was washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. The yellow residue was used in the next step without further purification. LC-MS (ESI⁺): m/e 166 (M+H)⁺, R_t: 1.44 min.

a3.6) Compound (7)

A mixture of compound **6** (100 mg, crude) and thionyl chloride (1 mL) in DCM (3 mL) was stirred at room temperature for 3 h. The mixture was concentrated *in vacuo*.

- 5 The residue was diluted with EtOAc (20 mL) and washed with saturated NaHCO₃ solution (6 mL×4) and brine (6 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The red residue was used in the next step without further purification. LC-MS (ESI+): m/e 184 (M+H)⁺, R_t: 1.88 min.

10 a3.7) Compound (8)

A mixture of compound **7** (580 mg, 3.157 mmol) and NaCN (170 mg, 3.473 mmol) in EtOH (12 mL) and H₂O (4 mL) was stirred at 50 °C for 60 h. The mixture was diluted with EtOAc (50 mL) and washed with brine (15 mL×4). The organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was purified on a
15 silica column (PE/EtOAc = 10: 1, v/v) to afford the title product as an off-white solid (280 mg, yield 51%). LC-MS (ESI+): m/e 175 (M+H)⁺, R_t: 1.89 min.

a3.8) Compound (9)

- A mixture of compound **8** (200 mg, 1.148 mmol), sodium hydroxide (459 mg, 11.48 mmol) in EtOH (4 mL) and water (0.5 mL) was stirred at 70°C overnight. The
20 solvent was concentrated, the residue was adjusted to pH=3. The solution was concentrated. The product was used in the next step without further purification
LC-MS (ESI+): m/e 194 (M+H)⁺, R_t: 1.16 min

25 a3.9) Compound (10)

- To a mixture of 2-(thieno[3,2-b]pyridin-5-yl)acetic acid from Example a3.8 (77 mg, 0.399 mmol) in MeOH (5 mL) was added SOCl₂ (0.5 mL, 6.85 mmol) dropwise at 0 °C. The reaction mixture was stirred at room temperature for 5h. The excess of solvent was removed under reduced pressure. The residue was diluted with EtOAc (100 mL)
30 and washed with saturated NaHCO₃ aqueous solution (5 mL×2) and brine (30 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue

was purified by Pre-TLC (PE/EtOAc = 2:1, v/v) to afford the title product as an oil (55 mg, yield 65%).

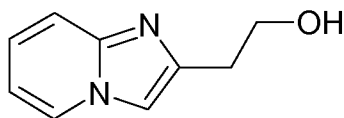
LC-MS (ESI+): m/e 208 (M+H)⁺, R_t: 1.69 min.

5 a3.10) 2-Thieno[3,2-b]pyridin-5-yl-ethanol

To a solution of methyl 2-(thieno[3,2-b]pyridin-5-yl)acetate (70 mg, 0.338 mmol) from Example a3.9) in THF (4 mL) was added LiBH₄ (8.09 mg, 0.372 mmol) in one portion. The mixture was allowed to stir at room temperature overnight. The reaction was quenched with saturated NH₄Cl solution, and then extracted with EtOAc (3×10
10 mL). The organic layer was washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. The yellow residue was used in the next step without further purification.

LC-MS (ESI+): m/e 180 (M+H)⁺, R_t: 1.57 min

15 a4) 2-(Imidazo[1,2-a]pyridin-2-yl)ethanol



a4.1) Ethyl 2-(imidazo[1,2-a]pyridin-2-yl)acetate

A mixture of ethyl 4-chloro-3-oxobutanoate (15 g, 91 mmol) and pyridin-2-amine (8.58 g, 91 mmol) in THF (80 mL) was refluxed overnight. Then, the reaction mixture
20 was concentrated and the residue purified by silica gel chromatography (PE:EA=1:1) to afford ethyl 2-(imidazo[1,2-a] pyridine-2-yl)acetate (5 g, yield 26.9 %).

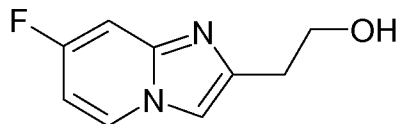
LC-MS (ESI+): m/e 205 (M+H)⁺, R_t: 0.54 min.

a4.2) 2-(Imidazo[1,2-a]pyridin-2-yl)ethanol

25 To a solution of ethyl 2-(imidazo[1,2-a]pyridin-2-yl)acetate (3.1 g, 15.18 mmol) in THF (30 mL), LiBH₄ (0.661 g, 30.4 mmol) was added and the mixture was stirred at room temperature overnight. Saturated NH₄Cl was added dropwise to quench the reaction. The solution was extracted with EA (3×100 mL). The organic phase was collected, dried over Na₂SO₄, filtered and concentrated. The title compound was used
30 without further purification in the next step.

LC-MS (ESI+): m/e 163 (M+H)⁺, R_t: 1.35 min

a5) 2-(7-Fluoroimidazo[1,2-a]pyridin-2-yl)ethanol



a5.1) 4-Fluoropyridin-2-amine

- 5 A mixture of N-(diphenylmethylene)-4-fluoropyridin-2-amine (2.0 g, 7.24 mmol) in THF (50 mL) and 1N HCl (aq) (50 mL) was stirred at about room temperature overnight. The aqueous layer was adjusted to pH>10 with 5N NaOH. The aqueous layer was extracted with ethyl acetate (3x50 mL), concentrated. The mixture was purified by column chromatography (PE/EA=4/1) to give the title compound (300 mg, yield: 37%).
- 10 LC-MS: m/e 113 (M+H); R_t : 1.36 min. ^1H NMR (CDCl_3): 4.62 (s, 2H), 6.16 (dd, $J=10.8$ Hz, 2.4, 1H) 6.38-6.42 (m, 1H), 8.00 (dd, $J=9.2$ Hz, 6 Hz, 1H).

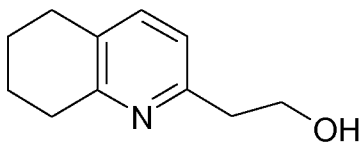
a5.2) Ethyl 2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)acetate

- 15 A mixture of 4-fluoropyridin-2-amine (1.0 g, 8.92 mmol) and ethyl 4-chloro-3-oxobutanoate (1.46 mL, 10.7 mmol) in THF (20 mL) was stirred at about reflux overnight. The residue was concentrated and was chromatographed on the C18 ISCO Combiflash system using the following gradient: A: Water (0.1% NH_4HCO_3); B: Methanol; 10%B to 60% B over 20 min to give 350 mg product as brown oil (350 mg, yield: 17.6%).
- 20 LC-MS: m/e 223 (M+H); R_t : 1.62 min; ^1H NMR (CDCl_3): 1.29 (t, 3H), 3.84 (s, 2H), 4.21 (q, 2H), 7.66-7.69 (m, 1H), 7.19 (dd, $J=8.2, 2.4$ Hz, 1H), 7.56 (s, 1H), 8.01-8.04 (m, 1H).

a5.3) 2-(7-Fluoroimidazo[1,2-a]pyridin-2-yl)ethanol

- 25 LiAlH_4 (0.171 g, 4.50 mmol) was added to the solution of ethyl 2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)acetate (0.5 g, 2.25 mmol) in THF (15 mL) and the reaction was stirred for about 2 h. The reaction was quenched with H_2O and concentrated. The residue was diluted with methanol (3 mL) and filtered. The filtrate was purified by C18 ISCO Combiflash system using the following gradient: A: Water
- 30 (0.1% NH_4HCO_3); B: Methanol; 10%B to 50%B over 20 min (100 mg, yield: 24.6%).

a6) 2-(5,6,7,8-Tetrahydroquinolin-2-yl)ethanol



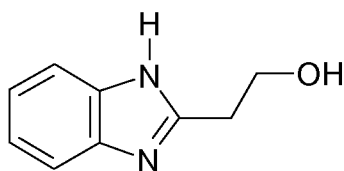
a6.1) Ethyl 2-(5,6,7,8-tetrahydroquinolin-2-yl)acetate

A solution of 7.56 g (74.7 mmol) of diisopropylamine in 100 mL of water-free THF was cooled to -30°C and n-BuLi (31.9 g, 15% solution in n-hexane, 74.7 mmol) was added via a syringe. The mixture was allowed to stir for 30 min. After cooling to -70°C, 8.68 g (74.7 mmol) tetramethylethylenediamine in 20 mL of THF were added and the mixture was allowed at -70°C for 1 h. Then, 5 g (34.00 mmol) of 2-methyl-5,6,7,8-tetrahydroquinoline and 3.87 g (35.7 mmol) of ethyl carbonochloridate were added. The mixture was allowed to warm to room temperature within 2 h while being stirring. The reaction mixture was poured onto conc. cold aqueous ammonium chloride solution and extracted with EA (3 times). The combined organic phase was once extracted with a saturated ammonium chloride solution, washed with a saturated sodium bicarbonate solution and dried (magnesium sulfate). After removal of the solvent, the crude product was purified by flash column chromatography (eluent: heptane/EA 1/2) to provide 2.16 g (29%) of the title compound).

a6.2) 2-(5,6,7,8-Tetrahydroquinolin-2-yl)ethanol

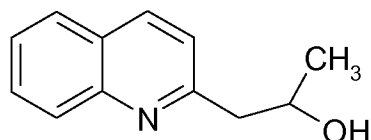
Under N₂, 4.56 mL (4.56 mmol) of lithium aluminium hydride (1M in THF) was cooled to 0°C and ethyl 2-(5,6,7,8-tetrahydroquinolin-2-yl)acetate (1 g, 4.56 mmol) dissolved in a small quantity of THF was slowly added. The mixture was allowed to stir for 1.5 h. To the reaction mixture 173 mg of H₂O in THF, 173 mg of 10% NaOH and 3x 173 mg of H₂O were added. The mixture was then stirred for 30 min. Magnesium sulfate was added. After removal of the solvent, the crude product (0.78 g, 96%) was purified by chromatography (eluent: EA/heptane 3/1) to give the title compound.

a7) 2-(1H-benzo[d]imidazol-2-yl)ethanol



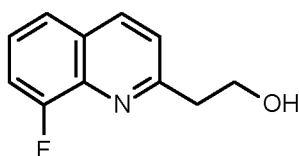
Commercially available from Sigma-Aldrich.

a8) 1-(quinolin-2-yl)propan-2-ol



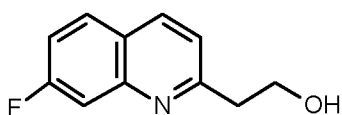
5 CAS-No.: 156538-90-8, commercially available from Enamine (Ukraine, Kiev, order number EN300-95420.

a9) 2-(8-fluoroquinolin-2-yl)ethanol



10 To a solution of formaldehyde and paraformaldehyde (0.187 g, 6.20 mmol) in 2 mL of water was added 8-fluoro-2-methylquinoline (1 g, 6.20 mmol) and then sodium hydroxide (0.37 g, 9.31 mmol) dissolved in 2 mL of water. Then 2-3 mL of ethanol were added. The mixture was stirred at 85°C for 48 hours. After cooling to room temperature, the reaction mixture was poured onto ice-water. The reaction mixture was
15 mixed with DCM and water. The organic phase was washed with water, dried and concentrated. The residue was purified by chromatography (eluent: DCM/methanol) to give 0.316 g (26.6%) of the title compound as bright yellow oily compound.

a10) 2-(7-fluoroquinolin-2-yl)ethanol



20

a10.1) tert-butyl 2-(7-fluoroquinolin-2-yl) acetate

To a solution of diisopropylamine (0.753 g, 7.45 mmol) in THF was added at -78°C n-butyl lithium (0.437 g, 6.82 mmol, 2.5 molar) over a period of 15 min. Then
25 the mixture was stirred for further 30 min at -78°C. A solution of 7-fluoro-2-

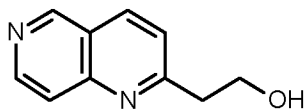
131

methylquinoline (1 g, 6.20 mmol) in 2 mL of THF was added at -78°C. After stirring for a further hour solution of di-tert-butyl dicarbonate (1.49 g, 6.82 mmol) in 1 mL of THF was added. The reaction mixture was allowed to warm up to room temperature over a period of 2 h. The reaction mixture was mixed with water and EA. The aqueous phase
5 was extracted with EA. The combined organic phases were dried and concentrated to give the title compound (790 mg, 48.7%) as red oil.

a10.2) 2-(7-fluoroquinolin-2-yl)ethanol

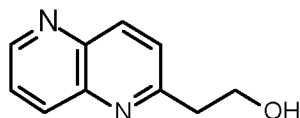
To 3.03 mL of lithiumaluminiumhydride in THF (1 molar, 115 mg, 3.03 mmol)
10 was added the compound of example a10.1 at 0°C. Then the mixture was stirred for 2 h at 0°C and then stirred at room temperature for 20 h. The reaction mixture was mixed with water and 10% by weight aq. NaOH solution. The mixture was stirred for 30 min, dried and concentrated to give 250 mg of the title compound (43.2%).

15 a11) 2-(1,6-naphthyridin-2-yl)ethanol



The title compound was prepared in analogy to the method described in example a9).

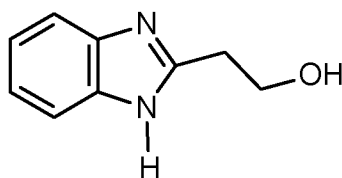
20 a12) 2-(1,5-naphthyridin-2-yl)ethanol



The title compound was prepared in analogy to the method described in example a9).

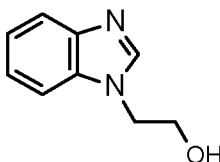
25 a13) 2-(1H-benzo[d]imidazole-2-yl)ethanol

132



Commercially available from Matrix Scientific, catalogue number 27653

a14) 2-(1H-benzo[d]imidazol-1-yl)ethanol

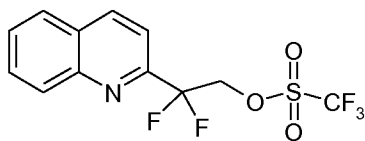


5

Commercially available from Matrix Scientific, catalogue number 054768.

b) Preparation of compounds of the general formula Het-A¹-OS(O)₂CF₃

10 b1) Trifluoromethanesulfonic acid 2,2-difluoro-2-quinolin-2-yl ethyl ester



b1.1) Difluoroquinolin-2-yl acetic acid ethyl ester

2-Bromoquinoline (5.0 g, 24.0 mmol), ethyl 2-bromodifluoroacetate (5.8 g, 28.8 mmol) and copper powder (3.5 g, 55.2 mmol) in DMSO (20 mL) were stirred at 55°C for 5 hours. The solid was filtered off, water (100 mL) and EA (150 mL) were added. The organic layer was separated, dried over sodium sulfate and concentrated to give the title compound as a yellow oil (4.2 g, 70%), which was used in the next step without further purification. LC-MS (ESI⁺): m/e 252 (M+H)⁺, R_t: 0.93 min.

20 b1.2) 2,2-Difluoro-2-quinolin-2-ylethanol

To a solution of difluoroquinolin-2-yl acetic acid ethyl ester (2 g, 7.9 mmol) in ethanol (20 mL) was added NaBH₄ (317 mg, 1.0 mmol) at 0°C under N₂. The mixture was stirred for 1 hour and then at room temperature for 1.5 hours. The solution was quenched with dilute HCl (0.1 N, 20 mL). The mixture was neutralized with saturated

NaHCO₃ solution and extracted with EtOAc (3*100 mL). The combined organic layer was dried over sodium sulfate. The solvent was evaporated and the residue was purified by column chromatography on silica gel (PE: EA=10: 1) to give the title compound as a yellow solid (0.7 g, 44%). LC-MS (ESI⁺): m/e 210 (M+H)⁺, R_t: 0.75 min.

5

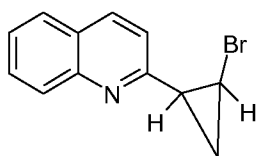
b1.3) Trifluoromethanesulfonic acid 2,2-difluoro-2-quinolin-2-yl ethyl ester

To a solution of 2,2-difluoro-2-quinolin-2-ylethanol (300 mg, 1.4 mmol) and triethylamine (217 mg, 2.1 mmol) in anhydrous DCM (5 mL) was added dropwise trifluoromethanesulphonic anhydride (606 mg, 2.1 mmol) at -70 °C. The reaction mixture was stirred for 1 hour. The resulting solution was warmed slowly to room temperature and stirred for 1 hour. The solid was removed by filtration. Water (5 mL) and DCM (30 mL) were added, the organic layer was separated, dried over sodium sulfate and evaporated to give the crude title compound as an orange oil (450 mg, 92%), which was used in the next step without further purification. LC-MS (ESI⁺): m/e 342 (M+H)⁺, R_t: 1.01 min.

10
15

c) Preparation of compounds of the general formula Het-A⁴-Br

c1) syn-2-(2-Bromocyclopropyl)quinoline



20

c1.1) (Z)-2-(2-Bromovinyl)quinoline

A suspension of 24.97 g (57.3 mmol) of (bromomethyl)triphenylphosphonium bromide in 160 mL of THF was chilled to -70 °C under argon. Then, 6.43 g (57.3 mmol) of potassium tert-butoxide were added portionwise and the suspension was allowed to stir at this temperature for 1 h. A solution of 7.5 g of (47.7 mmol) quinoline-2-carbaldehyde in 40 mL of THF was slowly added dropwise. The mixture was allowed to stir at -75 °C for further 5 hours and then warmed to room temperature overnight. 160 mL of PE were added. The precipitate formed was sucked off. The mother liquid was evaporated and the residue was stirred with diisopropyl ether. The residue formed was

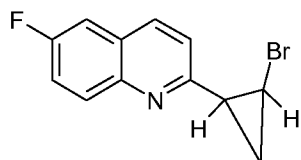
25

sucked off. Purification by chromatography (heptane/EA 3/1) yielded 6.6 g (59.1%) of the title compound.

c1.2) syn 2-(2-Bromocyclopropyl)quinoline

5 A solution of diethylzinc in hexane (5.54 g, 44.9 mL, 44.9 mmol) was chilled to 0°C under argon. Trifluoroacetic acid (5.11 g, 3.46 mL, 44.9 mmol) was added dropwise over 20 minutes. The mixture was stirred for further 20 minutes at 0° C. Then, a solution of diiodomethane (12.01 g, 3.62 mL, 44.9 mmol) in dichloromethane was added at 0°C over a period of 20 minutes. A solution of (Z)-2-(2-bromovinyl)quinoline
10 (2.1 g, 8.97 mmol) in DCM was added dropwise and the mixture was stirred over night at room temperature. The total amount of DCM was 350 mL. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride and then extracted with DCM. The organic phase was washed with water. The combined organic phases were evaporated. The residue was stirred with EA. Active charcoal was added and the
15 mixture was stirred for some further minutes. The solids were filtered off and the filtrate was concentrated. Purification by chromatography (CombiFlash Rf, normal phase chromatography, gradient elution using cyclohexane in EA up to a concentration of 15%) yielded 0.78 g (34.8%) of the title compound.

20 c2) syn 2-(2-bromocyclopropyl)-6-fluoroquinoline



c2.1) (Z)-2-(2-bromovinyl)-6-fluoroquinoline

To a suspension of (bromomethyl)triphenylphosphonium bromide (14.94 g, 34.3 mmol) in 100 mL of THF was added potassium tert-butoxide (3.84 g, 34.3 mmol)
25 portionwise under Ar. Then the reaction mixture was stirred for 1 h at this temperature. 6-Fluoroquinoline-2-carbaldehyde (5 g, 28.5 mmol) in 40 mL of THF was added. The resulting reaction mixture was stirred for 5 h at -75°C and allowed to warm up overnight. The reaction mixture was diluted with petrol ether and the solid was sucked off. The mother liquid was concentrated, diisopropyl ether was added and the formed
30 precipitate was sucked off. The mother liquid was purified by column chromatography

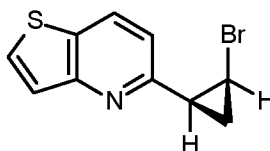
135

(cyclohexane/EA) to give 4.7 g (65.3%) of the title compound as brown solid. LC-MS: m/e 254.0.

c2.2) syn 2-(2-bromocyclopropyl)-6-fluoroquinoline

5 The title compound was prepared in analogy to the method described for example c1.2. LC-MS: 268.0

c3) syn 5-(2-bromocyclopropyl)thieno[3,2-b]pyridine

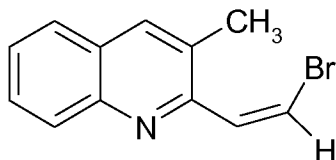


10 The title compound was prepared in analogy to the method described in example c1.2 starting from (Z)-5-(2-bromovinyl)thieno[3,2-b]pyridine. LC-MSM m/e 255.9 (M+H)⁺

d) Preparation of compounds of the general formula Het-A³-Br

15

d1) (Z)-2-(2-bromovinyl)-3-methylquinoline

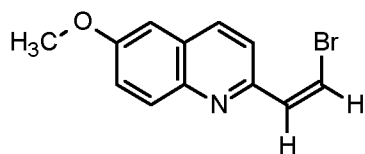


To a suspension of (bromomethyl)triphenylphosphonium bromide (3.06 g, 7.01 mmol) in 30 mL of THF, potassium tert-butoxide (0.78 g, 7.01 mmol) was added
20 portionwise at -75°C under argon. After completion of the addition, the mixture was stirred for 1 h at -75°C. Then, a solution of 3-methylquinoline-2-carbaldehyde (1 g, 5.84 mmol) in 20 mL of THF was added. The reaction mixture was stirred for 5 h at -75°C and then allowed to warm up to room temperature overnight. For work-up, the reaction mixture was diluted with diisopropyl ether (1:1) and the precipitate formed was sucked
25 off. The filtrate was concentrated and triturated in diisopropyl ether. The precipitate was sucked off. The filtrate was purified by column chromatography (normal phase, eluent:

136

cyclohexane/EA) to give 492.5 mg (34%) of the title compound as yellow solid. LC-MS: m/e 248.0 (M+H)⁺; R_t 1.561 min.

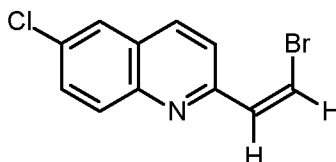
d2) (Z)-2-(2-bromovinyl)-6-methoxyquinoline



5

The title compound was prepared in analogy to the method described in example d1 but using 6-methoxyquinoline-2-carbaldehyde instead of 3-methylquinoline-2-carbaldehyde. LC-MS: m/e 265.1 (M+H)⁺; R_t 1.78 min

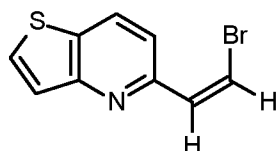
10 d3) (Z)-2-(2-bromovinyl)-6-chloroquinoline



The title compound was prepared in analogy to the method described in example d1 but using 6-chloroquinoline-2-carbaldehyde instead of 3-methylquinoline-2-carbaldehyde. LC-MS: m/e 268.1 R_t 4.609 min.

15

d4) (Z)-5-(2-bromovinyl)thieno[3,2-b]pyridine



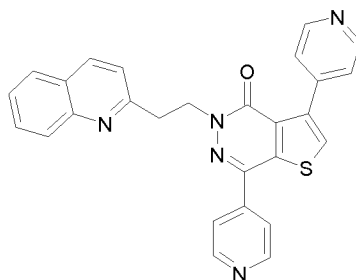
The title compound was prepared in analogy to the method described in example d1 but using thieno[3,2-b]pyridine-5-carbaldehyde. LC-MS: m/e 239.9.

20

II. Preparation of compounds of the formula I

II.1 Preparation of compounds of the formula I in which A is A¹, X¹ is N, and X³ is S

EXAMPLE 1: 3,7-Di(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one



1.1 4-Bromothiophene-3-carboxylic acid

5 To a mixture of Mg (1.4 g, 60 mmol) and I₂ (0.1 g) in anhydrous THF (2 mL) was added dropwise a solution of 2-bromo-propane (7.4 g, 60 mmol) in anhydrous THF (60 mL) at room temperature under nitrogen during a period of 30 min. After the addition, the mixture was refluxed until the most of magnesium was consumed. The resulting Grignard reagent was added dropwise to a solution of 3,4-dibromo-thiophene (12.1 g, 10 50 mmol) in anhydrous THF (60 mL) at 0 °C under nitrogen within about 30 min. The mixture was allowed to stir at 0 °C for 1.5 h. Excessive CO₂ was purged into the mixture at -30 °C and the reaction mixture was stirred until the temperature rose to room temperature. Then the reaction was quenched with water (30 mL) and basified with 8% *aq.* NaOH solution to pH 11 and was washed with ethyl acetate (3×60 mL). The 15 aqueous layer was acidified with 5% *aq.* HCl to pH 1~2, the precipitate was filtered and was dried to give the title compound as off-white solid (5.8 g, yield 56%).

LC-MS (ESI⁺): *m/e* 209 (M+H)⁺, R_t: 0.69 min.

1.2 4-Bromo-2-isonicotinoylthiophene-3-carboxylic acid

20 To a solution of diisopropylamine (5.3 g, 53 mmol) in anhydrous THF (40 mL) at -30°C was added *n*-BuLi (23.2 mL, 58 mmol, 2.5M in hexanes) dropwise. The mixture was stirred at the same temperature for 0.5 h, then cooled to -78 °C and HMPA (0.86 g, 4.8 mmol) was added slowly. Then the solution of 4-bromothiophene-3-carboxylic acid (5.0 g, 24 mmol) in anhydrous THF (50 mL) was added slowly. The mixture was stirred 25 at the same temperature for 1 h, *N*-methoxy-*N*-methyl-4-pyridinecarboxamide (8.0 g, 48 mmol) was added dropwise into the stirring mixture at -78°C. The reaction mixture was stirred for another 1 h at room temperature and was then quenched with H₂O (10 mL). The aqueous layer was acidified with 5% *aq.* HCl to pH 1~2, the precipitate was

138

collected by filtration. The filter cake was washed with DCM (10*50 mL). The title compound was dissolved in DCM; the solid insoluble in DCM was the side product. The filtrate was extracted with DCM (3*200 mL). The organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was washed with
5 DCM to give the title compound (0.8 g, yield 10.7 %) as a yellow solid.

LC-MS (ESI+): m/e 312 (M+H)⁺, R_t: 1.45 min.

1.3 Ethyl 4-bromo-2-isonicotinoylthiophene-3-carboxylate

To a solution of the compound from example 1.2 (2.5 g, 8 mmol) and Cs₂CO₃ (5.2 g, 16
10 mmol) in CH₃CN (500 mL) was added CH₃CH₂I (3.0 g, 19.2 mmol) dropwise. The mixture stirred at 30 °C for 48 h. The mixture was filtered and concentrated to give the title compound as yellow oil (2 g, 73.5% yield).

LC-MS (ESI+): m/e 340 (M+H)⁺, R_t: 0.81 min

1.4 Ethyl 2-isonicotinoyl-4-(pyridin-4-yl)thiophene-3-carboxylate

A mixture of the compound from example 1.3 (500 mg, 1.47 mmol), 4-pyridineboronic acid (271 mg, 2.21 mmol), Na₂CO₃ (390 mg, 3.68 mmol) and Pd(dppf)Cl₂ (122 mg, 0.15 mmol) in dioxane/H₂O (3:1) (12 mL) was stirred at 100°C under argon for 2 h. The mixture was concentrated and the residue was purified by Prep-HPLC to give the title
20 product as white solid (318 mg, 64 % yield).

LC-MS (ESI+): m/e 339 (M+H)⁺, R_t: 0.61 min

1.5 3,7-Di(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one

A mixture of the compound from example 1.4 (200 mg, 0.59 mmol) in
25 NH₂NH₂·H₂O (2 mL) and EtOH (10 mL) was stirred at room temperature for 30 min. The mixture was filtered and the solid was dried to obtain the title compound as a white solid (150 mg, 83.1%). LC-MS (ESI+): m/e 307 (M+H)⁺, R_t: 1.56 min.

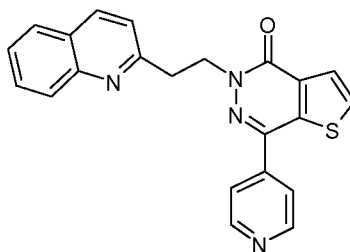
1.6 3,7-Di(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

30 To a solution of 3,7-di(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one from example 1.5 (100 mg, 0.32 mmol), 2-quinolin-2-yl-ethanol from example a1 (58 mg, 0.33 mmol) and PPh₃ (256 mg, 0.98 mmol) in DCM (10 mL), DIAD (198 mg, 0.98

mmol) was added dropwise. The mixture was stirred at room temperature for 3h, concentrated and the residue was purified by Prep-HPLC to give the title compound as white solid (26 mg, 17.6% yield).

LC-MS (ESI+): m/e 462 (M+H)⁺, R_t : 2.00 min; ¹H-NMR(DMSO-*d*, 400MHz): δ
5 3.46 (t, J = 7.2 Hz, 2H), 4.71 (t, J = 7.2 Hz, 2H), 7.49-7.51 (m, 3H), 7.54-7.57 (m, 1 H),
7.62 (dd, J = 4.4, 1.6 Hz, 2H), 7.68-7.72 (m, 1 H), 7.84 (d, J = 8.4 Hz, 1H), 7.94 (d, J =
7.2 Hz, 1H), 8.28-8.30 (m, 2H), 8.60 (dd, J = 4.6, 1.6 Hz, 2H), 8.70 (dd, J = 4.6, 1.6 Hz,
2H).

10 EXAMPLE 2: 7-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-
4(5H)-one



2.1 2-Isonicotinoylthiophene-3-carboxylic acid

To a solution of diisopropylamine (5.2 g, 51.5 mmol) in anhydrous THF (40 mL)
15 at -30°C was added n-BuLi (23.2 mL, 56.2 mmol, 2.5M in THF) dropwise. The mixture
was stirred at the same temperature for 0.5 h, then cooled to -78°C and HMPA (0.8 g,
4.7 mmol) was added slowly. Then a solution of thiophene-3-carboxylic acid (3.0 g,
23.4 mmol) in anhydrous THF (50 mL) was added slowly. The mixture was stirred at
the same temperature for 1 h, *N*-methoxy-*N*-methyl-4-pyridinecarboxamide (5.0 g, 46.9
20 mmol) was added drop wise into the stirring mixture at -78°C. The reaction mixture
was stirred for another 1 h at room temperature and was then quenched with H₂O (10
mL). The aqueous layer was acidified with 5% *aq.* HCl to pH 1~2, the precipitate was
collected by filtration. The filter cake wash with DCM and the filtrate was extracted
with DCM (3×200 mL). The organic layers were dried over Na₂SO₄ and concentrated
25 under reduced pressure. The crude product was washed with DCM to give the title
product (2.2 g, yield 40 %) as a white solid.

LC-MS (ESI+): m/e 234 (M+H)⁺, R_t : 0.57 min.

140

2.2 Ethyl 2-isonicotinoylthiophene-3-carboxylate

To a solution of 2-isonicotinoylthiophene-3-carboxylic acid (2.2 g, 9.4 mmol) from example 2.1 and Cs_2CO_3 (6.2 g, 18.9 mmol) in CH_3CN (500 mL) was added $\text{CH}_3\text{CH}_2\text{I}$ (2.9 g, 18.9 mmol) dropwise. The mixture was stirred at 30 °C for 48 h. The mixture was filtered and concentrated to give the title compound as yellow oil (2.1 g, 85.5% yield).

LC-MS (ESI+): m/e 340 ($\text{M}+\text{H}$)⁺, R_t : 0.81 min

2.3 7-(Pyridin-4-yl)thieno[3,2-d]pyridazin-4(5H)-one

The mixture of ethyl 2-isonicotinoylthiophene-3-carboxylate (200 mg, 0.77 mmol) from example 2.2 in $\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$ (2 mL) and EtOH (10 mL) was stirred at room temperature for 30 min. The mixture was filtered and the solid dried to obtain the title compound (150 mg, 85.1% yield).

LC-MS (ESI+): m/e 230 ($\text{M}+\text{H}$)⁺, R_t : 1.52 min.

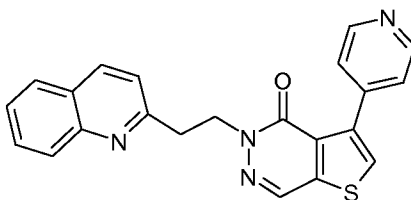
2.4 7-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

To a solution of 7-(pyridin-4-yl)thieno[3,2-d]pyridazin-4(5H)-one (100 mg, 0.44 mmol) from example 2.3, 2-quinolin-2-yl-ethanol from example a1 (83 mg, 0.48 mmol) and PPh_3 (343 mg, 1.31 mmol) in DCM (10 mL), DEAD (228 mg, 1.31 mmol) was added dropwise. The mixture stirred at room temperature for 3 h, concentrated and the purified by Prep-HPLC to give the title compound as a white solid (20 mg, 11.8% yield).

LC-MS (ESI+): m/e 385 ($\text{M}+\text{H}$)⁺, R_t : 1.87 min; $^1\text{H-NMR}$ (DMSO-*d*₆, 400 MHz): δ 3.49 (t, J = 7.2 Hz, 2H), 4.76 (t, J = 7.2 Hz, 2H), 7.49-7.57 (m, 2H), 7.58 (dd, J = 4.4, 1.6 Hz, 2H), 7.67-7.72 (m, 1 H), 7.78 (d, J = 5.2 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 7.6 Hz, 1H), 8.21 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 8.66 (dd, J = 4.2, 1.6 Hz, 2H).

EXAMPLE 3: 3-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

141



3.1 4-Bromo-2-formyl-thiophene-3-carboxylic acid

To a solution of (i-Pr)₂NH (1.09 g, 10.8 mmol) in anhydrous THF (15 mL) was added dropwise n-BuLi (5.0 mL, 12.5 mmol, 2.5M in hexane) at -30°C. The mixture was stirred at the same temperature for 0.5 h. Then, the mixture was cooled to -78°C and the solution of 4-bromothiophene-3-carboxylic acid from example 1.1 (1.0 g, 4.85 mmol) and HMPA (0.17 g, 0.95 mmol) in anhydrous THF (20 mL) was added slowly. The mixture was stirred at the same temperature for 1 h, anhydrous DMF (0.6 g, 8.22 mmol) was added dropwise into the stirring mixture at -78°C. The reaction mixture was stirred for another 45 min at room temperature and then quenched with water. The aqueous layer was acidified with 5% *aq.* HCl to pH 1~2, the precipitate was collected by filtration, the filtrate was extracted with DCM (3×50 mL). The organic layers were dried over Na₂SO₄ and concentrated under reduced pressure. The crude product was washed with CH₂Cl₂ to give the title product (0.68 g, 60.2 %) as a solid.

LC-MS: m/e (M+H)⁺: 235.7; R_t: 0.64 min.

3.2 4-Bromo-2-formyl-thiophene-3-carboxylic acid ethyl ester

4-Bromo-2-formyl-thiophene-3-carboxylic acid (0.16 g, 0.68 mmol), K₂CO₃ (0.188 g, 1.36 mmol), and 4 mL of anhydrous DMF were stirred at room temperature for 10 min, then iodoethane was added (0.128 g, 0.8 mmol) dropwise. The reaction solution was stirred at 50 °C for 3h. The reaction mixture was cooled, extracted with EA (3 x 50 mL), concentrated and the residue was purified by TLC (PE/EA =8/1) to give 0.4 g of the title compound (yield: 63.5%).

LC-MS: m/e (M+H)⁺: 263.7, R_t: 0.88 min.

3.3 3-Bromo-5H-thieno[2,3-d]pyridazin-4-one

4-Bromo-2-formyl-thiophene-3-carboxylic acid ethyl ester (1.0 g, 3.8 mmol), NH₂NH₂·H₂O (0.27 g, 4.58 mmol) and 20 mL of EtOH were refluxed under nitrogen

for 5h. The reaction mixture was cooled and precipitate formed, then filtered to give the title compound (0.2 g, yield: 23%).

LC-MS: m/e (M+H)⁺: 231.7, R_t : 1.29 min

5 3.4 3-Bromo-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

To a stirred solution of PPh₃ (977 mg, 3.73 mmol) and DEAD (1.13 mL) in 15 mL of anhydrous THF was added a solution of 3-bromo-5H-thieno[2,3-d]pyridazin-4-one (429 mg, 1.86 mmol) and 2-quinolin-2-yl-ethanol from example a1 (355 mg, 2.05 mmol) in 15 mL of anhydrous THF while being cooled with an ice-bath. Then the
10 resulting mixture was stirred in nitrogen atmosphere at 45°C overnight. The reaction mixture was concentrated and the product was recrystallized from EA to give the title compound (370 mg, 53.6%).

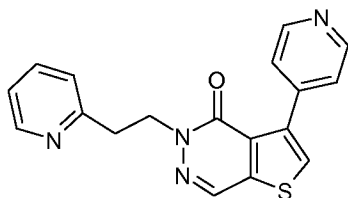
LC-MS: m/e (M+H)⁺: 386.7, R_t : 2.02 min

15 3.5 3-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

3-Bromo-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one (130 mg, 0.33 mmol), pyridine-4-ylboronic acid (45.7 mg, 0.37 mmol), Pd(dppf)Cl₂ (15 mg) and K₂CO₃ (93 mg, 0.67 mmol) were dissolved in dioxane/H₂O (3/1, 2.8 mL). The mixture was stirred in nitrogen atmosphere at 120°C for 1h in a microwave tube. The solution
20 was concentrated and purified by TLC (DCM/MeOH =10/1) and recrystallized from MeOH to give the title product (90 mg, 69.4%).

LC-MS: m/e (M+H)⁺: 385.7, R_t : 1.90 min. ¹H NMR (DMSO, 400MHz) δ : 8.48-8.45 (m, 3H), 8.25 (d, J= 8.4Hz, 1H), 8.02 (s, 1H), 7.93-7.88 (m, 2H), 7.72 (t, J= 8.4Hz, 1H), 7.58 (t, J=7.2Hz, 1H), 7.48-7.42 (m, 3H), 4.72 (t, J= 7.0 Hz, 2H), 3.49 (t, J= 7.0
25 Hz, 2H)

EXAMPLE 4: 3-(Pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one



143

4.1 3-Bromo-5-(2-pyridin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one

The title compound was prepared in analogy to the process described in Example 3.4 starting from 3-bromo-5H-thieno[2,3-d]-pyridazin-4-one and 2-pyridin-2-yl-ethanol. Yield: 76.3%.

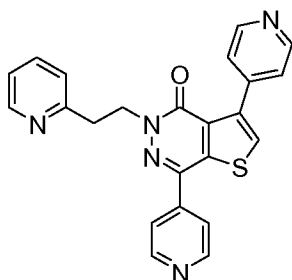
5 LC-MS: m/e (M+H)⁺: 336.7, R_t: 1.51 min

4.2 3-(Pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

The title compound was prepared in analogy to the process described in Example 3.5 starting from 3-bromo-5-(2-pyridin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one and pyridine-4-ylboronic acid. Yield: 33.1%.

LC-MS: m/e (M+H): 335.7, R_t: 1.69 min. ¹H NMR (DMSO, 400MHz) δ : 8.60 (d, J= 5.2Hz, 2H), 8.47 (d, J= 4.4Hz, 1H), 8.16 (s, 1H), 7.53-7.48 (m, 2H), 7.43 (d, J=5.2Hz, 2H), 7.11-7.04 (m, 2H), 4.57 (t, J= 7.6 Hz, 2H), 3.24 (t, J= 7.4 Hz, 2H).

15 EXAMPLE 5: 3,7-Di(pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one



5.1 3-Bromo-7-pyridin-4-yl-5H-thieno[2,3-d]pyridazin-4-one

The title compound was prepared in analogy to the process described in Example 3.3 starting from ethyl 4-bromo-2-isonicotinoyl-thiophene-3-carboxylic acid from Example 1.3. Yield: 56.8%.

LC-MS: m/e (M+H)⁺: 308.7, R_t: 1.59 min.

25 5.2 3-Bromo-7-pyridin-4-yl-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

The title compound was prepared in analogy to the process described in Example 3.4 starting from 3-bromo-7-pyridin-4-yl-5H-thieno[2,3-d]pyridazin-4-one and 2-pyridin-2-yl-ethanol. Yield: 70%.

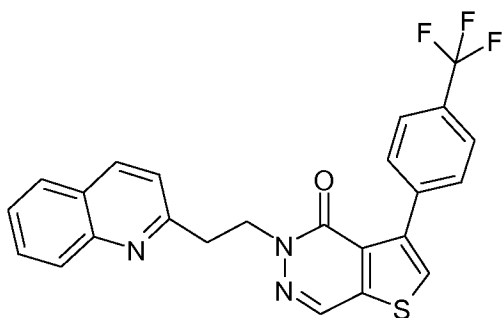
LC-MS: m/e (M+H)⁺: 413.7; R_t : 1.84 min.

5.3 3,7-Di(pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

The title compound was prepared in analogy to the process described in Example 3.5 starting from 3-bromo-7-pyridin-4-yl-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one and pyridine-4-ylboronic acid. Yield: 75.2%.

LC-MS: m/e (M+H)⁺: 412.7, R_t : 1.71 min; ¹H NMR (DMSO, 400MHz) δ : 8.78 (d, J = 5.2Hz, 2H), 8.71 (d, J = 4.4Hz, 2H), 8.56 (d, J = 4.8Hz, 1H), 7.70-7.67 (m, 3H), 7.60 (t, J = 7.6Hz, 1H), 7.51 (d, J = 5.2 Hz, 2H), 7.21 (d, J = 7.6 Hz, 1H), 7.17-7.14 (m, 1H), 4.75 (t, J = 7.6 Hz, 2H), 3.37 (t, J = 7.4 Hz, 2H).

EXAMPLE 6: 5-[2-(Quinolin-2-yl)ethyl]-3-[4-(trifluoromethyl)phenyl]thieno[2,3-d]pyridazin-4(5H)-one



3-Bromo-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one Example 3.4 (100 mg, 0.26 mmol), 4-(trifluoromethyl)phenylboronic acid (0.26 mmol), Pd(dppf)Cl₂ (12.7 mg) and K₂CO₃ (72 mg, 0.527 mmol) were dissolved in dioxane/H₂O (3/1, 2.8 mL). The mixture was stirred at 110°C for 0.5 h in a microwave tube. The solution was concentrated and purified by prep-TLC to give the title product.

LC-MS: m/e (M+H)⁺: 452, R_t : 2.36, ¹H NMR (CDCl₃, 400 MHz) δ : 3.50 (t, 2H, J = 7.6 Hz), 4.75 (t, 2H, J = 7.6 Hz), 7.33 (d, 1H, J = 4.4 Hz), 7.48-7.53 (m, 2H), 7.59-7.69 (m, 5H), 7.78 (d, 1H, J = 7.6 Hz), 8.00 (d, 1H, J = 8.0), 8.06 (d, 1H, J = 8.0 Hz), 8.23 (s, 1H)

Examples 7 to 92 were prepared analogously to the method described for Example 6.

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
7	3-(4-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	398 / 2.32	2.40 (s, 3H), 3.50 (t, 2H, J=7.6 Hz), 4.73 (t, 2H, J=7.6 Hz), 7.22 (d, 2H, J=8.0 Hz), 7.32 (d, 1H, J=7.6 Hz), 7.40 (d, 2H, J=7.6 Hz), 7.45 (s, 1H), 7.49 (t, 1H, J=7.2 Hz), 7.67 (t, 1H, J=7.2 Hz), 7.77 (d, 1H, J=7.6 Hz), 8.01-8.06 (m, 2H), 8.19 (s, 1H)
8	3-[4-(propan-2-yl)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	426 / 2.46	1.29 (d, 6H, J=6.8 Hz), 2.95 (m, 1H), 3.49 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=8 Hz), 7.27~7.31 (m, 3H), 7.44~7.49 (m, 4H), 7.66 (t, 1H, J=8.4 Hz), 7.75 (d, 1H, J=8 Hz), 8.01~8.04 (m, 2H), 8.18 (s, 1H)
9	3-(4-ethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	412 / 2.34	1.28 (t, 3H, J=7.6 Hz), 2.70 (q, 2H, J=7.6 Hz), 3.49 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.25 (d, 2H, J=8.0 Hz), 7.31 (d, 1H, J=8.4 Hz), 7.44-7.50 (m, 4H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.4 Hz), 8.00-8.05 (m, 2H), 8.19 (s, 1H)
10	4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl} benzonitrile	409 / 2.11	3.49 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.33 (d, 1H, J=8.0 Hz), 7.50-7.58 (m, 4H), 7.66-7.68 (m, 3H), 7.79 (d, 1H, J=7.6 Hz), 7.98 (d, 1H, J=8.0 Hz), 8.07 (d, 1H, J=8.0 Hz), 8.25 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
11	3-(4-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	414 / 2.18	3.50 (t, 2H, J=7.6 Hz), 3.85 (s, 3H), 4.74 (t, 2H, J=7.6 Hz), 6.94 (d, 2H, J=8.4 Hz), 7.31 (d, 1H, J=8.4 Hz), 7.42-7.51 (m, 4H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.4 Hz), 8.00-8.06 (m, 2H), 8.19 (s, 1H)
12	3-(4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	402 / 2.21	3.50 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.06-7.11 (m, 2H), 7.32 (d, 1H, J=8.4 Hz), 7.45-7.52 (m, 4H), 7.65-7.69 (m, 1H), 7.78 (d, 1H, J=8.4 Hz), 8.01 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.21 (s, 1H)
13	3-(4-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	428 / 2.26	1.44 (t, 3H, J=6.8 Hz), 3.49 (t, 2H, J=7.6 Hz), 4.05~4.11 (m, 2H), 4.74 (t, 2H, J=7.6 Hz), 6.93 (d, 2H, J=8.4 Hz), 7.32 (d, 1H, J=8.4 Hz), 7.42~7.51 (m, 4H), 7.67 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=8 Hz), 8.00~8.06 (m, 2H), 8.19 (s, 1H)
14	3-[4-(dimethylamino)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	427 / 2.26	2.99 (s, 6H), 3.50 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=7.6 Hz), 6.77 (d, 2H, J=8.8 Hz), 7.31 (d, 1H, J=8.8 Hz), 7.38 (s, 1H), 7.43-7.51 (m, 3H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.0 Hz), 8.01-8.05 (m, 2H), 8.16 (s, 1H).

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
15	(4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}phenyl)acetonitrile	423 / 2.10	3.49 (t, 2H, J=7.6 Hz), 3.79 (s, 3H), 4.73 (t, 2H, J=7.6 Hz), 7.31-7.37 (m, 3H), 7.48-7.51 (m, 4H), 7.65-7.69 (m, 1H), 7.99 (d, 1H, J=8.4 Hz), 8.05 (d, 1H, J=8.4 Hz), 8.22 (s, 1H)
16	3-(4-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	400 / 2.00	2.17 (s, 1H), 3.53 (t, 2H, J=7.6 Hz), 4.77 (t, 2H, J=7.6 Hz), 7.80 (d, 2H, J=8.8 Hz), 7.33~7.42 (m, 4H), 7.51 (t, 1H, J=7.2 Hz), 7.69 (t, 1H, J=7.2 Hz), 7.79 (d, 1H, J=7.6 Hz), 8.08 (d, 2H, J=8.4 Hz), 8.22 (s, 1H)
17	3-(2-chlorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	418 / 2.22	3.47 (t, 2H, J=7.6 Hz), 4.71 (t, 2H, J=7.6 Hz), 7.28-7.36 (m, 4H), 7.46-7.50 (m, 3H), 7.64-7.68 (m, 1H), 7.76 (d, 1H, J=8.0 Hz), 8.00-8.04 (m, 2H), 8.21 (s, 1H).
18	3-(2-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	398 / 2.29	2.09 (s, 3H), 3.48 (t, 2H, J=7.6 Hz), 4.69 (t, 2H, J=7.6 Hz), 7.17-7.33 (m, 5H), 7.37 (s, 1H), 7.49 (t, 1H, J=7.2 Hz), 7.67 (t, 1H, J=7.2 Hz), 7.76 (d, 1H, J=8.0 Hz), 7.99-8.05 (m, 2H), 8.22 (s, 1H)
19	3-(2-ethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	412 / 2.36	1.02 (t, 3H, J=7.6 Hz), 2.36~2.49 (m, 2H), 3.47 (t, 2H, J=7.6 Hz), 4.65~4.71 (m, 2H), 7.15 (d, 1H, J=7.2 Hz), 7.02~7.38 (m, 6H), 7.49 (m, 1H, J=7.6 Hz), 7.77 (d, 1H, J=8 Hz), 7.99~8.04 (m, 2H), 8.22 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
20	3-(2-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	402 / 2.16	3.49 (t, 2H, J=7.6 Hz), 4.73 (t, 2H, J=7.6 Hz), 7.14~7.21 (m, 2H), 7.26~7.31 (m, 1H), 7.38 (t, 2H, J=7.6 Hz), 7.48 (t, 1H, J=7.6 Hz), 7.54 (s, 1H), 7.67 (t, 1H, J=7.6 Hz), 7.76 (d, 1H, J=8 Hz), 8.02 (t, 2H, J=7.6 Hz), 8.20 (s, 1H)
21	3-(2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	414 / 2.22	3.47 (t, 2H, J=7.2Hz), 3.74(s, 3H), 4.69 (t, 2H, J=7.6Hz), 6.97~7.02 (m, 2H), 7.28 (t, 2H, J=8.4Hz), 7.38 (t, 1H, J=8Hz), 7.48 (t, 2H, J=7.6Hz), 7.67 (t, 1H, J=7.6Hz), 7.76 (d, 1H, J=8Hz), 8.03 (d, 2H, J=8.4Hz), 8.17 (s, 1H)
22	3-(2-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	428 / 2.31	1.18 (t, 3H, J=6.8 Hz), 3.47 (t, 2H, J=7.6 Hz), 4.01~4.06 (m, 2H), 4.69 (t, 2H, J=7.6 Hz), 6.96~7.01 (m, 2H), 7.27~7.36 (m, 3H), 7.48 (t, 2H, J=8.8 Hz), 7.67 (t, 1H, J=7.2 Hz), 7.76 (d, 1H, J=8.4 Hz), 8.03 (d, 2H, J=8 Hz), 8.18 (s, 1H)
23	3-(2-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	400 / 2.04	3.52 (t, 2H, J=7.6 Hz), 4.83 (t, 2H, J=7.6 Hz), 7.05 (t, 1H, J=8 Hz), 7.17 (d, 1H, J=7.6 Hz), 7.27~7.38 (m, 3H), 7.48~7.55 (m, 2H), 7.68 (t, 1H, J=7.6 Hz), 7.78 (d, 1H, J=7.2 Hz), 8.01~8.08 (m, 2H), 8.32 (s, 1H), 8.71 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
24	5-[2-(quinolin-2-yl)ethyl]-3-[2-(trifluoromethyl)phenyl]thieno[2,3-d]pyridazin-4(5H)-one	452 / 2.30	3.47 (t, 2H, J=7.6 Hz), 4.67 (t, 2H, J=7.6 Hz), 7.25-7.29 (m, 2H), 7.47-7.57 (m, 4H), 7.66-7.58 (m, 3H), 8.02=8.04 (m, 2H), 8.22 (s, 1H)
25	3-[3-(methoxymethyl)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	428 / 2.16	3.42 (s, 1H), 3.49 (t, 2H, J=7.6 Hz), 4.52 (s, 2H), 3.79 (s, 3H), 4.74 (t, 2H, J=7.6 Hz), 7.31 (d, 1H, J=8.4 Hz), 7.35-7.51 (m, 6H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.0 Hz), 7.99-8.05 (m, 2H), 8.20 (s, 1H)
26	3-(3-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	414 / 2.19	3.50 (t, 2H, J=7.6 Hz), 3.83 (s, 3H), 4.74 (t, 2H, J=7.6 Hz), 6.92-6.95 (m, 1H), 7.07-7.12 (m, 2H), 7.31-7.35 (m, 2H), 7.47-7.51 (m, 2H), 7.66-7.70 (m, 1H), 7.77 (d, 1H, J=8.4 Hz), 8.01-8.06 (m, 2H), 8.20 (s, 1H)
27	3-(3-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	428 / 2.27	1.43 (t, 3H, J=6.8 Hz), 3.50 (t, 2H, J=7.2 Hz), 4.06 (q, 2H, J=6.8 Hz), 4.74 (t, 2H, J=7.2 Hz), 6.91-6.94 (m, 2H), 7.07-7.09 (m, 2H), 7.29-7.33 (m, 2H), 7.47-7.51 (m, 2H), 7.65-7.78 (m, 2H), 8.01-8.06 (m, 2H), 8.20 (s, 1H)

150

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
28	3-[3-(dimethylamino)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	427 / 2.26	2.97 (s, 6H), 3.49 (t, 2H, J=7.2 Hz), 4.73 (t, 2H, J=7.6 Hz), 6.77 (dd, 1H, J=2.4 Hz, J=8.4 Hz), 6.85-6.88 (m, 2H), 7.26-7.32 (m, 2H), 7.47-7.51 (m, 2H), 7.65-7.77 (m, 2H), 8.03 (t, 2H, J=7.6 Hz), 8.19 (s, 1H)
29	3-[4-Oxo-5-(2-quinolin-2-yl-ethyl)-4,5-dihydro-thieno[2,3-d]pyridazin-3-yl}-benzonitrile	409 / 2.11	3.49 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.35 (d, 1H, J=8.4 Hz), 7.47~7.52 (m, 3H), 7.65~7.73 (m, 4H), 7.79 (d, 1H, J=8 Hz), 7.97 (d, 1H, J=8.4 Hz), 8.08 (d, 1H, J=8.4 Hz), 8.24 (s, 1H)
30	3-(3-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	402 / 2.21	3.49 (t, 2H, J=7.6 Hz), 4.47 (t, 2H, J=7.6 Hz), 7.06-7.11 (m, 1H), 7.20-7.24 (m, 1H), 7.27-7.39 (m, 3H), 7.47-7.51 (m, 2H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.0 Hz), 8.00 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.21 (s, 1H)
31	3-(3-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	400 / 2.00	3.51 (t, 2H, J=7.6 Hz), 3.76 (s, 1H), 4.72 (t, 2H, J=7.6 Hz), 6.85 (d, 1H, J=1.6 Hz, J=8.0 Hz), 6.99-7.02 (m, 2H), 7.23 (t, 1H, J=8.0 Hz), 7.34 (d, 1H, J=8.8 Hz), 7.48-7.53 (m, 2H), 7.66-7.70 (m, 1H), 7.78 (d, 1H, J=8.0 Hz), 8.03-8.08 (m, 2H), 8.21 (s, 1H)

151

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
32	N,N-dimethyl-3-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}benzamide	455 / 1.97	3.09 (d, 6H, J=17.6 Hz), 3.50 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.31 (d, 1H, J=8.4 Hz), 7.43~7.51 (m, 6H), 7.65~7.69 (m, 1H), 7.78 (d, 1H, J=8.4 Hz), 8.00 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.21 (s, 1H)
33	3-(3-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	398 / 2.08	2.40 (s, 3H), 3.49 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.19-7.21 (m, 1H), 7.30-7.33 (m, 4H), 7.45 (s, 1H), 7.49 (t, 1H, J=7.6 Hz), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=7.6 Hz), 8.01 (d, 1H, J=8.4 Hz), 8.04 (d, 1H, J=8.4 Hz), 8.19 (s, 1H)
34	5-[2-(quinolin-2-yl)ethyl]-3-(thiophen-2-yl)thieno[2,3-d]pyridazin-4(5H)-one	390 / 1.53	3.92 (t, 2H, J=6.4 Hz), 4.81 (t, 2H, J=6.4 Hz), 7.02-7.04 (m, 1H), 7.32 (d, 1H, J=3.6 Hz), 7.38 (d, 1H, J=3.6 Hz), 7.62 (s, 1H), 7.71 (d, 1H, J=8.4 Hz), 7.82 (t, 1H, J=7.6 Hz), 8.01-8.05 (m, 2H), 8.17 (s, 1H), 8.52 (d, 1H, J=8.4 Hz), 8.64 (d, 1H, J=8.4 Hz)
35	3-(1-methyl-1H-indol-5-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one	437 / 2.23	3.49 (t, 2H, J=7.8 Hz), 3.82 (s, 3H), 4.73 (t, 2H, J=8 Hz), 6.51 (d, 1H, J=2.8 Hz), 7.07 (d, 1H, J=2.8 Hz), 7.26~7.48 (m, 5H), 7.65~7.77 (m, 3H), 8.01~8.04 (m, 2H), 8.20 (s, 1H)
36	3-(1H-indol-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	423 / 2.14	3.49 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 6.57 (s, 1H), 7.25-7.32 (m, 2H), 7.48-7.52 (m, 2H), 7.59 (s, 1H), 7.65-7.70 (m, 2H), 7.78 (d, 1H, J=8.0 Hz), 8.04 (t, 2H, J=8.4 Hz), 8.22 (s, 1H), 8.28 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
37	3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	386 / 1.73,	3.50 (t, 2H, J=7.6 Hz), 4.76 (t, 2H, J=7.6 Hz), 7.34 (d, 1H, J=8.4 Hz), 7.49 (t, 1H, J=8.0 Hz), 7.61 (s, 1H), 7.66 (t, 1H, J=8.0 Hz), 7.78 (d, 2H, J=8.4 Hz), 7.96 (d, 1H, J=8.4 Hz), 8.07 (d, 1H, J=8.4 Hz), 8.26 (s, 1H), 8.76 (s, 2H), 9.22 (s, 1H)
38	3-(2-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	415 / 2.06	3.48 (t, 2H, J=7.6 Hz), 3.90 (s, 3H), 4.71 (t, 2H, J=7.6 Hz), 6.93-6.96 (m, 1H), 7.30 (d, 1H, J=8.4 Hz), 7.49 (t, 1H, J=7.6 Hz), 7.56-7.59 (m, 2H), 7.67 (t, 2H, J=7.6 Hz), 7.77 (d, 1H, J=8.0 Hz), 8.00-8.05 (m, 2H), 8.19 (s, 1H), 8.21 (dd, 1H, J=1.2, J=5.2 Hz)
39	3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	385 / 1.91	3.49 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=7.6 Hz), 7.32-7.36 (m, 2H), 7.49 (t, 1H, J=8.0 Hz), 7.55 (s, 1H), 7.64-7.69 (m, 1H), 7.77 (d, 1H, J=8.0 Hz), 7.88 (d, 1H, J=8.0 Hz), 8.06 (d, 1H, J=8.8 Hz), 8.23 (s, 1H), 8.62 (br, 1H), 8.73 (br, 1H).
40	3-(4-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	415 / 1.90	3.47 (t, 2H, J=7.6 Hz), 3.79 (s, 3H), 4.70 (t, 2H, J=7.6 Hz), 6.91 (d, 1H, J=5.6 Hz), 7.30 (d, 1H, J=8 Hz), 7.47~7.51 (m, 2H), 7.68 (t, 1H, J=7.2 Hz), 7.77 (d, 1H, J=7.6 Hz), 8.00~8.06 (m, 2H), 8.20 (s, 1H), 8.37 (s, 1H), 8.54 (d, 1H, J=5.6 Hz)

153

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
41	3-(furan-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	374 / 2.14	3.53 (t, 2H, J=7.6 Hz), 4.77 (t, 2H, J=7.6 Hz), 6.76 (d, 1H, J=1.2 Hz), 7.35 (d, 1H, J=8.8 Hz), 7.46~7.52 (m, 3H), 7.68 (t, 1H, J=7.6 Hz), 7.78 (d, 1H, J=8 Hz), 8.02~8.08 (m, 2H), 8.15 (s, 1H), 8.23 (s, 1H)
42	3-(quinolin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	435 / 1.93	3.50 (t, 2H, J=7.6 Hz), 4.76 (t, 2H, J=7.6 Hz), 7.32 (d, 1H, J=8.4 Hz), 7.49 (t, 1H, J=7.6 Hz), 7.57 (t, 1H, J=7.6 Hz), 7.65~7.69 (m, 4H), 7.85 (d, 1H, J=8.4 Hz), 7.99 (d, 1H, J=8.4 Hz), 8.05 (d, 1H, J=8.4 Hz), 8.14 (d, 1H, J=8.4 Hz), 8.31 (s, 1H), 9.06 (s, 1H)
43	3-(isoquinolin-4-yl)-5-[2-(quinolin-2-yl)ethyl]-thieno[2,3-d]pyridazin-4(5H)-one	435 / 1.89	3.42 (t, 2H, J=7.6 Hz), 4.62~4.68 (m, 2H), 7.25 (d, 1H, J=8.0 Hz), 7.47~7.68 (m, 7H), 7.76 (d, 1H, J=8.4 Hz), 7.95~8.04 (m, 3H), 8.29 (s, 1H), 8.45 (s, 1H), 8.30 (s, 1H)
44	3-(isoquinolin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	435 / 1.87	3.43 (t, 2H, J=7.6 Hz), 4.65 (t, 2H, J=7.6 Hz), 7.25~7.30 (m, 2H), 7.47~7.51 (m, 1H), 7.56 (s, 1H), 7.63~7.68 (m, 3H), 7.76 (d, 1H, J=8.0 Hz), 7.95~8.05 (m, 2H), 8.30 (s, 1H), 8.36 (d, 1H, J=7.0 Hz), 8.30 (s, 1H)
45	3-(1H-indol-4-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one	423 / 2.10	3.47 (t, 2H, J=7.6 Hz), 4.71 (t, 2H, J=7.6 Hz), 6.26 (s, 1H), 7.05 (s, 1H, J=2.4 Hz), 7.15~7.33 (m, 4H), 7.46 (t, 1H, J=7.2 Hz), 7.61~7.67 (m, 2H), 7.74 (d, 1H, J=8.4 Hz), 8.00 (d, 2H, J=8.4 Hz), 8.22 (s, 1H), 8.49 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
46	3-(2,3-dihydrobenzofuran-5-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one	426 / 2.19	3.26 (t, 2H, J=8.4 Hz), 3.50 (t, 2H, J=7.6 Hz), 4.61 (t, 2H, J=8.8 Hz), 4.74 (t, 2H, J=7.6 Hz), 6.81 (d, 1H, J=8.4 Hz), 7.23~7.40 (m, 4H), 7.49 (t, 1H, J=7.6 Hz), 7.67 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=8 Hz), 8.00~8.06 (m, 2H), 8.19 (s, 1H)
47	3-(quinolin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	435 / 1.88	3.43 (t, 2H, J=7.6 Hz), 3.98 (s, 3H), 4.74 (t, 2H, J=7.6 Hz), 7.21-7.27 (m, 2H), 7.47-7.51 (m, 2H), 7.55 (s, 1H), 7.64-7.77 (m, 3H), 7.83 (d, 1H, J=8.4 Hz), 7.97 (d, 1H, J=8.4 Hz), 8.01 (d, 1H, J=8.4 Hz), 8.18 (d, 1H, J=8.8 Hz), 8.29 (s, 1H), 8.90 (d, 1H, J=2.8 Hz)
48	3-(3,5-dimethyl-1,2-oxazol-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	403 / 2.01	2.07 (s, 3H), 2.25 (s, 3H), 3.49 (t, 2H, J=7.6 Hz), 4.71~4.75 (m, 2H), 7.35 (t, 2H, J=8.4 Hz), 7.49 (t, 1H, J=8 Hz), 7.66 (t, 1H, J=8.4 Hz), 7.77 (d, 1H, J=8.4 Hz), 7.98 (d, 1H, J=8 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.22 (s, 1H)
49	3-(6-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	415 / 2.09	3.49 (t, 2H, J=7.6 Hz), 4.65 (t, 2H, J=7.6 Hz), 6.79 (d, 1H, J=8.4 Hz), 7.33 (d, 1H, J=8.8 Hz), 7.47-7.52 (m, 2H), 7.65-7.69 (m, 2H), 7.75-7.79 (m, 2H), 8.00 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.22 (s, 1H), 8.28 (d, 1H, J=2.0 Hz)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
50	3-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	442 / 2.17	3.50 (t, 2H, J=7.6 Hz), 4.30 (s, 4H), 4.74 (t, 2H, J=7.6 Hz), 6.90 (d, 1H, J=8.8 Hz), 7.00~7.02 (m, 1H), 7.08 (d, 1H, J=2 Hz), 7.32 (d, 1H, J=8 Hz), 7.42 (s, 1H), 7.49 (t, 1H, J=8Hz), 7.67 (t, 1H, J=6.8 Hz), 7.77 (d, 1H, J=8 Hz), 8.01~8.06 (m, 2H), 8.18 (s, 1H)
51	3-(2-methylpyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	399 / 1.97	2.61 (s, 3H), 3.50 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=7.6 Hz), 7.22-7.28 (m, 2H), 7.33 (d, 1H, J=8.0 Hz), 7.47-7.51 (m, 1H), 7.56 (s, 1H), 7.65-7.69 (m, 1H), 7.78 (d, 1H, J=7.6 Hz), 7.98 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.23 (s, 1H), 8.52 (d, 1H, J=5.2 Hz).
52	3-(5-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	415 / 1.96	3.50 (t, 2H, J=7.6 Hz), 3.87 (s, 3H), 4.75 (t, 2H, J=7.6 Hz), 7.45-7.51 (m, 2H), 7.57 (s, 1H), 7.67 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=8.0 Hz), 7.99 (d, 1H, J=8.4 Hz), 8.05 (d, 1H, J=8.4 Hz), 8.23 (s, 1H), 8.33 (m, 2H)
53	3-[6-(morpholin-4-yl)pyridin-3-yl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	470 / 2.05	3.50 (t, 2H, J=7.6Hz), 3.58 (t, 4H, J=4.8 Hz), 3.84 (t, 4H, J=4.8 Hz), 4.75 (t, 2H, J=7.6 Hz), 6.69 (d, 1H, J=8.8 Hz), 7.32 (d, 1H, J=8.4 Hz), 7.44 (s, 1H), 7.49 (t, 1H, J=7.2 Hz), 7.68 (m, 1H, J=8.4 Hz), 7.76~7.79 (m, 2H), 8.00~8.07 (m, 2H), 8.20 (s, 1H), 8.33 (d, 1H, J=2 Hz)

156

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
54	3-(1,3-benzodioxol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	428 / 2.16	3.50 (t, 2H, J=7.6Hz), 4.74(t, 2H, J=7.6Hz), 6.00 (s, 2H), 6.84 (d, 1H, J=8Hz), 6.95~7.01 (m, 2H), 7.33 (d, 1H, J=8.4Hz), 7.42 (s, 1H), 7.49 (t, 1H, J=7.6Hz), 7.67 (t, 1H, J=7.2Hz), 7.77 (d, 1H, J=8.4Hz), 8.00~8.06 (m, 2H), 8.19 (s, 1H)
55	3-(quinolin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	435 / 2.03	3.50 (t, 2H, J=7.6 Hz), 3.95 (d, 2H, J=7.2 Hz), 4.75 (t, 2H, J=7.6 Hz), 7.21 (d, 1H, J=8.4 Hz), 7.40-7.50 (m, 2H), 7.60 (s, 1H), 7.65-7.69 (m, 1H), 7.77-7.84 (m, 2H), 7.94 (d, 1H, J=2.4 Hz), 7.99 (d, 1H, J=8.4 Hz), 8.05 (d, 1H, J=8.4 Hz), 8.12 (d, 1H, J=8.4 Hz), 8.17 (d, 1H, J=8.0 Hz), 8.25 (s, 1H), 8.93-8.94 (m, 1H)
56	3-(1-methyl-1H-pyrazol-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	388 / 1.93	3.52 (t, 2H, J=7.6 Hz), 3.95 (s, 3H), 4.77 (t, 2H, J=7.6 Hz), 7.34 (d, 1H, J=8.4 Hz), 7.48-7.55 (m, 2H), 7.66-7.71 (m, 1H), 7.77-7.80 (m, 2H), 8.02-8.08 (m, 2H), 8.16 (s, 1H), 8.23 (s, 1H)
57	3-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	430 / 2.17	0.95 (d, 6H, J=6.8 Hz), 2.26 (m, 1H), 3.54 (t, 2H, J=7.6 Hz), 3.95 (d, 2H, J=7.2 Hz), 4.78 (t, 2H, J=7.6 Hz), 7.34 (d, 1H, J=8.4 Hz), 7.50-7.54 (m, 2H), 7.69 (t, 1H, J=7.6 Hz), 7.78 (d, 1H, J=8.4 Hz), 7.82 (s, 1H), 8.02-8.08 (m, 2H), 8.14 (s, 1H), 8.28 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
58	tert-butyl 2-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}-1H-pyrrole-1-carboxylate	473 / 2.11	1.35 (s, 9H), 3.46 (t, 2H, J=7.6 Hz), 4.68 (t, 2H, J=7.6 Hz), 6.23~6.28 (m, 2H), 7.29 (d, 1H, J=8.4 Hz), 7.45~7.51 (m, 3H), 7.69 (t, 1H, J=8 Hz), 7.77 (d, 1H, J=7.6 Hz), 8.05 (d, 2H, J=8 Hz), 8.15 (s, 1H)
59	3-(2-methoxypyrimidin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	416 / 1.95	3.50 (t, 2H, J=7.6 Hz), 4.07 (s, 3H), 4.75 (t, 2H, J=7.6 Hz), 7.35 (d, 1H, J=8.4 Hz), 7.54 (s, 1H), 7.67 (t, 2H, J=9.2 Hz), 7.79 (d, 1H, J=7.6 Hz), 7.98 (d, 1H, J=8.4 Hz), 8.07 (d, 1H, J=8.4 Hz), 8.24 (s, 1H), 8.67 (s, 2H)
60	5-[2-(quinolin-2-yl)ethyl]-3-(2,3,4-trifluorophenyl)thieno[2,3-d]pyridazin-4(5H)-one	438 / 1.60	3.88 (t, 2H, J=6.0 Hz), 4.76 (t, 2H, J=6.0 Hz), 6.88-7.02 (m, 2H), 7.55 (s, 1H), 7.68 (d, 1H, J=7.6 Hz), 7.82 (t, 1H, J=7.6 Hz), 7.98-8.06 (m, 2H), 8.24 (s, 1H), 8.48 (d, 1H, J=8.4 Hz), 8.63 (d, 1H, J=8.4 Hz)
61	3-(4-fluoro-3-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	416 / 2.28	2.24 (d, 3H, J=1.6 Hz), 3.42 (t, 2H, J=7.6 Hz), 4.66 (t, 2H, J=7.6 Hz), 6.95 (t, 1H, J=8.8 Hz), 7.19~7.24 (m, 3H), 7.35 (s, 1H), 7.44 (t, 1H, J=6.8 Hz), 7.58~7.62 (m, 1H), 7.70 (d, 1H, J=8.4 Hz), 7.93~7.99 (m, 2H), 8.13 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
62	3-(4-fluoro-2-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	416 / 1.61	3.87 (t, 2H, J=6.0 Hz), 4.73 (t, 2H, J=6.0 Hz), 6.78-7.03 (m, 3H), 7.38 (s, 1H), 7.68 (d, 1H, J=8.4 Hz), 7.82 (t, 1H, J=7.6 Hz), 7.98-8.04 (m, 2H), 8.25 (s, 1H), 8.48 (d, 1H, J=8.4 Hz), 8.60 (d, 1H, J=8.4 Hz)
63	3-(3-chloro-4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	436 / 2.09	3.50 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.15 (t, 1H, J=8.8 Hz), 7.33-7.38 (m, 2H), 7.47-7.53 (m, 3H), 7.68 (t, 1H, J=7.6 Hz), 7.79 (d, 1H, J=7.6 Hz), 7.99-8.08 (m, 2H), 8.22 (s, 1H)
64	3-(2-chloro-4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	436 / 2.24	3.47 (t, 2H, J=7.6 Hz), 4.71 (t, 2H, J=7.6 Hz), 6.99-7.04 (m, 1H), 7.31-7.44 (m, 2H), 7.47-7.51 (m, 2H), 7.64-7.69 (m, 1H), 7.76 (d, 1H, J=8.0 Hz), 7.98 (d, 1H, J=8.8 Hz), 8.03 (d, 1H, J=8.8 Hz), 8.22 (s, 1H)
65	3-(3,4-dimethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	412 / 2.13,	2.30 (s, 6H), 3.49 (t, 2H, J=7.6 Hz), 4.73 (t, 2H, J=7.6 Hz), 7.18 (d, 1H, J=7.6 Hz), 7.24-7.27 (m, 2H), 7.31 (d, 1H, J=8.4 Hz), 7.43 (s, 1H), 7.46-7.50 (m, 1H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.4 Hz), 8.03 (t, 2H, J=8.8 Hz), 8.18 (s, 1H).

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
66	3-(2,4-dimethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	412 / 2.12	2.05 (s, 3H), 2.36 (s, 3H), 3.47 (t, 2H, J=7.6 Hz), 4.69 (t, 2H, J=7.6 Hz), 7.02~7.08 (m, 4H), 7.29 (d, 1H, J=8.8 Hz), 7.35 (s, 1H), 7.48 (t, 1H, J=7.2 Hz), 7.66 (t, 1H, J=7.2 Hz), 7.76 (d, 1H, J=8 Hz), 8.01 (t, 1H, J=8.8 Hz), 8.21 (s, 1H)
67	3-(2,4-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	420 / 2.19	3.48 (t, 2H, J=7.6 Hz), 4.73 (t, 2H, J=7.6 Hz), 6.89-6.94 (m, 2H), 7.29-7.36 (m, 2H), 7.47-7.53 (m, 2H), 7.67-7.69 (m, 1H), 7.76 (d, 1H, J=8.0 Hz), 8.00 (d, 1H, J=8.4 Hz), 8.04 (d, 1H, J=8.4 Hz), 8.21 (s, 1H)
68	3-(2,4-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	444 / 2.17	3.47 (t, 2H, J=7.6 Hz), 3.72 (s, 3H), 3.84 (s, 3H), 4.69 (t, 2H, J=7.6 Hz), 6.52-6.55 (m, 2H), 7.19 (s, 1H, J=8.0 Hz), 7.30 (d, 1H, J=8.0 Hz), 7.44 (s, 1H), 7.46-7.50 (m, 1H), 7.65-7.77 (m, 2H), 8.03 (d, 2H, J=8.4 Hz), 8.16 (s, 1H)
69	3-(2,5-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	444 / 2.16	3.46~3.50 (m, 2H), 3.69 (s, 3H), 3.79 (s, 3H), 4.69 (t, 2H, J=7.6 Hz), 6.87 (d, 1H, J=2 Hz), 6.91 (s, 2H), 7.30 (d, 1H, J=8.4 Hz), 7.49 (t, 2H, J=6.8 Hz), 7.68 (t, 1H, J=8.4 Hz), 7.76 (d, 1H, J=8.4 Hz), 8.02~8.05 (m, 2H), 8.17 (s, 1H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
70	3-(2,3-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	420 / 2.19	3.50 (t, 2H, J=7.6 Hz), 4.73 (t, 2H, J=7.6 Hz), 7.10-7.13 (m, 2H), 7.18-7.23 (m, 1H), 7.31 (d, 1H, J=8.4 Hz), 7.49 (t, 1H, J=7.6 Hz), 7.57 (s, 1H), 7.68 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=7.6 Hz), 8.01-8.06 (m, 2H), 8.22 (s, 1H)
71	3-(3,4-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	444 / 1.95,	3.50 (t, 2H, J=7.6 Hz), 3.88 (s, 3H), 3.92 (s, 3H), 4.75 (t, 2H, J=7.6 Hz), 6.92 (d, 1H, J=8.4 Hz), 7.09~7.11 (m, 2H), 7.32 (d, 1H, J=8.4 Hz), 7.46~7.51 (m, 2H), 7.68 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=7.6 Hz), 8.04 (t, 2H, J=8.8 Hz), 8.20 (s, 1H)
72	3-(3,4-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	420 / 2.22	3.49 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.15-7.21 (m, 2H), 7.28-7.35 (m, 2H), 7.47 (s, 1H), 7.50 (d, 1H, J=7.2 Hz), 7.65-7.69 (m, 1H), 7.78 (d, 1H, J=8.0 Hz), 7.98 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.0 Hz), 8.22 (s, 1H)
73	3-(5-fluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	432 / 2.19	3.48 (t, 2H, J=7.6 Hz), 3.71 (s, 1H), 4.71 (t, 2H, J=7.6 Hz), 6.87-7.08 (m, 3H), 7.30 (d, 1H, J=8.8 Hz), 7.47-7.51 (m, 2H), 7.68 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=8.4 Hz), 8.03 (t, 2H, J=8.0 Hz), 8.18 (s, 1H).

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
74	3-(4-fluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	432 / 2.01,	3.47 (t, 2H, J=7.6Hz), 3.72 (s, 3H), 4.70 (t, 2H, J=7.6 Hz), 6.70-6.72 (m, 2H), 7.18-7.22 (m, 1H), 7.44 (s, 1H), 7.49 (t, 1H, J=7.6 Hz), 7.67 (d, 1H, J=7.6 Hz), 7.77 (d, 1H, J=8.4 Hz), 7.99 (d, 1H, J=8.4 Hz), 8.02 (t, 2H, J=8.8 Hz), 8.17 (s, 1H)
75	3-(3,5-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	444 / 2.20	3.50 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 6.50 (t, 1H, J=2.4 Hz), 6.68 (d, 2H, J=2.4 Hz), 7.31 (d, 1H, J=7.6 Hz), 7.46-7.50 (m, 2H), 7.65-7.69 (m, 1H), 7.76 (d, 1H, J=8.4 Hz), 8.00-8.05 (m, 2H), 8.19 (s, 1H)
76	3-(2,5-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	420 / 2.19	3.49 (t, 2H, J=6.0 Hz), 4.73 (t, 2H, J=6.0 Hz), 7.06-7.11 (m, 3H), 7.31 (d, 1H, J=8.4 Hz), 7.48 (t, 1H, J=8.4 Hz), 7.56 (s, 1H), 7.64-7.69 (m, 1H), 7.76 (d, 1H, J=8.0 Hz), 8.00 (d, 1H, J=8.4 Hz), 8.04 (d, 1H, J=8.4 Hz), 8.21 (s, 1H)
77	3-(2,3-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	444 / 2.15	3.48 (t, 2H, J=7.6 Hz), 3.59 (s, 3H), 3.89 (s, 3H), 4.71 (t, 2H, J=7.6 Hz), 6.86 (dd, 1H, J=1.2 Hz, J=7.6 Hz), 6.97 (d, 1H, J=8.0 Hz), 7.05-7.09 (m, 1H), 7.30 (d, 1H, J=8.0 Hz), 7.47-7.51 (m, 2H), 7.67 (t, 1H, J=7.6 Hz), 7.76 (d, 1H, J=8.0 Hz), 8.00-8.04 (m, 2H), 8.20 (s, 1H)

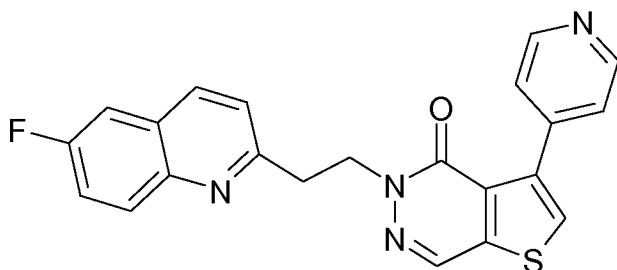
EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
78	3-(3-fluoro-4-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	432 / 2.19	3.50 (t, 2H, J=7.6 Hz), 3.93 (s, 3H), 4.74(t, 2H, J=7.6 Hz), 6.99 (t, 1H, J=8.4 Hz), 7.23-7.27 (m, 2H), 7.33 (d, 1H, J=8.4 Hz), 7.44 (s, 1H), 7.49 (t, 1H, J=7.6 Hz), 7.65-7.69 (m, 1H), 7.78 (d, 1H, J=8.0 Hz), 8.00 (d, 1H, J=8.0 Hz), 8.05 (d, 1H, J=8.4 Hz), 8.19 (s, 1H)
79	3-(2-fluoro-3-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	432 / 2.17	3.48 (t, 2H, J=7.6 Hz), 3.92 (s,3H), 4.72 (t,2H,J=7.6 Hz), 6.93-7.13 (m, 3H), 7.29 (d, 1H, J=8.0 Hz), 7.46-7.50 (m, 1H), 7.55 (s, 1H), 7.65-7.69 (m, 1H), 7.77 (d, 1H, J=8.0 Hz), 8.01-8.04 (m, 2H), 8.19 (s, 1H)
80	3-(3,5-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	420 / 2.24	3.50 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=7.6 Hz), 6.81-6.85 (m, 1H), 7.01-7.03 (m, 2H), 7.34 (d,1H, J=8.4 Hz), 7.47-7.51 (m, 2H), 7.66 (t, 1H, J=8.4 Hz), 7.77 (d, 1H, J=8.4 Hz), 7.98 (d, 1H, J=8.4 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.21 (s, 1H)
81	3-(3-fluoro-5-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	432 / 2.23	3.51 (t, 2H, J=7.6 Hz), 3.81 (s, 1H), 4.75 (t, 2H, J=7.6 Hz), 6.63-6.67 (m, 1H), 6.79-6.82 (m, 1H), 6.87 (s, 1H), 7.33 (d, 1H, J=8.4 Hz), 7.47-7.51 (m, 2H), 7.67 (t, 1H, J=7.6 Hz), 7.78 (d, 1H, J=8.0 Hz), 8.00-8.07 (m, 2H), 8.20 (s, 1H).

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
82	3-(2-methoxy-5-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	428 / 1.61	2.21 (s, 3H), 3.59 (s, 3H), 3.78 (t, 2H, J=6.0 Hz), 4.66 (t, 2H, J=6.0 Hz), 6.77 (d, 1H, J=8.4 Hz), 6.94 (s, 1H), 7.07 (d, 1H, J=8.4 Hz), 7.37 (s, 1H), 7.50 (d, 1H, J=8.4 Hz), 7.69 (t, 1H, J=7.6 Hz), 7.86-7.92 (m, 2H), 8.05 (s, 1H), 8.45 (m, 2H)
83	3-(2,5-dichlorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	452 / 2.09	3.48 (t, 2H, J=7.6 Hz), 4.72 (t, 2H, J=7.6 Hz), 7.29~7.33 (m, 3H), 7.39 (d, 1H, J=8 Hz), 7.48 (t, 2H, J=6.4 Hz), 7.66 (t, 1H, J=7.2 Hz), 7.76 (d, 1H, J=8 Hz), 7.98~8.04 (m, 2H), 8.22 (s, 1H)
84	3-(naphthalen-2-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	434 / 2.11	3.55 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=7.6 Hz), 7.35 (d, 1H, J=8.4 Hz), 7.48~7.63 (m, 5H), 7.71 (t, 1H, J=7.2 Hz), 7.79~7.87 (m, 4H), 7.94 (s, 1H), 8.09 (t, 2H, J=8.4 Hz), 8.23 (s, 1H)
85	3-phenyl-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	384 / 2.19	3.50 (t, 2H, J=7.6 Hz), 4.74 (t, 2H, J=7.6 Hz), 7.32 (d, 1H, J=8.4 Hz), 7.39~7.53 (m, 7 H), 7.67 (t, 1H, J=7.6 Hz), 7.77 (d, 1H, J=7.6 Hz), 8.04 (t, 2H, J=8.8 Hz), 8.20 (s, 1H)
86	3-(1-benzofuran-2-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	423 / 1.70	3.75 (t, 2H, J=6.8 Hz), 4.79 (t, 2H, J=6.8 Hz), 7.14-7.18 (m, 1H), 7.24 (t, 1H, J=7.2 Hz), 7.07 (d, 1H, J=8.4 Hz), 7.40-7.61 (m, 4H), 7.77-7.85 (m, 2H), 8.00 (s, 1H), 8.10 (s, 2H), 8.30-8.34 (m, 2H)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
87	3-(1H-indazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	424 / 2.00	3.50 (t, 2H, J=7.6 Hz), 4.75 (t, 2H, J=7.6 Hz), 7.32 (d, 1H, J=8.4 Hz), 6.63-6.67 (m, 1H), 6.79-6.82 (m, 1H), 6.87 (s, 1H), 7.33 (d, 1H, J=8.4 Hz), 7.47-7.51 (m, 2H), 7.67 (t, 1H, J=7.6 Hz), 7.78 (d, 1H, J=8.0 Hz), 8.00-8.07 (m, 2H), 8.20 (s, 1H).
88	3-(1-methyl-1H-pyrazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	388 / 1.89	3.49 (t, 2H, J=7.6 Hz), 3.56 (s, 3H), 4.73 (t, 2H, J=7.6 Hz), 6.31 (d, 1H, J=2.0 Hz), 7.34 (d, 1H, J=8.0 Hz), 7.47-7.52 (m, 2H), 7.56 (s, 1H), 7.64-7.69 (m, 1H), 7.77 (d, 1H, J=8.0 Hz), 7.96 (d, 1H, J=8.8 Hz), 8.06 (d, 1H, J=8.4 Hz), 8.25 (s, 1H)
89	3-(4,5-difluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	450 / 2.22	3.47 (t, 2H, J=7.6Hz), 3.60 (s, 3H), 4.70 (t, 2H, J=7.6Hz), 6.75~6.80 (m, 1H), 7.07 (t, 1H, J=7.6 Hz), 7.30 (d, 1H, J=8.4 Hz), 7.45~7.50 (m, 2H), 7.67 (t, 1H, J=7.2 Hz), 7.77 (d, 1H, j=8 Hz), 7.99~8.05 (m, 2H), 8.18 (s, 1H)
90	3-(2-fluoro-4-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	416 / 1.60	2.26 (s, 3H), 3.77 (t, 2H, J=6.0 Hz), 4.68 (t, 2H, J=6.0 Hz), 6.73 (d, 1H, J=8.4 Hz), 6.83 (d, 1H, J=8.0 Hz), 7.05 (t, 1H, J=8.0 Hz), 7.44(s,1H),7.60 (d, 1H, J=8.4 Hz), 7.75 (t,1 H, J=8.0 Hz),7.90-7.99 (m, 2H), 8.14 (s, 1H), 8.28 (d, 1H, J=8.4 Hz), 8.59 (d, 1H, J=8.4 Hz)

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]	¹ H NMR (CDCl ₃) δ:
91	3-(2-fluoro-5-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	432 / 2.18	3.49 (t, 2H, J=7.6 Hz), 3.80 (s, 3H), 4.73 (t, 2H, J=7.6 Hz), 6.88-6.93 (m, 2H), 7.08 (t, 1H, J=8.8 Hz), 7.30 (d, 1H, J=8.4 Hz), 7.46-7.51 (m, 1H), 7.65-7.69 (m, 1H), 7.55 (s, 1H), 7.65-7.69 (m, 1H), 7.76 (d, 1H, J=8.4 Hz), 8.03 (t, 2H, J=8.0 Hz), 8.20 (s, 1H).
92	3-methyl-4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}benzonitrile	423 / 1.54	1.99 (s, 3H), 3.84 (t, 2H, J=6.0 Hz), 4.73 (t, 2H, J=6.0 Hz), 7.15 (d, 1H, J=8.0 Hz), 7.39-7.46 (m, 3H), 7.77 (d, 1H, J=8.4 Hz), 7.87 (t, 1H, J=8.0 Hz), 8.02-8.09 (m, 2H), 8.32 (s, 1H), 8.36 (d, 1H, J=8.4 Hz), 8.69 (d, 1H, J=8.4 Hz)

EXAMPLE 93: 5-[2-(6-Fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one



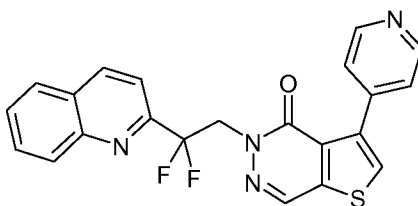
- 5 93.1 3-Bromo-5-(2-(6-fluoroquinolin-2-yl)ethyl)thieno[2,3-d]pyridazin-4(5H)-one
- 2-(6-Fluoroquinolin-2-yl)ethanol (182 mg, 0.952 mmol) from Example a2) and 3-bromo-5H-thieno[2,3-d]pyridazin-4(5H)-one (200 mg, 0.865 mmol) from Example 3.3 were dissolved in THF (10 mL) and stirred for about 10 min. Then Ph₃P (342 mg, 1.305 mmol) and DEAD (226 mg, 1.298 mmol) were each added sequentially rapidly to the
- 10 solution. The reaction mixture was stirred under nitrogen atmosphere overnight. The reaction solution was concentrated and purified by TLC (PE/EA=1/1). The crude product was recrystallized from methanol (130 mg, yield: 37.1%). LC-MS: m/e (M+H)⁺; R_t : 1.90 min.

93.2 5-[2-(6-Fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-*d*]pyridazin-4(5*H*)-one

3-Bromo-5-(2-(6-fluoroquinolin-2-yl)ethyl)thieno[2,3-*d*]pyridazin-4(5*H*)-one (66 mg, 0.163 mmol) was dissolved in dioxane (2.1 mL) and H₂O (0.7 mL), pyridin-4-yl boronic acid (20.07 mg, 0.163 mmol), K₂CO₃ (45.1 mg, 0.327 mmol) and Pd(dppf)Cl₂ (7.23 mg, 9.80 μmol) were each added sequentially to the suspension. The suspension was heated in a microwave tube at about 110 °C for 1 h. The crude product was purified by TLC (EA) to give the title compound (45 mg, yield: 68.5%).

10 LC-MS: *m/e* (M+H)⁺: 403.7, *R*_t: 1.81 min; ¹H NMR (CDCl₃, 400 MHz) δ: 8.65 (d, *J* = 6.0 Hz, 2H), 8.24 (s, 1H), 8.02-7.96 (m, 2H), 7.61 (s, 1H), 7.46-7.42 (m, 3H), 7.41-7.38 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 4.75 (t, *J* = 7.4 Hz, 2H), 3.48 (t, *J* = 7.4 Hz, 2H).

15 EXAMPLE 94: 5-[2,2-Difluoro-2-(quinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-*d*]pyridazin-4(5*H*)-one



94.1 3-Bromo-5-(2,2-difluoro-2-(quinolin-2-yl)ethyl)thieno[2,3-*d*]pyridazin-4(5*H*)-one

A mixture of 3-bromothieno[2,3-*d*]pyridazin-4(5*H*)-one (10mg, 0.043 mmol) from Example 3.3, trifluoromethanesulfonic acid 2,2-difluoro-2-quinolin-2-yl ethyl ester (14.77 mg, 0.043 mmol) from Example b1 and Cs₂CO₃ (28.2 mg, 0.087 mmol) in DMF (0.5 mL) was stirred at room temperature for 5 h. The solution was purified by Pre-TLC (PE/EA =1/2) to give a dark yellow oil (4 mg, yield 22%).

LC-MS (ESI⁺): *m/e* 422 (M+H)⁺, *R*_t: 1.96 min.

25

94.2 5-[2,2-Difluoro-2-(quinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-*d*]pyridazin-4(5*H*)-one

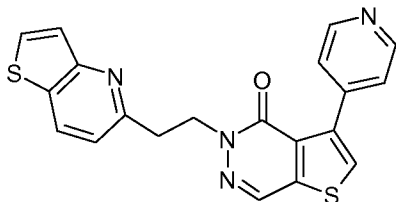
A mixture of 3-bromo-5-(2,2-difluoro-2-(quinolin-2-yl)ethyl)thieno[2,3-*d*]pyridazin-4(5*H*)-one (0.118 mmol), pyridin-4-yl boronic acid (0.118 mmol), Na₂CO₃

(31.4 mg, 0.296 mmol) and PdCl₂(dppf)-CH₂Cl₂ adduct (9.67 mg, 0.012 mmol) in dioxane (1.5 mL) and water (0.5 mL) was stirred at 100 °C for 2h. The solvent was evaporated and the residue was purified by Pre-TLC (PE/EA=1/1) to give a crude yellow solid. The solid was dissolved in DCM (1.5 mL) and filtered. The white solid
5 obtained was the title compound (40 mg, yield 80%).

LC-MS (ESI+): m/e 421 (M+H)⁺, R_t: 2.00 min; ¹H NMR (CDCl₃, 400MHz) δ: 8.70 (s, 1H), 8.61 (d, *J* = 8.4 Hz, 1H), 8.50 (dd, *J* = 4.4 Hz, 1.2Hz, 1H), 8.22 (s, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.88-7.84 (m, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.76-7.73 (m, 1H), 7.30 (dd, *J* = 4.4 Hz, 2.0Hz, 2H), 5.15 (t, *J* = 14 Hz, 2H).

10

EXAMPLE 95: 3-(Pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one



95.1 3-Bromo-5-[2-(thieno[3,2-b]pyridin-5-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

15 To a mixture of 3-bromothieno[2,3-d]pyridazin-4(5H)-one (100 mg, 0.433 mmol) from Example 3.3 and triphenylphosphine (227 mg, 0.866 mmol) in THF (2 mL) was added (E)-diethyl diazene-1,2-dicarboxylate (151 mg, 0.866 mmol) dropwise at 0°C. After the addition, the mixture was stirred for 1h at 0°C. Then 2-(thieno[3,2-b]pyridin-5-yl)ethanol from Example a3 (78 mg, 0.433 mmol) in THF(1 mL) was added
20 dropwise. The mixture was stirred at room temperature overnight. The solution was filtered to obtain the title compound (80 mg, yield 47.1 %).

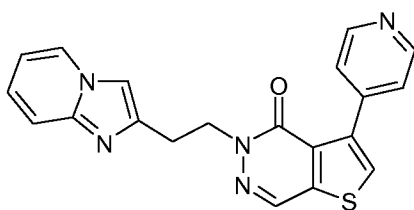
LC-MS (ESI+): m/e 392 (M+H)⁺, R_t: 1.60 min; ¹H NMR (CDCl₃, 400MHz) δ: 8.67 (d, *J* = 4.4 Hz, 2H), 8.24 (s, 1H), 8.09 (d, *J* = 6.4 Hz, 1H), 7.72 (d, *J* = 4.4 Hz, 1H), 7.60 (s, 1H), 7.49 (d, *J* = 4.4 Hz, 1H), 7.45 (d, *J* = 4.8 Hz, 2H), 7.17 (d, *J* = 6.4 Hz, 1H),
25 4.7 (t, *J* = 6.4 Hz, 2H), 3.44 (t, *J* = 6.0 Hz, 2H).

95.2 3-(Pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one

A mixture of pyridin-4-ylboronic acid (37.6 mg, 0.306 mmol), the compound from Example 95.1 (80 mg, 0.204 mmol), Na₂CO₃ (54.0 mg, 0.510 mmol) and PdCl₂(dppf)-CH₂Cl₂ adduct (16.65 mg, 0.020 mmol) in dioxane (3 mL) and water (1 mL) was stirred at 100 °C in a microwave for 10 min. The solvent was evaporated and the residue was washed with methanol, filtered, the filtrate was concentrated and purified by HPLC to afford the title compound (59 mg, yield 74.1 %) as a white solid.

LC-MS (ESI+): m/e 391 (M+H)⁺, R_t: 1.86 min.

EXAMPLE 96: 5-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one



96.1 2-(2-Chloroethyl)imidazo[1,2-a]pyridine

A mixture of 2-(imidazo[1,2-a]pyridin-2-yl)ethanol (400mg, 2.466 mmol) from Example a4) and SOCl₂ (2 mL, 27.4 mmol) in DCM (10 mL) was stirred at room temperature for 2 days. The mixture was concentrated *in vacuo*. The residue was diluted with EtOAc (3×100 mL) and washed with saturated NaHCO₃ solution (6 mL×4) and brine (6 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was purified by Pre-TLC (PE/EA=1/1, v/v) to give the title compound as an oil (300 mg, yield 70%).

LC-MS (ESI+): m/e 181 (M+H)⁺, R_t: 1.68 min.

96.2 3-Bromo-5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5H-thieno[2,3-d]pyridazin-4(5H)-one

A mixture of 2-(2-chloroethyl)imidazo[1,2-a]pyridine (90 mg, 0.498 mmol), 3-bromothieno[2,3-d]pyridazin-4(5H)-one from Example 3.4 (115 mg, 0.498 mmol) and Cs₂CO₃ (325 mg, 0.996 mmol) in DMF (3 mL) was stirred at 60 °C for 16h. The solvent was evaporated. The residue was purified by Pre-TLC (PE/EA=1/2, v/v) to give the title compound as an oil (140 mg, yield 80%).

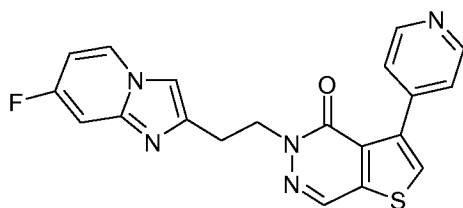
LC-MS (ESI+): m/e 374 (M+H)⁺, R_t: 1.79 min.

96.3 5-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one

A mixture of pyridin-4-ylboronic acid (29.5 mg, 0.240 mmol), the compound
 5 from Example 96.2 (60 mg, 0.160 mmol), Na₂CO₃ (42.4 mg, 0.400 mmol) and
 PdCl₂(dppf)-CH₂Cl₂ adduct (13.06 mg, 0.016 mmol) in dioxane (3 mL) and water (1
 mL) was stirred at 100 °C in a microwave for 10 min. The solvent was evaporated and
 the residue was purified by Pre-TLC (PE/EA=1/4) and purified by HPLC to afford the
 title product as a white solid (45 mg, yield 75%).

10 LC-MS (ESI+): m/e 374 (M+H)⁺, R_t: 1.70 min; ¹H NMR (DMSO-d₆, 400MHz):
 8.68 (s, 1H), 8.60 (d, *J* = 6.0 Hz, 2H), 8.46 (d, *J* = 6.4 Hz, 1H), 8.21 (s, 1H), 7.74 (s,
 1H), 7.75 (d, *J* = 6.0 Hz, 2H), 7.46 (d, *J* = 9.2 Hz, 1H), 7.19-7.15 (m, 1H), 6.84-6.80 (m,
 1H), 4.47 (t, *J* = 7.6 Hz, 2H), 3.13 (t, *J* = 7.6 Hz, 2H).

15 EXAMPLE 97: 5-[2-(7-Fluoroimidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one



97.1 3-Bromo-5-(2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)ethyl)thieno[2,3-d]pyridazin-4(5H)-one

20 A mixture of 3-bromothieno[2,3-d]pyridazin-4(5H)-one from Example 3.4 (231
 mg, 1 mmol), 2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)ethanol from Example a5 (180 mg,
 1.00 mmol) and Ph₃P (525 mg, 2.00 mmol) was dissolved in THF (6 mL). Then DEAD
 (0.317 mL, 2.00 mmol) in THF (1 mL) was added. The resulting mixture was stirred at
 room temperature under nitrogen overnight. The mixture was concentrated and purified
 25 on the ISCO Combiflash system using a 40g C-18 column using the following gradient:
 A: Water(0.1%NH₄HCO₃); B: Methanol; 30%B to 80%B over 20 min (160 mg,
 yield:17.7%).

LC-MS: m/e 393 (M+H)⁺; R_t:1.74 min; ¹H NMR(DMSO-d₆) δ: 3.12(t, 2H), 4.44 (t, 2H), 6.88-6.92 (m, 1H), 7.32 (dd, J=10, 2, 1H), 7.74(s, 1H), 8.17 (s, 1H), 8.52-8.56 (m, 1H), 8.62 (s,1H).

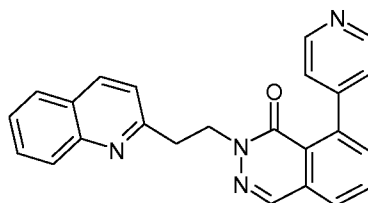
- 5 97.2 5-[2-(7-Fluoroimidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one

A mixture of 3-bromo-5-(2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)ethyl)thieno[2,3-d]pyridazin-4(5H)-one (80 mg, 0.203 mmol), pyridin-4-ylboronic acid (37.5 mg, 0.305 mmol), PdCl₂(dppf)-CH₂Cl₂ adduct (16.61 mg, 0.020 mmol) and Cs₂CO₃ (133 mg, 0.407 mmol) in 1,4-dioxane (3 mL) and water(1.5mL) was heated under microwave at about 110 °C for about 15min. The mixture was concentrated and was chromatographed on the ISCO Combiflash system using a 40 g Silicycle SiliaSep Silica gel column C-18 column using the following gradient: A: Water(0.1%NH₄HCO₃); B: Methanol; 30%B to 80%B over 20 min (15 mg, 18.8%).

- 15 LC-MS: m/e 392 (M+H); R_t:1.74 min; ¹H NMR(CDCl₃) δ: 3.30 (t, 2H), 4.64 (t, 2H), 6.61-6.65 (m, 1H), 7.15 (dd, J=9.6 Hz, 2.4 Hz, 1H), 7.38 (s, 1H), 7.50 (d, J=6 Hz, 2H), 7.61 (s, 1H), 7.96-7.99 (m, 1H), 8.26 (s, 1H), 8.68 (d, J=6 Hz, 2H).

- II.2 Preparation of compounds of the formula I in which A is A¹, X¹ is N, R¹ is Y¹-
20 Cyc¹ and X³ is -C(R⁹)=C(R⁸)-

EXAMPLE 98: 8-(Pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one



- 25 98.1 N-tert-Butyl-2-chlorobenzamide

The mixture of 2-chlorobenzoic acid (20 g, 128 mmol), HOBT (34.6 g, 256 mmol), EDCI (48.8 g, 256 mmol), 2-methylpropan-2-amine (9.3 g, 128 mmol) and TEA (25.9 g, 256 mmol) in THF (600 mL) was stirred at room temperature overnight. After solvent evaporation, the mixture was diluted with ethyl acetate (600 mL) and washed

with water (3 x 300 mL). The organic layer was dried over Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography on silica gel, eluting with EtOAc/PE (1:5) to give the title product as a white solid (23.9 g, yield: 88.5%).

LC-MS: $m/e = 212$ (M+H)⁺; R_t=0.85 min.

5

98.2 2-tert-Butyl-7-chloro-3-hydroxy-2,3-dihydroisoindol-1-one

N-tert-Butyl-2-chlorobenzamide (5.4 g, 25.6 mmol) was dissolved in THF (280 mL) and the solution was added with TMEDA (12.4 mL, 81.9 mmol) and then added with sec-butyllithium-hexane solution (1.0 mol/L, 82.7 mL, 81.9 mmol) dropwise at
10 -78°C for 40 minutes under argon atmosphere, followed by stirring at the same temperature for 2.5 hours. Then, the mixture was added with DMF (4.36 mL, 56.3 mmol) and warmed from -78°C to room temperature over 2 hours. The reaction mixture was added with water (200 mL), and extracted with ethyl acetate (100 mL*3). The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate.
15 The solvent was evaporated under reduced pressure and the residue was purified by crystallization using diisopropyl ether to obtain product 3 (5.0 g, Yield: 81%).

LC-MS: $m/e = 240$ (M+H)⁺; R_t=1.74 min; ¹H NMR (400MHz, DMSO-*d*₆): δ 7.58-7.54 (m, 1H), 7.49-7.45 (m, 2H), 6.35 (d, J=8.4 Hz, 1H), 5.98 (d, J=8.4 Hz, 1H), 1.52 (s, 9H).

20

98.3 8-Chloro-2H-phthalazin-1-one

The compound from Example 98.2 (5 g, 21 mmol) was suspended in 20 mL acetic acid under nitrogen. The resulting thick slurry was heated to 90°C. At approximately 80°C, a homogeneous solution was obtained. Hydrazine monohydrate (64%, 3.2 mL, 63
25 mmol) was added dropwise (exotherm), keeping the internal temperature between 90 and 93°C over approximately 4 h. The resulting suspension was continued to stir at 90°C as the conversion of starting material was monitored by LC (<1%). Water (40 mL) preheated to 80°C was added, maintaining the mixture at 80-90°C followed by ramping down to 20°C over approximately 3h time. At this point, the resulting suspension was
30 transferred onto a filter. The filter cake was rinsed with water (10mL*3). The wet product was air-dried overnight to afford the title product (2.6 g, Yield: 69%).

LC-MS: $m/e = 181$ ($M+H$)⁺; $R_t = 1.51$ min; ^1H NMR (400 MHz, DMSO- d_6) δ : 12.61 (s, 1H), 8.32 (s, 1H), 7.88-7.83 (m, 3H).

98.4 8-Chloro-2-(2-quinolin-2-yl-ethyl)-2H-phthalazin-1-one

5 To a solution of triphenylphosphine (9.00 g, 34.3 mmol) in THF (100 mL), DEAD (5.44 mL, 34.3 mmol) was added at 0°C. After stirring for 15 min, 2-(quinolin-2-yl)ethanol from Example a1 (2.97 g, 17.17 mmol) was added. After another 15 min, 8-chlorophthalazin-1(2H)-one (3.1 g, 17.17 mmol) was added. The mixture was stirred overnight at room temperature; LC-MS indicated complete conversion to the product. 1
10 N HCl was added (pH= 4). The mixture was extracted with EtOAc (3 x 50 mL), the EtOAc layers were discarded. The aqueous layer was neutralized by aq. NaHCO₃ and extracted with ethyl acetate (3 x 500 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was suspended in EtOAc. The solid was filtered through a Büchner
15 funnel. The purity of the title product was 95%.

LC-MS: $m/e = 336$ ($M+H$)⁺; $R_t = 1.54$ min; ^1H NMR (400 MHz, DMSO- d_6) δ : =8.35 (s, 1H), 8.29-8.26 (d, $J=8.8$ Hz, 1H), 7.94-7.90 (m, 2H), 7.88-7.86 (m, 3H), 7.73-7.69 (m, 1H), 7.57-7.55 (m, 1H), 7.48-7.46 (m, 1H), 4.58-4.55 (t, $J=5.4$ Hz, 2H), 3.42-3.38 (t, $J=5.4$ Hz, 2H).

20

98.5 8-(Pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one

A reaction tube was charged with pyridin-4-ylboronic acid (0.223 mmol), K₂CO₃ (61.7 mg, 0.447 mmol) under a dry nitrogen atmosphere. A solution of 8-chloro-2-(2-quinolin-2-yl-ethyl)-2H-phthalazin-1-one (50 mg, 0.186 mmol) in 1,4-dioxane (5 mL)
25 along with PdCl₂(dppf) (5.45 mg, 7.45 μ mol) was added. After addition of water (1 mL), the resulting mixture was heated at 100°C overnight. After removal of the solvent under reduced pressure, the title compound was obtained as a crude product. It was purified by Prep-HPLC.

LC-MS $m/e = 379.1$ ($M+H$)⁺; $R_t = 1.80$ min; ^1H NMR (400 MHz, CDCl₃) δ ppm
30 8.58 (s, 2 H), 8.18 (s, 1 H), 8.04 (d, $J=8.0$ Hz, 1 H), 7.94 (d, $J=8.0$ Hz, 1H), 7.74-7.78 (m, 3 H), 7.66 (d, $J=1.6$ Hz, 1 H), 7.46-7.52 (m, 2 H), 7.30 (d, $J=8.4$ Hz, 1 H), 7.11 (d, $J=5.2$ Hz, 2 H), 4.65 (t, $J=7.4$ Hz, 2 H), 3.45 (t, $J=7.4$ Hz, 2 H).

Examples 99 to 164 were prepared analogously to the method for Example 98.

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]
99	2-[2-(Quinolin-2-yl)ethyl]-8-[4-(trifluoromethyl)phenyl]phthalazin-1(2H)-one	446 / 2.34
100	8-(4-Methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	392 / 2.30
101	8-[4-(Propan-2-yl)phenyl]-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	420 / 2.45
102	8-(4-Ethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	406 / 2.15
103	4-{4-Oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl} benzonitrile	403 / 1.96
104	8-(4-Methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	408 / 2.19
105	8-(4-Fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	396 / 2.22
106	(4-{4-Oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl}phenyl)acetonitrile	417 / 2.11
107	8-(4-Hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	394 / 1.99
108	8-(2-chlorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	412 / 2.06
109	8-(2-Methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	392 / 2.08
110	8-(2-Ethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	406 / 2.35
111	8-(2-Fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	396 / 2.20
112	8-(2-Methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	408 / 2.20

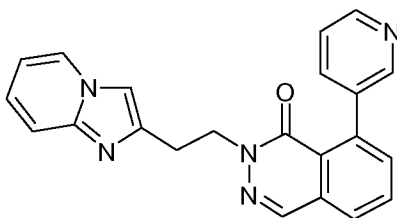
EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]
113	8-(3-Methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	408 / 2.02
114	3-{4-Oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl}benzonitrile	403 / 1.96
115	8-(3-Fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	396 / 2.04
116	8-(3-Hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	394 / 1.87
117	N,N-Dimethyl-3-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl}benzamide	449 / 1.98
118	8-(3-Methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	392 / 2.10
119	2-[2-(Quinolin-2-yl)ethyl]-8-(thiophen-2-yl)phthalazin-1(2H)-one	384 / 2.19
120	8-(1-Methyl-1H-indol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	431 / 2.26
121	8-(3,5-Dimethyl-1H-pyrazol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	396 / 1.90
122	8-(1H-Indol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	417 / 1.97
123	8-(1H-Indol-6-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	417 / 1.98
124	8-(Pyrimidin-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	380 / 1.82
125	8-(2-Methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	409 / 2.07
126	8-(Pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	379 / 1.81
127	8-(Furan-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	368 / 1.95

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]
128	8-(Quinolin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	439
129	8-(1H-Indol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	417 / 2.12
130	8-(2,3-Dihydro-1-benzofuran-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	420 / 2.19
131	8-(3,4-Dihydro-2H-1,5-benzodioxepin-7-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	450 / 2.19
132	8-(1-Benzofuran-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	418 / 2.25
133	8-(6-Methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	409 / 2.10
134	8-(2,3-Dihydro-1,4-benzodioxin-6-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	436 / 1.99
135	8-(2-Methylpyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	393 / 1.95
136	8-(5-Methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	409 / 1.97
137	8-(5-Fluoropyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	397 / 2.00
138	8-(1,3-Benzodioxol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	422 / 2.00
139	8-(1-Methyl-1H-pyrazol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	382 / 1.90
140	8-[1-(2-Methylpropyl)-1H-pyrazol-4-yl]-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	424 / 2.14
141	tert-Butyl 2-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl}-1H-	467 / 2.34

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]
	pyrrole-1-carboxylate	
142	8-(3-Chloro-4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	430 / 2.32
143	8-(2-Chloro-4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	430 / 2.28
144	8-(3,4-dimethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	406 / 2.37
145	8-(2,4-Dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	438 / 2.20
146	8-(2,5-Dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	438 / 2.18
147	8-(2,3-Difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	414 / 2.23
148	8-(3,4-Dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	438 / 2.11
149	8-(3,4-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	414 / 2.25
150	8-(5-Fluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	426 / 2.21
151	8-(4-Fluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	426 / 2.22
152	8-(3,5-Fimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	438 / 2.21
153	8-(2,5-Difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	414 / 2.23
154	8-(3-Fluoro-4-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	426 / 2.20
155	8-(2-Fluoro-3-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	426 / 2.19
156	8-(3,5-Difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	414 / 2.06

EX.	Name	LC-MS: m/ e (M+H) ⁺ / R _t [min]
157	8-(3-Fluoro-5-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	426 / 2.25
158	8-(Naphthalen-2-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	428 / 2.35
159	8-Phenyl-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	378 / 2.21
160	8-(1-Benzofuran-2-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	418 / 2.29
161	8-(1-Methyl-1H-pyrazol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	382 / 1.90
162	8-(4,5-Difluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	434
163	8-(2-Fluoro-4-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	410 / 2.28
164	8-(2-Fluoro-5-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	442

EXAMPLE 165: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yl)phthalazin-1(2H)-one



5 165.1 8-Chloro-2-(2-imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one

To a solution of triphenylphosphine (5.81 g, 22.15 mmol) in THF (150 mL), DIAD (7.54 mL, 38.8 mmol) was added at 0°C. After stirring for 15 min, 2-(imidazo[1,2-a]pyridin-2-yl)ethanol from Example a4 (2.00 g, 11.07 mmol) was added. After another 15 min, 8-chlorophthalazin-1(2H)-one from Example 98.3 (1.80 g, 11.07 mmol) was added. The mixture was stirred overnight at room temperature. LC-MS indicated complete conversion to the product. 1 N HCl was added (pH= 4).The mixture

10

was extracted with EtOAc, the EtOAc layers were discarded. The aqueous layer was neutralized by aq. NaHCO₃ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude title product was recrystallized from ethyl acetate to give
 5 3.1 g (yield: 86%) of a bright beige solid.

165.2 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yl)phthalazin-1(2H)-one

A reaction tube was charged with 8-chloro-2-(2-imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one (80 mg, 0.246 mmol) and a mixture of 1.5 mL of ethanol
 10 and 1.5 mL of toluene under argon. To this suspension, pyridin-3-ylboronic acid (30.3 mg, 0.246 mmol) and Na₂CO₃ (39.2 mg, 0.369 mmol) were added. Then, tetrakis-(triphenylphosphine)palladium (28.5 mg, 0.025 mmol) was added. The reaction mixture was heated in a Biotage microwave at about 130 °C for about 30 min. The reaction was monitored by TLC (DCM/methanol = 9:1). After completion of the reaction, EA was
 15 added followed by the addition of 1 N HCl. The mixture was extracted twice with EtOAc. The aqueous layer was basified with 2N NaOH and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was triturated from ethyl acetate to give the title compound as a white solid (12 mg, 13.26%).

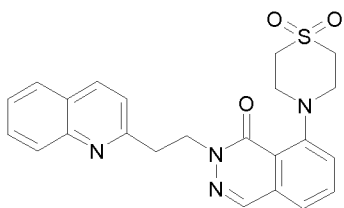
20 LC-MS: m/e = 368.1 (M+H)⁺

The compound of Examples 166-172 were prepared in analogy to the method described in Example 165.2.

EX.	Name	LC-MS: m/ e (M+H) ⁺
166	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-yl)phthalazin-1(2H)-one	368.1
167	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(3-methoxypyridin-4-yl)phthalazin-1(2H)-one	398.1
168	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyrimidin-5-yl)phthalazin-1(2H)-one	368.8

EX.	Name	LC-MS: m/ e (M+H) ⁺
169	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-methyl-1H-pyrazol-3-yl)phthalazin-1(2H)-one	371.1
170	8-(Furan-3-yl)-2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	357.1
171	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxo-2,3-dihydro-1H-indol-6-yl)phthalazin-1(2H)-one	422.1
172	8-(3,4-Dihydro-2H-chromen-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	423.2

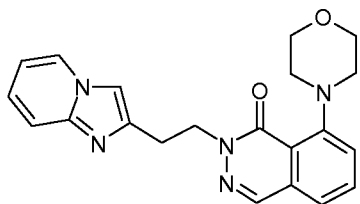
EXAMPLE 173: 8-(1,1-Dioxidothiomorpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]-phthalazin-1(2H)-one



- 5 A microwave reaction vial was charged with the 8-chloro-2-(2-(quinolin-2-yl)ethyl)phthalazin-1(2H)-one from Example 98.4 (100 mg, 0.30 mmol), Cs₂CO₃ (194 mg, 0.59 mmol), Pd₂(dba)₃ (5.45 mg, 5.96 μmol) and BINAP (11.13 mg, 0.018 mmol). The solids were purged with argon for 1 h. A separate flask was charged with toluene (993 μl) and thiomorpholin 1,1-dioxide (48.3 mg, 0.36 mmol), degas with argon for 1 h
- 10 and then transferred to the microwave reaction vial under inert conditions. The resulting reaction mixture was heated on microwave at 100 °C for 20 h. The reaction mixture was poured into water and extracted with DCM. The solids were removed. The organic layer was washed with water, dried over MgSO₄, filtered and concentrated *in vacuo*. The residue was purified on a silica column (eluent: DCM/methanol) and then recrystallized
- 15 from EA to afford the title product (87 mg, 67.2%).

LC-MS: m/e = 435.1 (M+H)⁺

EXAMPLE 174: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(morpholin-4-yl)phthalazin-1(2H)-on



A microwave reaction vial was charged with the 8-chloro-2-(2-imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one from Example 165.1 (100 mg, 0.31 mmol), Cs₂CO₃ (201 mg, 0.62 mmol), Pd₂(dba)₃ (5.64 mg, 6.16 μmol) and BINAP (11.50 mg, 0.018 mmol). The solids were purged with argon for 1 h. A separate flask was charged with toluene (993 μl) and morpholine (32.2 mg, 0.37 mmol), degas with argon for 1 h and then transferred to the microwave reaction vial under inert conditions. The resulting reaction mixture was heated on microwave at 100 °C for 20 h. The reaction mixture was poured into water and extracted with DCM. The solids were removed. The organic layer was washed with water, dried over MgSO₄, filtered and concentrated *in vacuo*. The residue was purified on a silica column (eluent: DCM/methanol) and then recrystallized from EA to afford the title product (11 mg, 9.52 %).

LC-MS: m/e = 376.1 (M+H)⁺

The compound of Examples 175 to 191 were prepared in analogy to the method described in Example 174.

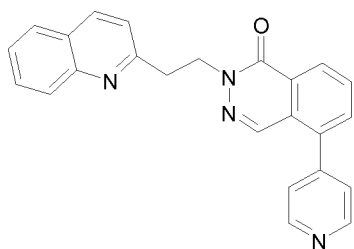
EX.	Name	LC-MS: m/ e (M+H) ⁺
175	8-(1,1-Dioxidothiomorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	424.1
176	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)phthalazin-1(2H)-one hydrochloride	402.2
177	8-(5,5-Difluorohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	436.2
178	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperazin-1-yl)phthalazin-1(2H)-one	375.2

EX.	Name	LC-MS: m/ e (M+H) ⁺
	hydrochloride	
179	8-(4,4-Difluoropiperidin-1-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	410.2
180	8-[4-(Chloromethyl)-4-(hydroxymethyl)piperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	451.9
181	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-1-yl)phthalazin-1(2H)-one hydrochloride	374.2
182	8-(2,3-Dihydro-4H-1,4-benzoxazin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	424.1
183	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[4-(trifluoromethyl)piperidin-1-yl]phthalazin-1(2H)-one hydrochloride	442.2
184	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(4-methylpiperazin-1-yl)phthalazin-1(2H)-one hydrochloride	389.2
185	8-(1,3-Dihydro-2H-isoindol-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	408.2
186	8-(7-Benzyl-2,7-diazaspiro[4.4]non-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	505.3
187	8-({[(3aR,4S,6aS)-2-benzyl-octahydro-cyclopenta[c]pyrrol-4-yl]methyl} amino)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	519.3

EX.	Name	LC-MS: m/ e (M+H) ⁺
188	tert-butyl (3R)-3-({3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl} amino)pyrrolidine-1-carboxylate	475.2
189	8-(2,6-Dimethylmorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	404.2
190	2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,4-oxazepan-4-yl)phthalazin-1(2H)-one hydrochloride	390.2
191	tert-Butyl 4- {3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl} -3,6-dihydropyridine-1(2H)-carboxylate	472.2

II.3 Preparation of compounds of the formula I in which A is A¹, X¹ is N and X³ is -C(R⁹)=C(R⁸)- with R⁹ being Y³-Cyc³

5 EXAMPLE 192: 5-(Pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride



192.1 4-Bromo-3-hydroxy-3H-isobenzofuran-1-one

10 To a stirred solution of *n*-butyllithium 1.6 M in hexanes (17.5 mL, 28.1 mmol) was added at -20 °C under argon 2,2,6,6-tetramethylpiperidine (4.7 mL, 28.1 mmol) in anhydrous THF (40 mL). After cooling (-50 °C), 3-bromobenzoic acid (2.54 g, 12.8 mmol) in anhydrous THF (10 mL) was added dropwise and the mixture was stirred for 1 h. The mixture was then treated with an excess of DMF (3.7 g, 50.4 mmol). The
15 resulting solution was allowed to warm up to ambient temperature, after which water

was added. The aqueous layer was washed with diethyl ether, and then acidified with 4M HCl. The mixture was diluted with diethyl ether and the organic layer was separated and dried with MgSO₄. The residue was purified by crystallization using with EtOAc/PE to give the crude title product (1.18 g, yield: 41 %).

5 LC-MS: $m/e = 229$ (M+H)⁺; R_t=1.47 min.

192.2 5-Bromo-2H-phthalazin-1-one

The compound from Example 192.1 (1 g, 4.4 mmol) was suspended in 5 mL acetic acid under nitrogen. The resulting thick slurry was heated to 90°C. At approximately 80°C, a homogeneous solution was obtained. Hydrazine monohydrate (64%, 0.66 mL, 13.2 mmol) was added dropwise (exotherm), keeping the internal temperature between 90 and 93°C over approximately 4h. The resulting suspension was continued to stir at 90°C as the conversion of starting material was monitored by LC (<1%). Water (10 mL) preheated to 80°C was added, maintaining the mixture at 80-15 90°C followed by cooling down to 20°C over approximately 2h time. At this point, the resulting suspension was transferred onto a filter. The filter cake was rinsed with water (10 mL*3). The wet product was air-dried overnight to afford the title product (570 mg, Yield: 58 %).

LC-MS: $m/e = 227$ (M+H)⁺; R_t=1.65 min, ¹H NMR (400MHz, DMSO-*d*₆): δ
20 12.94 (s, 1H), 8.41 (s, 1H), 8.25-8.19 (m, 2H), 7.77-7.73 (m, 1H).

192.3 5-Bromo-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one

To a mixture of PPh₃ (699 mg, 2.67 mmol) in THF (50 mL) and DIAD (198 mg, 0.98 mmol), 5-bromo-2H-phthalazin-1-one (300 mg, 1.33 mmol) and then 2-quinolin-2-yl-ethanol from example a1 (254 mg, 1.46 mmol) were added dropwise at 15°C under nitrogen. The mixture was stirred at room temperature overnight. Water was added and the mixture was extracted with EtOAc. The organic phase was washed with HCl (1 N). The aqueous phase was basified and extracted with DCM. The organic phase was washed with a NaHCO₃-solution, dried over Na₂SO₄, filtered and concentrated. The crude product was recrystallized from EA and dried to give the title compound as bright beige solid (300 mg, 59.2% yield).
30

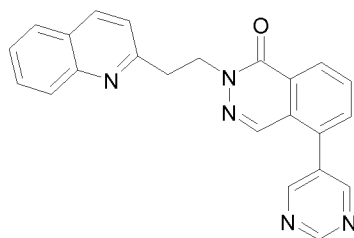
192.4 5-(Pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one
hydrochloride

A reaction tube was charged with a solution of 5-bromo-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one (70 mg, 0.184 mmol) in 1.5 mL of ethanol and 1.5 mL of toluene under argon. To this suspension, pyridin-4-ylboronic acid (22.63 mg, 0.184 mmol) and a 2M solution of Na₂CO₃ (39.2 mg, 0.369 mmol) were added. Then, tetrakis-(triphenylphosphine)palladium (21.27 mg, 0.018 mmol) was added. The reaction mixture was heated in a Biotage microwave at about 130 °C for about 30 min. The reaction was monitored by TLC (DCM/methanol = 9:1). After completion of the reaction, EA was added followed by the addition of 1 N HCl. The mixture was extracted twice with EtOAc. The organic layer was basified with NaHCO₃ and extracted with brine. The organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was dissolved in isopropanol. Isopropanol containing HCl was added. The precipitate was sucked off and recrystallized from hot isopropanol to give a bright gray solid (55 mg, 72.0%).

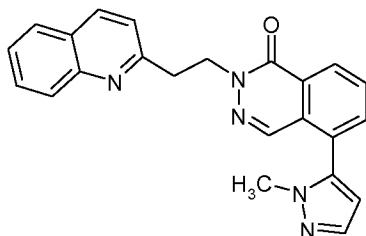
LC-MS: $m/e = 379.1$ (M+H)⁺

EXAMPLE 193: 5-(Pyrimidin-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one
hydrochloride

The title compound was prepared in analogy to the method described in Example 192. LC-MS: $m/e = 380.1$ (M+H)⁺

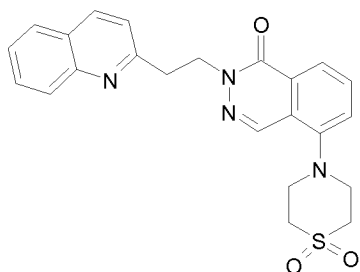


EXAMPLE 194: 5-(1-Methyl-1H-pyrazol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one



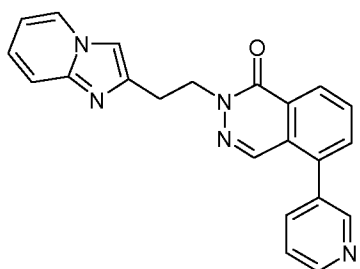
The title compound was prepared in analogy to the method described in Example 192. LC-MS: $m/e = 382.2$ ($M+H$)⁺

5 EXAMPLE 195: 5-(1,1-Dioxidothiomorpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one



The title compound was prepared in analogy to the method described in Example 173 but using 5-bromo-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one instead of 8-chloro-2-(2-(quinolin-2-yl)ethyl)phthalazin-1(2H)-one. LC-MS: $m/e = 435.1$ ($M+H$)⁺.

EXAMPLE 196: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-3-yl)phthalazin-1(2H)-one



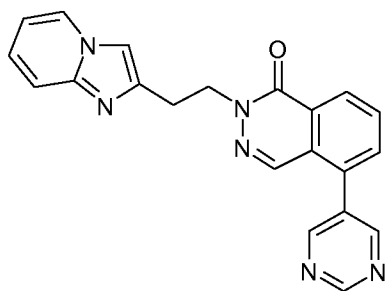
15 196.1 5-Bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one

The title compound was prepared in analogy to the method described in Example 192.3 but using 2-(imidazo[1,2-a]pyridin-2-yl)ethanol from Example a4. Yield: 84%.

196.2 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-3-yl)phthalazin-1(2H)-one

The title compound was prepared in analogy to the method described in Example 192.4 but using 5-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one. LC-MS: $m/e = 368.1$ (M+H)⁺

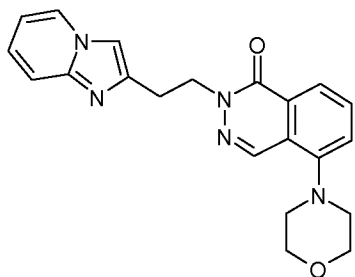
5 EXAMPLE 197: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyrimidin-5-yl)phthalazin-1(2H)-one



The title compound was prepared in analogy to the method described in Example 196 but using 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidine. Yield: 73.9%.

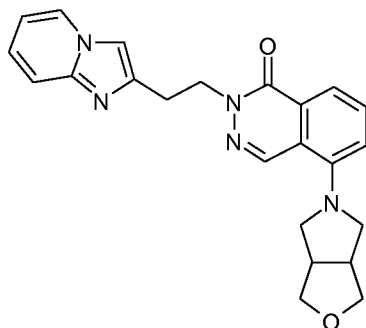
10 LC-MS: $m/e = 368.8$ (M+H)⁺

EXAMPLE 198: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(morpholin-4-yl)phthalazin-1(2H)-one hydrochloride



15 The title compound was prepared in analogy to the method described in Example 174 but using 5-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one from Example 196.1 instead of 8-chloro-2-(2-imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one. Yield: 2.1%. LC-MS: $m/e = 376.2$ (M+H)⁺

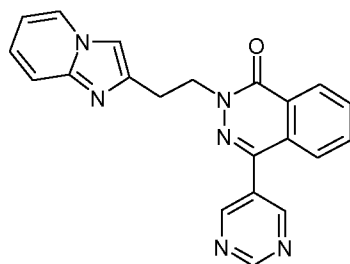
20 EXAMPLE 199: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)phthalazin-1(2H)-one hydrochloride



The title compound was prepared in analogy to the method described in Example 176 but using 5-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one from Example 196.1 instead of 8-chloro-2-(2-imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one. Yield: 11.8%. LC-MS: $m/e = 402.2$ (M+H)⁺

II.4 Preparation of compounds of the formula I in which A is A¹, X¹ is N, X² is C-R⁷ with R⁷ being Y²-Cyc² and X³ is -C(R⁹)=C(R⁸)-

10 EXAMPLE 200: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(pyrimidin-5-yl)phthalazin-1(2H)-one



200.1 4-Bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-phthalazin-1(2H)-one

To a solution of triphenylphosphine (1165 mg, 4.44 mmol) in THF (60 mL),
 15 DIAD (1.5 mL, 7.78 mmol) was added at 0°C under nitrogen. After stirring for 30 min, 4-bromophthalazin-1(2H)-1-one (0.5 g, 2.22 mmol) was added. After further stirring, 2-(2-imidazo[1,2-a]pyridin-2-yl)ethanol from Example a4 (396 mg, 2.44 mmol) was added. The mixture was stirred for 12 h at room temperature. LC-MS indicated complete conversion to the product. EA and water were added. The organic phase was washed
 20 with 1 N HCl. The EtOAc layers were discarded. The aqueous layer was neutralized by aq.NaHCO₃ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The

crude title product was recrystallized from diisopropyl ether/ EA (1:1) to give 710 mg (yield: 87%) of a white solid.

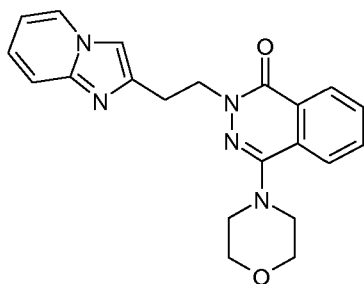
200.2 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(pyrimidin-5-yl)phthalazin-1(2H)-one

5 The title compound was prepared in analogy to the method described in Example 168 but using 4-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-phthalazin-1(2H)-one. Yield: 35.1%. LC-MS: $m/e = 369.1$ (M+H)⁺

EXAMPLE 201: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(morpholin-4-yl)phthalazin-1(2H)-one

10

The title compound was prepared in analogy to the method described in Example 198 but using 4-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-phthalazin-1(2H)-one. Yield: 48.2%. LC-MS: $m/e = 376.2$ (M+H)⁺

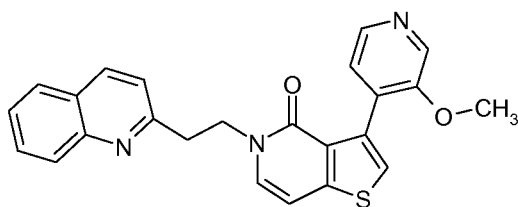


15

II.5 Preparation of compounds of the formula I in which A is A¹, X¹ is CH, R¹ is Y¹-Cyc¹ and X³ is S

EXAMPLE 202: 3-(3-Methoxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one

20



202.1 (E)-3-(4-Bromothiophen-2-yl)acrylic acid

Piperidine (1.036 mL, 10.47 mmol) was added to a mixture of 4-bromothiophene-2-carbaldehyde (20 g, 105 mmol) and malonic acid (13.07 g, 126 mmol) at 80°C under nitrogen atmosphere. The reaction mixture was stirred for 2 h at 100°C. The reaction

25

mixture was cooled to room temperature and extracted with EA/water. The organic phase was washed with 2N NaOH. The aqueous phase was acidified and a precipitate was formed. The solid was stirred in a mixture of DCM and diisopropyl ether (1:1). The solid was sucked off and dried under reduced pressure to give a bright beige solid (12.3 g, 50.4%).

202.2 (E)-3-(4-Bromothiophen-2-yl)acryloyl azide

To a solution of (E)-3-(4-bromothiophen-2-yl)acrylic acid (9.30 g, 39.9 mmol) in acetone (100 mL), triethylamine (4.24 g, 41.9 mmol) was added under nitrogen atmosphere. At 0°C, isobutyl chloroformate (5.72 g, 41.9 mmol) was slowly added and then, the mixture was stirred for 1 h. 4.67 g (71.8 mmol) of sodium azide dissolved in 10 mL of water was slowly added at 0°C, the mixture was stirred at 0°C for a further hour and then warmed up to room temperature overnight. The reaction mixture was extracted with EA/water. The organic phase was washed aq. NaHCO₃ solution and then with brine. The organic phase was dried over MgSO₄, concentrated to dryness and the residue was purified by trituration with diisopropyl ether to afford a bright beige solid (9.00 g, 34.9 mmol). Yield: 87%.

202.3 3-Bromothieno[3,2-c]pyridin-4(5H)-one

100 mL of diphenyl ether were warmed to 210°C and then a solution of (E)-3-(4-bromothiophen-2-yl)acryloyl azide (9.95 g, 38.6 mmol) in 50 mL of diphenyl ether was added under nitrogen. The reaction mixture was held at this temperature for 15 min. After cooling to room temperature, the reaction mixture was diluted with 100 mL of cyclohexane. The precipitate was sucked off and dried in vacuo to give 6.6 g (yield: 74.4%) of the title compound as brown solid.

202.4 3-Bromo-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one

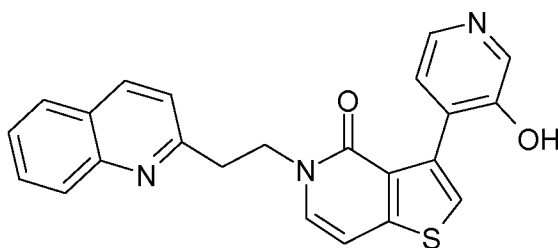
The title compound was prepared in analogy to the method described in Example 192.3 but using 3-bromothieno[3,2-c]pyridin-4(5H)-one. Yield: 26.6%. As a byproduct, 3-bromo-4-(2-quinolin-2-yl)ethoxythieno[3,2-c]pyridine was obtained (yield: 23.3%). Using a Companion® chromatography system (normal phase, eluent cyclohexane/ethyl acetate), the title compound was obtained as a bright beige solid.

202.5 3-(3-Methoxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one

A reaction tube was charged with a solution of 3-bromo-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-on (100 mg, 0.260 mmol) in 1.5 mL of ethanol and 1.5 mL of toluene under argon. To this suspension, 3-methoxypyridin-4-ylboronic acid (39.7 mg, 0.260 mmol) and a 2M solution of Na₂CO₃ (41.3 mg, 0.389 mmol) were added. Then, tetrakis(triphenylphosphine)palladium (30.0 mg, 0.026 mmol) was added. The reaction mixture was heated in a Biotage microwave at about 130 °C for about 30 min. The reaction was monitored by TLC (DCM/methanol = 9:1). After completion of the reaction, EA was added followed by the addition of 1 N HCl. The mixture was extracted twice with EtOAc. The organic layer was basified with NaHCO₃ and extracted with brine. The organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was dissolved in isopropanol. Isopropanol containing HCl was added. The precipitate was sucked off and recrystallized from hot ethyl acetate to give a white solid (32 mg, 29.8%).

LC-MS: $m/e = 414.1$ (M+H)⁺

20 EXAMPLE 203: 3-(3-Hydroxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one hydrochloride



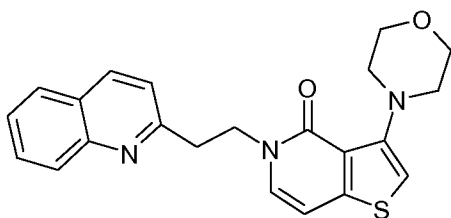
To 3-(3-methoxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one (50.0 mg, 0.121 mmol) in DCM (20 mL) was added 1M BBr₃ in DCM (0.363 mmol, 91 mg). The reaction mixture was stirred for 2 h under nitrogen. The reaction mixture was poured onto water and basified with 1N NaOH, extracted with DCM and dried. The organic phase was concentrated to dryness and the residue was purified by column chromatography (normal phase) on silica using DCM/methanol to give the title compound (13 mg, 0.030 mmol).

LC-MS: $m/e = 400.1$ (M+H)⁺

The compounds of Example 204 to 210 were prepared in analogy to the method described above.

EX.	Name	LC-MS: m/ e (M+H) ⁺
204	3-(1-Methyl-1H-pyrazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one hydrochloride	387.1
205	3-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one hydrochloride	384.1
206	3-(Pyrimidin-5-yl)-5-(2-quinolin-2-yl)ethylthieno[3,2-c]pyridin-4(5H)-one	385.1
207	3-(2-Oxoindolin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one	438.1
208	3-(3-Hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one hydrochloride	399.1
209	5-[2-(5-Ethylpyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one hydrochloride	362.1
210	5-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one hydrochloride	373.1

5 EXAMPLE 211: 3-(Morpholin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one hydrochloride



211.1 3-Morpholinothieno[3,2-c]pyridin-4(5H)-one

3-Bromothieno[3,2-c]pyridin-4(5H)-one from Example 202.3 (411 mg, 1.786 mmol) and morpholine 81501 mg, 17.23 mmol) were stirred in a microwave for 3 h at 220°C. The mixture was poured onto water and extracted with DCM. The organic phase was concentrated and the residue was recrystallized from EA to give 180 mg (yield: 42.6%) of the title compound.

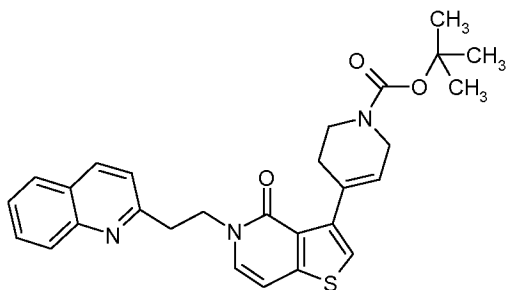
211.2 3-(Morpholin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one hydrochloride

The title compound was prepared in analogy to the method described in Example 1.6 but using THF as solvent. Yield: 20.5%. LC-MS: $m/e = 392.1$ (M+H)⁺

5

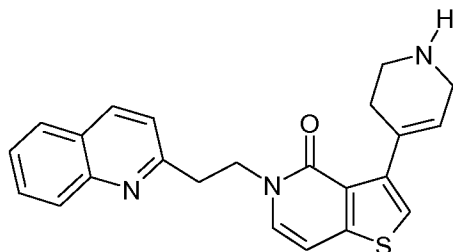
EXAMPLE 212: tert-Butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-5,6-dihydropyridine-1(2H) carboxylate

The title compound was prepared in analogy to the method described in Example 202.5.



10

EXAMPLE 213: 5-(2-(Quinolin-2-yl)ethyl)-3-(1,2,3,6-tetrahydropyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one hydrochloride



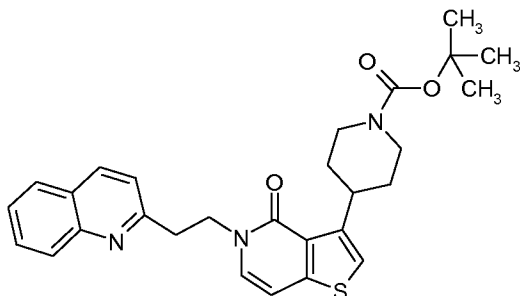
15

Tert-butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-5,6-dihydropyridine-1(2H) carboxylate from Example 212 (120 mg, 0.246 mmol) in 1 mL of HCl containing isopropanol was stirred under nitrogen for 12 h at room temperature. The reaction mixture was extracted with DCM, the aqueous phase was basified with 1N NaOH and extracted with DCM. The organic phase was dried, concentrated and the residue was recrystallized from HCl-isopropanol to give the title compound as hydrochloride salt as yellow solid (90 mg, 86%).

20

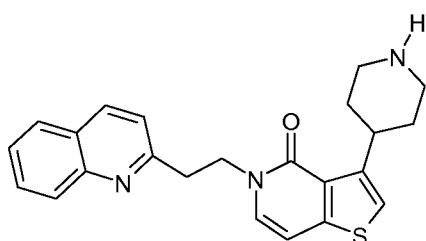
LC-MS: $m/e = 388.1$ (M+H)⁺

EXAMPLE 214: tert-Butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-piperidine-1 carboxylate



The title compound was prepared in analogy to the method described in Example 202.5

EXAMPLE 215: 3-(Piperidin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one trifluoroacetate



Route a)

Under nitrogen, 5-(2-(quinolin-2-yl)ethyl)-3-(1,2,3,6-tetrahydropyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one hydrochloride from Example 213 (80 mg, 0.189 mmol) in methanol (15 mL) was hydrogenated at room temperature for 12 h. The title compound was obtained as 2,2,2-trifluoroacetate salt a bright beige solid (4.1 mg, 4.32%) .

LC-MS: $m/e = 390.2$ (M+H)⁺

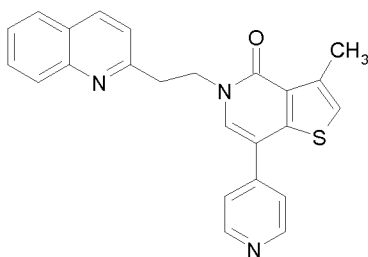
Route b)

The title compound was prepared in analogy to the method described in Example 213 starting from tert-butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-piperidine-1 carboxylate from Example 214.

LC-MS: $m/e = 390.2$ (M+H)⁺

II.6 Preparation of compounds of the formula I in which A is A¹, X¹ is CH, R⁷ is Y²-Cyc² and X³ is S

EXAMPLE 216: 3-Methyl-7-(pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)thieno[3,2-c]pyridin-4(5H)-one



216.1 7-Iodo-3-methyl-5-(2-(quinolin-2-yl)ethyl)thieno[3,2-c]pyridin-4(5H)-one

- 5 To a mixture of triphenylphosphine (901 mg, 3.44 mmol) and DIAD (1.2 mL, 6.01 mmol) in THF (10 mL), 7-iodo-3-methyl-thieno[3,2-c]pyridin-4(5H)-one (500 mg, 1.72 mmol) was added followed by the addition of 2-(quinolin-2-yl)ethanol from example a1 (327 mg, 1.89 mmol) at 15°C under nitrogen. The mixture was stirred overnight at room temperature. The mixture was extracted with EtOAc/H₂O, the EtOAc
- 10 layers were washed with 1N HCl and then discharged. The aqueous layer was neutralized by aq. NaHCO₃ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude title product was recrystallized from ethyl acetate to give the title compound as bright beige solid (yield: 14.35%). LC-MS: *m/e* = 447.0 (M+H)⁺;
- 15 R_t: 2.11 min.

216.2 3-Methyl-7-(pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)thieno[3,2-c]pyridin-4(5H)-one

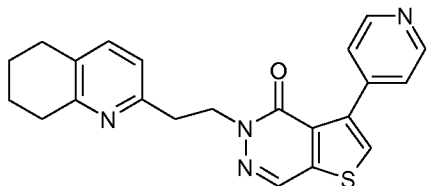
- The title compound was prepared in analogy to the method described in Example
- 20 165.2 but using 7-iodo-3-methyl-5-(2-(quinolin-2-yl)ethyl)thieno[3,2-c]pyridin-4(5H)-one (0.22 mmol) and pyridin-4-ylboronic acid (0.22 mmol). The title compound was obtained as white solid (yield: 22.9%).

LC-MS: *m/e* = 398.1 (M+H)⁺

- 25 II.7 Preparation of compounds of the formula I in which A is A¹, X¹ is N, R¹ is Y¹-Cyc¹

195

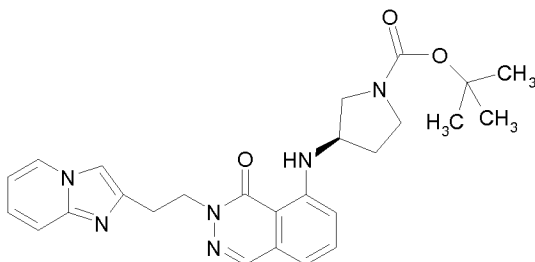
EXAMPLE 217: 3-(Pyridin-4-yl)-5-[2-(5,6,7,8-tetrahydroquinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one hydrochloride



The title compound was prepared in analogy to the method described in Example 1.6 but starting from 3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)one (obtainable by Suzuki coupling of 3-bromo-5H-thieno[2,3-d]pyridazin-4-one from Example 3.3 and pyridin-4-yl boronic acid as described above) and 2-(5,6,7,8-tetrahydroquinolin-2-yl)ethanol from example a6). The title compound was obtained as white solid.

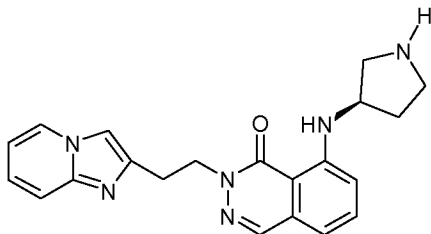
LC-MS: $m/e = 389.1$ (M+H)⁺

EXAMPLE 218: (R)-tert-butyl 3-(3-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)-4-oxo-3,4-dihydrophthalazin-5-ylamino)pyrrolidine-1-carboxylate



A reaction tube was charged with 8-chloro-2-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)phthalazin-1(2H)-one (155 mg, 0.48 mmol), BINAP (17.83 mg, 0.029 mmol), tris(dibenzylideneacetone)dipalladium(0) (8.74 mg, 9.55 μ mol) and cesium carbonate (311 mg, 0.955 mmol) in 1591 μ l of toluene. The mixture was stirred for 1 h under argon. To this mixture, (R)-tert-butyl 3-aminopyrrolidine-1-carboxylate (89 mg, 0.477 mmol) was added. The reaction mixture was heated in a microwave at 105 °C for 20 h. After completion of the reaction, the reaction mixture was extracted with water and DCM. The organic layers were washed with water, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using a normal phase Companion® system (4 g gold, gradient elution: DCM to 10% methanol). Yield: 24.73%. LC-MS: $m/e = 475.2$ (M+H)⁺.

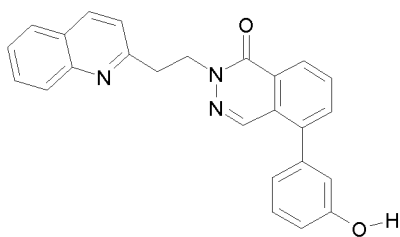
EXAMPLE 219: 2-[2-(Imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3R)-pyrrolidin-3-ylamino]phthalazin-1(2H)-one dihydrochloride



A solution of (R)-tert-butyl 3-(3-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)-4-oxo-3,4-dihydrophthalazin-5-ylamino)pyrrolidine-1-carboxylate from Example 218 (52 mg, 0.110 mmol) in 20 mL of DCM was mixed with 1 mL of HCl containing isopropanol and the reaction mixture was stirred under nitrogen for 12 h at room temperature. The reaction mixture was mixed with diisopropyl ether and the supernatant was discharged. Then, the residue was dissolved in isopropanol and diisopropyl ether was added. The supernatant was discharged. The precipitate was dried to give 24 mg of a yellow salt as solid foam. LC-MS: $m/e = 357.2$ (M+H)⁺

II.8 Preparation of compounds of the formula I in which A is A¹, X¹ is N, X³ is -C(R⁹)=C(R⁸)- with R⁹ being Y³-Cyc³

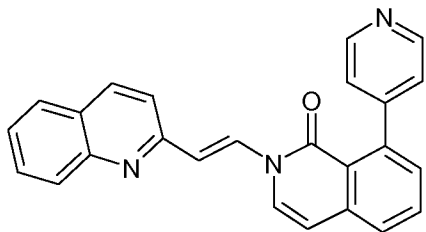
EXAMPLE 220: 5-(3-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one



The title compound was prepared in analogy to the method described in Example 192.

II.9 Preparation of compounds of the formula I in which A is A³, X¹ is CH and R¹ is Y¹-Cyc¹

EXAMPLE 221: (E)-8-(Pyridin-4-yl)-2-(2-(quinolin-2-yl)vinyl)isoquinolin-1(2H)-one



221.1 8-(Pyridin-4-yl)isoquinolin-1(2H)-one

A reaction tube was charged with 8-bromoisoquinolin-1(2H)-one (1 g, 4.46 mmol) and a mixture of 3 mL of ethanol and 3 mL of toluene under argon. To this, an aqueous sodium bicarbonate solution (2 M, 710 mg, 3.35 mL, 6.69 mmol) was added and then pyridin-4-ylboronic acid (549 mg, 4.46 mmol). Then, tetrakis(triphenylphosphine)palladium (516 mg, 4.46 mmol) was added. The reaction mixture was heated in a Biotage microwave at 130 °C for 30 min. The reaction was monitored by TLC (DCM/methanol = 9:1). After completion of the reaction, the reaction mixture was mixed with water and dichloromethane. The solid was sucked off. The organic phase was washed with an aqueous NaHCO₃ solution, brine, dried (MgSO₄) and evaporated. The residue was taken up with EA and the precipitate was sucked off. The crude product was purified by chromatography (Campanion normal phase, gradient elution, using 3-10% DCM in methanol) to yield 465 mg (46.9%) of the title compound.

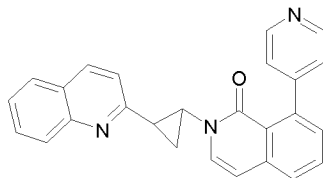
15

221.2 (E)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)vinyl)isoquinolin-1(2H)-one

8-(Pyridin-4-yl)isoquinolin-1(2H)-one (40 mg, 0.180 mmol) and (E)-2-(2-bromovinyl)quinoline (50.6 mg, 0.216 mmol) were dissolved in 2 mL of DMF under argon. The reaction mixture was stirred for 10 h at 115°C. Then, water and EA were added. The organic phase was washed with water and brine, dried (MgSO₄) and concentrated. The crude product was purified by chromatography (CombiFlash, normal phase, gradient elution, using 3-5% DCM in methanol) to yield the title compound as yellow solid (27 mg, 40.0%). LCMS: 376.1; R_t = 1.497.

25 II.10 Preparation of compounds of the formula I in which A is A⁴, X¹ is CH and R¹ is Y¹-Cyc¹

EXAMPLE 222: anti (rac) 8-(Pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



8-(Pyridin-4-yl)isoquinolin-1(2H)-one (200 mg, 0.900 mmol) and syn-2-(2-bromocyclopropyl)quinoline (223 mg, 0.900 mmol) from Example c1) were dissolved in 10 mL of DMF under argon. The reaction mixture was stirred for 1 h at 115°C. Then,
 5 an aqueous solution of sodium chloride and DCM were added. The phases were separated. The organic phase was washed with brine, dried (MgSO₄) and evaporated. The crude product was taken up in a small amount of EA. The precipitate formed was sucked off and dried to yield anti (rac) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one as bright beidge solids (248 mg, 70.8%). LCMS:
 10 390.2.

Separation of anti (rac) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

230 mg (0.591 mmol) of anti (rac) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one dissolved in 60 µl of trifluoroacetic acid were
 15 separated by chromatography (chiral chromatography, Chiralpack AD-H, n-heptane/EtOH) to give 76 mg (33.0%) of compound 222a with positive rotation and 62 mg (27%) of compound 222b with negative rotation.

Compound 222a: (+) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one
 20

[α] = + 87.8° (methanol, 1 mg/mL); yellow solid.

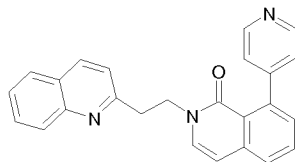
Compound 222b: (-) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

[α] = - 98.3° (methanol, 1 mg/mL); bright yellow solid.

25

II.11 Preparation of compounds of the formula I in which A is A¹, X¹ is CH and R¹ is Y¹-Cyc¹

EXAMPLE 223: 8-(Pyridin-4-yl)-2-(2-(quinolin-2-yl-ethyl)isoquinolin-1(2H)-one



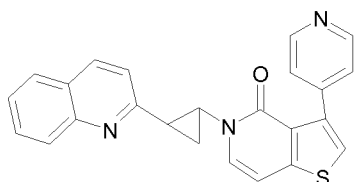
A flask was charged with 8-(pyridin-4-yl)isoquinolin-1(2H)-one (0,113 mmol, 50 mg) in NH_3 /ethanol (2 mol/L) (15 mL, 30,0 mmol). Then, Raney-Nickel in water (5 drops) was added. At room temperature, the hydrogen flow was turned on. The hydrogenation reaction was stopped after 4 days. Under nitrogen, the reaction mixture was filtered over Celite and evaporated to yield 52 mg (80% yield) of the crude title product as soli, yellow oil. The crude product was purified by Combi-flash chromatography (gradient elution using methanol/DCM up to a concentration of 10%). LC-MS: 378.2.

10

II.12 Preparation of compounds of the formula I in which A is A^4 , X^1 is CH and R^1 is Y^1 -Cyc¹

15

EXAMPLE 224: anti (*rac*) 3-(Pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one



224.1 3-(Pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one

3-Bromothieno[3,2-c]pyridin-4(5H)-one (1000 mg, 4.35 mmol) from Example 202.3 was suspended in 2 mL of toluene and 2 mL of ethanol under argon. Then, an aqueous solution of sodium carbonate (691 mg, 6.52 mmol, 2 M) was added. To the suspension, pyridin-4-boronic acid (534 mg, 4.35 mmol) and then tetrakis(triphenyl phosphine)palladium(0) (502 mg, 0.435 mmol) were added. The reaction mixture was heated in a Biotage microwave at 130 °C for 30 min. Water and EA were added. The precipitate formed was collected to give 480 mg of the title compound. The filtrate was acidified with 2 M HCl and extracted with EA (twice). The aqueous phase was basified and extracted three times with EA. The organic phases were combined, washed with

25

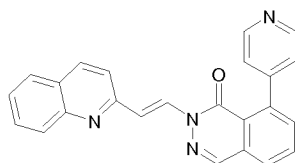
HCl, dried (MgSO₄) and evaporated to give further 43 mg of the title compound. Total yield: 523 mg (52.4%). LC-MS: 229.1 [M+H]⁺; R_t: 0.427.

224.2 anti (rac) 3-(Pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one

The title compound was prepared in analogy to the method described in Example 222. Yield: 57.7%, LC-MS: 396.1.

II.13 Preparation of compounds of the formula I in which A is A³, X¹ is N and R¹ is Y¹-Cyc¹

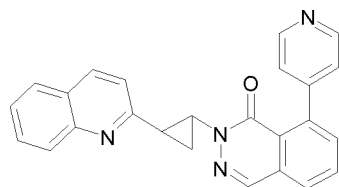
EXAMPLE 225: (E)-8-Pyridin-4-yl-2-((2-quinolin-2-yl-vinyl)-2H-phthalazin-1-one



The title compound was prepared according to the general procedure given above but starting from 8-pyridin-4-yl-2H-phthalazin-1-one. Yield: 5%. LC-MS: 377.1

II.14 Preparation of compounds of the formula I in which A is A⁴, X¹ is N and R¹ is Y¹-Cyc¹

EXAMPLE 226: anti (rac) 8-Pyridin-4-yl-2-(2-(quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one 2,2,2,-trifluoroacetate

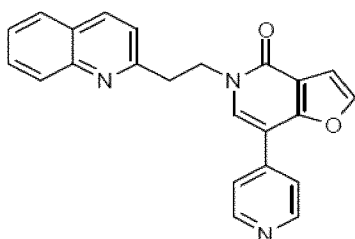


Under argon, a flask was charged with (E)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)vinyl)phthalazin-1(2H)-on (85 mg, 0.226 mmol) in dichloroethane, extra dry, (2,823 mL) at 0°C. Then, diethylzinc (1mol/L in hexane) (1,129 mL, 1,129 mmol) was added within 5min at -3 to 0°C. The reaction mixture was stirred for 10 min at 0°C. Diiodomethane (0,182 mL, 2,258 mmol) was added at 0°C within 2 min. The reaction

mixture was warmed to room temperature and stirred overnight at room temperature. Then, a further portion of diethyl zinc (1 mol/L in hexane) (1,129 mL, 1,129 mmol) was added at 0°C followed by a further portion of diiodomethane (0,182 mL, 2,259 mmol), and the reaction mixture was warmed to room temperature. The reaction mixture was stirred for further 3 days at room temperature. The reaction mixture was poured onto an ice-cold aqueous solution of NaHCO₃ (5%). The reaction mixture was extracted with DCM (3 times). The organic phase was washed with brine, water, dried over sodium sulfate and evaporated. Purification by prep. HPLC yielded 7.1 mg (6.23% yield) of the title compound. LC-MS: 391.1.

II.15 Preparation of compounds of the formula I in which A is A¹, X¹ is CH, R⁷ is Y²-Cyc² and X³ is O

EXAMPLE 227: 7-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]furo[3,2-c]pyridin-4(5H)-one



227.1 7-Bromo-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one

DIAD (4.91 mmol, 992 mg) was added dropwise to PPh₃ (753 mg, 2,80 mmol) in 20 mL of THF. The mixture was stirred for 30 min. Then 7-bromofuro[3,2-c]pyridine-4(5H)-one (300 mg, 1.402 mmol) was added followed by the addition of 2-(quinolin-2-yl)ethanol (243 mg, 1.402 mmol). The reaction mixture was stirred overnight at room temperature. The reaction mixture was extracted with water/ ethyl acetate. The organic phase was extracted with 1N HCl. The acidic aqueous phase was basified with 1N NaOH and extracted with DCM. The organic phase was extracted with water, dried over MgSO₄, filtered, concentrated and purified by chromatography to give the title compound as white solid (119 mg, 23%).

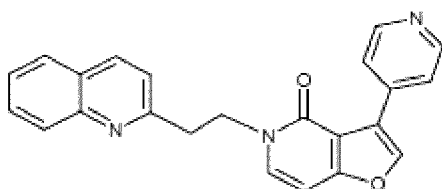
227.2 7-(Pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]furo[3,2-c]pyridin-4(5H)-one

The title compound was prepared in analogy to the method described in Example 165.2 but using 7-bromo-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one (61.7 mg, 0.167 mmol) and pyridin-4-ylboronic acid (22.82 mg, 0.167 mmol). The title compound was obtained as yellowish solid (yield: 22 mg, 35.8.9%).

5 LC-MS: $m/e = 368.1$ (M+H)⁺

II.16 Preparation of compounds of the formula I in which A is A¹, X¹ is CH, R¹ is Y¹-Cyc¹ and X³ is O

10 EXAMPLE 228: 3-(Pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one hydrochloride



228.1 (E)-3-(4-Bromofuran-2-yl)acryloyl chloride

To a solution of (E)-3-(4-bromofuran-2-yl)acrylic acid (3.8 g, 17.51 mmol) in 35 mL of trichloromethane was added a solution of 2.6 mL of thionyl chloride in 200 μ L of DMF. The reaction mixture was refluxed for 1 h and after cooling to room temperature concentrated to give 4 g (97% yield) of the title compound as light brown oil.

228.2 (E)-3-(4-Bromofuran-2-yl)acryloyl azide

20 A solution of (E)-3-(4-bromofuran-2-yl)acryloyl chloride (4.0 g, 16.99 mmol) in 10 mL of 1,4-dioxane was added to a solution of sodium azide (2.21 g, 34.0 mmol) in 10 mL of water and 10 mL of 1,4-dioxane. The reaction mixture was stirred for 2.5 h at room temperature. The reaction mixture was mixed with ethyl acetate and water. Phases were separated and the aqueous phase was extracted with ethyl acetate (twice). The combined organic phases were washed with brine, dried, filtrated and concentrated to give 4 g of the title compound (yield: 97%).

228.3 3-Bromofuro[3,2-c]pyridin-4(5H)-one

203

A solution of (E)-3-(4-bromofuran-2-yl)acryloyl azide (4 g, 16.53 mmol) in 20 mL of diphenyl ether was slowly added to 80 mL of diphenyl ether at 230°C. The mixture was stirred for further 15 min. The reaction mixture was allowed to cool down to room temperature. 100 mL of cyclohexane were added and the reaction mixture was stirred overnight. A precipitate was formed, filtered off and suspended in 50 mL of cyclohexane. The mixture was stirred for 1 h at room temperature. The precipitate was filtered off to give 2.76 g (78%) of the title compound as brownish solid.

LC-MS: m/e 215.9 (M+H)⁺

10 228.4 3-(Pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one

A reaction tube was charged with 3-bromofuro[3,2-c]pyridin-4(5H)-one (1000 mg, 4.67 mmol) and a mixture of 1 mL of ethanol and 1 mL of toluene under argon. To this mixture, pyridin-4-ylboronic acid (574 mg, 4.67 mmol) and a 2 M solution of Na₂CO₃ (743 mg, 7.01 mmol) were added followed by the addition of tetrakis-(triphenylphosphine)palladium (540 mg, 0.467 mmol). The reaction mixture was heated in a Cem microwave at about 130 °C for about 30 min. After completion of the reaction, EA was added followed by the addition of 2 N HCl. The mixture was extracted twice with EtOAc. The aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography to give the title compound as dark yellow solid (430 mg, 43.4%).

228.5 3-(Pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one

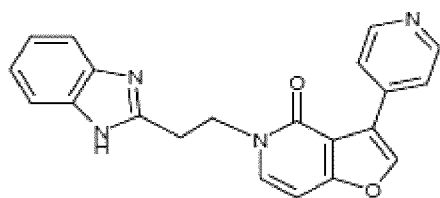
To a solution of triphenylphosphine (247 mg, 0.942 mmol) in THF (10 mL), DIAD (0.321 mL, 1.65 mmol) was added. The mixture was cooled to 15°C. 3-(Pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one (100 mg, 0.471 mmol) and 2-(quinolin-2-yl)ethanol from example from example a1 were added. After stirring overnight at room temperature, EA and 2M HCl were added. The phases were separated and extracted with EA. The organic phase was washed with water. The acidic aqueous phase was basified with 2M NaOH and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced

pressure. The residue was purified by chromatography to give 69 mg of the title compound (36.3%) as hydrochloride salt as dark yellow solid.

LC-MS: m/e 368.1 (M+H)⁺

- 5 The compounds of examples 229 to 231 were prepared in analogy to the method described in example 228.

EXAMPLE 229: 5-(2-(1H-Benzo[d]imidazol-2-yl)ethyl)-3-(pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one hydrochloride



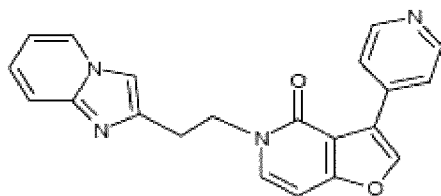
10

The title compound was obtained as grey solid (Yield: 3.46%).

LC-MS: m/e 357.1 (M+H)⁺

EXAMPLE 230: 5-(2-(Imidazo[1,2-a]pyridin-2-yl)ethyl)-3-(pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one hydrochloride

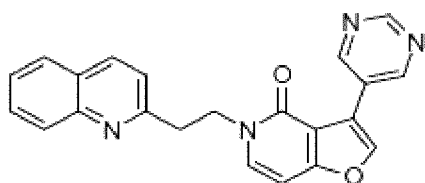
15



The title compound was obtained as grey solid (Yield: 30.3%)

LC-MS: m/e 357.1 (M+H)⁺

20 EXAMPLE 231: 3-(Pyrimidin-5-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one



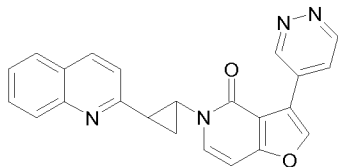
The title compound was obtained as bright yellow solid (Yield: 28.1.3%)

LC-MS: m/e 369.1 (M+H)⁺

II.17 Preparation of compounds of the formula I in which A is A⁴, X¹ is CH, R¹ is Y¹-Cyc¹ and X³ is O

5

EXAMPLE 232: anti 3-(Pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one



232.1 anti 3-Bromo-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one

10 A microwave reaction tube was charged with 3-bromofuro[3,2-c]pyridin-4(5H)-one (300 mg, 1.402 mmol) from Example 228.3, syn 2-(2-bromocyclopropyl)quinoline (348 mg, 1.402 mmol) from example c1), cesium carbonate (913 mg, 2.80 mmol) and 5 mL of DMF. The reaction mixture was stirred for 1.5 h at 110°C. EA and water were added. The phases were separated. The aqueous phase was washed with EA (twice).

15 The organic phases were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by chromatography to give 450 mg (84%) of the title compound as light brown yellow solid

20 232.2 anti 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one

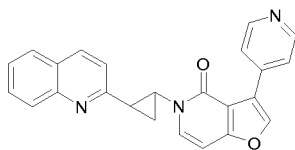
The compound from Example 232.1 was suspended in 1 mL of toluene and 1 mL of methanol under argon. Then, an aqueous solution of sodium carbonate (41.7 mg, 0.39 mmol, 2 M) was added. To the suspension, 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridazine (54 mg, 0.26 mmol) and then tetrakis(triphenylphosphine)palladium(0) (30.3 mg, 0.026 mmol) were added. The reaction mixture was heated in a Biotage microwave at 130 °C for 30 min. Water and EA were added. The aqueous phase was extracted twice with EA. The organic phases were combined, washed with HCl, dried (MgSO₄) and evaporated. The residue was purified by chromatography to give 15.5 mg

25

30 (yield: 15.53%) of the title compound as light brownish solid.

LC-MS: m/e 380.8 (M+H)⁺

EXAMPLE 233: anti 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one



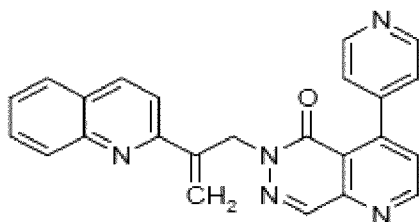
5

The title compound was prepared according to the method described for example 232.2. The title compound was obtained as yellow solid. LC-MS: m/e 379.9 (M+H)⁺

II.18 Preparation of compounds of the formula I in which A is A⁵, X¹ is N, R¹ is Y¹-Cyc¹ and X³ is N=C(R⁸)

10

EXAMPLE 234: 4-(Pyridin-4-yl)-6-(2-(quinolin-2-yl)allyl)pyrido[2,3-d]pyridazin-5(6H)-one



234.1 (E)-Ethyl 2-((2-acetylhydrazono)methyl)-4-chloronicotinate

To 2.1 g (9.83 mmol) of ethyl 4-chloro-2-formylnicotinate in 60 mL of ethanol was added 0.874 g (11.80 mmol) of acetohydrazide at room temperature. Then, the reaction mixture was heated under reflux for 2h. The reaction mixture was extracted with water/DCM. The organic phase was washed with brine, dried, filtrated and concentrated to give 1.95 g (73.6%) of the title compound as white solid.

20

234.2 4-Chloropyrido[3,2-d]pyridazin-5(6H)-one

(E)-ethyl 2-((2-acetylhydrazono)methyl)-4-chloronicotinate (2850 mg, 10.57 mmol) in 15 mL of dioxane was mixed with aq. NaOH (42.3 mg, 1.06 mmol, 2 M). The reaction mixture was stirred in a microwave for 60 min at 145°C. After cooling to room temperature, the solid was filtered off. The solid was dissolved in methanol and the

25

residue was filtered off. The filtrate was concentrated and triturated with EA to give 1.4 g (73.0%) of the title compound as orange brown solid.

234.3 4-(Pyridin-4-yl)pyrido[3,2-d]pyridazin-5(6H)-one

5 A reaction tube was charged with a solution of 4-chloropyrido[3,2-d]pyridazin-5(6H)-one (0.354 mmol) in 1 mL of ethanol and 1 mL of toluene under argon. To this suspension, a 2M solution of Na₂CO₃ (0.531 mmol) and pyridin-4-ylboronic acid (0.354 mmol) were added. Then, tetrakis(triphenylphosphine)palladium (0.035 mmol) was added. The reaction mixture was heated in a CEM microwave at about 130 °C for about 10 20 min. The reaction was monitored by TLC (DCM/methanol = 9:1). After completion of the reaction, EA was added followed by the addition of water. The organic layer was basified with NaHCO₃. The organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (25.2%).

15

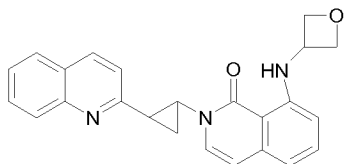
234.4 4-(Pyridin-4-yl)-6-(2-(quinolin-2-yl)allyl)pyrido[2,3-d]pyridazin-5(6H)-one

A reaction tube was charged with 307 mg (1.369 mmol) of 4-(pyridin-4-yl)pyrido[2,3-d]pyridazin-5(6H)-one, syn-2-(2-bromocyclopropyl)quinoline from example c1 and cesium carbonate (892 mg, 2.74 mmol). The reaction mixture was 20 heated for 6h at 110°C under argon. After cooling to room temperature, EA was added followed by the addition of water. The organic layer was basified with NaHCO₃. The organic layers were dried over MgSO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to give 106 mg of the title compound (yield: 19.78%).

25

II.19 Preparation of compounds of the formula I in which A is A⁴

EXAMPLE 235: anti 8-(Oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



30

235.1 anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one
8-bromoisoquinolin-1(2H)-one (300 mg, 1.339 mmol) and syn-2-(2-bromocyclopropyl)quinoline (332 mg, 1.339 mmol) from Example c1) were dissolved in 4 mL of DMF under argon. Cesium carbonate (873 mg, 2.68 mmol) was added. The
5 reaction mixture was stirred for 1 h at 115°C. Then, an aqueous solution of sodium chloride and DCM were added. The phases were separated. The organic phase was washed with brine, dried (MgSO₄) and evaporated. The crude product was taken up in a small amount of EA. The precipitate formed was sucked off and dried to yield anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one as bright beidge solid
10 (330 mg, 63.0%). LC-MS: 391.0 (M⁺); R_t: 1.6 min.

Separation of anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

33g of anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one were
15 suspended in isopropyl acetate/heptane 1:4 (5 mL/g). The racemate was separated by chiral chromatography to give 16.1 g of anti (+) 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (compound 235.1a) R_t = 4.885 min and 20.25 g of anti (-) 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (compound 235.1b), R_t = 9.253 min.

20

235.2 anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

A microwave reaction vial was charged with the anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one from Example 235.1 (70 mg, 0.18 mmol),
25 Cs₂CO₃ (175 mg mg, 0.54 mmol), Pd₂(dba)₃ (3.28 mg mg, 3.58 μmol) and BINAP (6.68 mg, 10.73 μmol). The solids were purged with argon for 1 h. A separate flask was charged with toluene (2 mL) and oxetan-3-amine (19.6 mg, 0.18 mmol), degas with argon for 1 h and then transferred to the microwave reaction vial under inert conditions. The resulting reaction mixture was heated on microwave at 105 °C for 48 h. The
30 reaction mixture was poured into water and extracted with DCM. The solids were removed. The organic layer was washed with water, dried over MgSO₄, filtered and

concentrated *in vacuo*. The residue was purified on a silica column (eluent: DCM/methanol) and then triturated with EA to afford the title product (35 mg, 51.0 %).

LC-MS: $m/e = 384.2$ (M+H)⁺.

5 Separation of anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

484 mg (0.591 mmol) of anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one dissolved in 20 mL of ethanol-DCM (1:1 mixture) and 1 mL of the solution were chromatographed on a Whelk-O (R,R) 2 x 25
10 cm (10 mkm particles) column in EtOH (containing 0.1% n-propylamine) at 40 mL/min and 254 nm detection. Peaks obtained were concentrated to give first-eluting compound 235a (220 mg, chiral purity 98.6%) and second-eluting compound 235b (230 mg, chiral purity 97.3%), recovery ~93%.

Compound 235a: (+) anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one
15

Compound 235b: (-) anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one.

20 EXAMPLE 236: anti (-) 8-(pyridazin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

The title compound was prepared according to the method described in example 232.2 starting from anti (-) 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (compound 235.1b). LC-MS: $m/e = 391.2$ (M+H)⁺.

25

EXAMPLE 237: anti (-) 8-(6-fluoropyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

The title compound was prepared according to the method described in example 232 starting from anti (-) 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (compound 235.1b) and 2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine. LC-MS: $m/e = 408.2$ (M+H)⁺
30

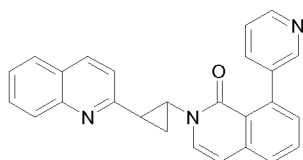
$[\alpha] = -107^\circ$ (methanol)

EXAMPLE 238: anti (-) 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

- 5 The title compound was prepared according to the method described in example 232 starting from anti (-) 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (compound 235.1b) and 2-fluoropyridin-4-ylboronic acid.

LC-MS: $m/e = 408.2$ ($M+H$)⁺

- 10 EXAMPLE 239: anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one hydrochloride



- 15 The title compound was prepared according to the method described in example 232 starting from anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one and pyridin-3-ylboronic acid. LC-MS: $m/e = 390.1$ ($M+H$)⁺

Separation of anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one:

- 20 320 mg of anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one were subjected to a chromatography on a Chiralpak IC column, eluent: 500 parts of n-heptane, 450 parts of DCM, 50 parts of methanol and 1 part of triethylamine to give 105 mg of compound 239a (R_t : 4.74 min), 98.8% ee and 120 mg of compound 239b (R_t : 4.68 min), 97.6% ee.

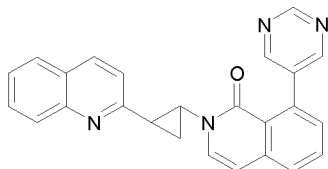
- 25 Compound 239a: (+) anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

$[\alpha] = +108.5^\circ$ (methanol)

Compound 239b: (-) anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

- 30 $[\alpha] = -94.8^\circ$ (methanol)

EXAMPLE 240: anti 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



- 5 The title compound was prepared according to the method described in example 232 starting from anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one and pyrimidin-5-ylboronic acid.

LC-MS: $m/e = 391.1$ ($M+H$)⁺

- 10 Separation of anti 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one:

- 330 mg of anti 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one were subjected to a chromatography on a Chiralpak IC column, eluent: 500 parts of n-heptane, 450 parts of DCM, 50 parts of methanol and 1 part of triethylamine to give 112 mg of compound 240a (R_t : 9.80), 95.6% ee and 98 mg of compound 240b (R_t : 5.52), 81.2% ee.

Compound 240a: anti (+) 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

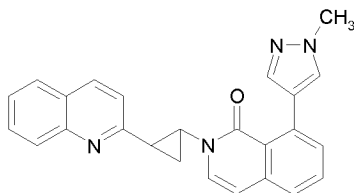
$[\alpha] = +118.3^\circ$ (methanol)

20

Compound 240b: anti (-) 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

$[\alpha] = -120.4^\circ$ (methanol)

- 25 EXAMPLE 241: anti 8-(1-methyl-1H-pyrazol-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



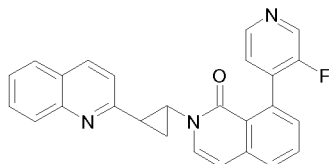
212

The title compound was prepared according to the method described in example 232 starting from anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one and 1-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole.

LC-MS: $m/e = 393.1$ (M+H)⁺

5

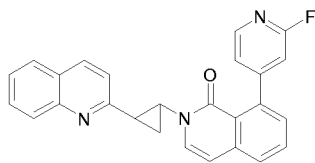
EXAMPLE 242: anti 8-(3-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



The title compound was prepared according to the method described in example 232 starting from anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one and 3-fluoro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine.

LC-MS: $m/e = 408.1$ (M+H)⁺

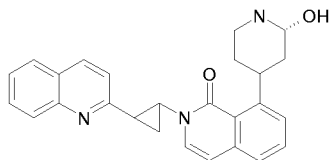
EXAMPLE 243: anti 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



The title compound was prepared according to the method described in example 232 starting from anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one and 2-fluoropyridin-4-ylboronic acid. LC-MS: $m/e = 408.1$ (M+H)⁺

20

EXAMPLE 244: anti 8-((3S)-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (2E)-but-2-enedioate



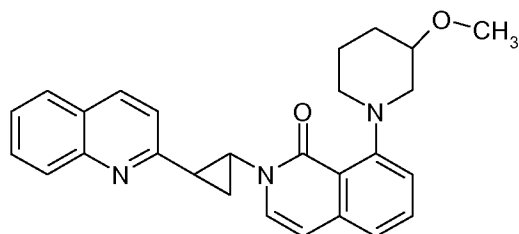
The title compound was prepared according to the method described in example 173 starting from anti 8-bromo-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

25

and (S)-piperidin-3-ol. The title compound was converted into the fumarate salt. LC-MS: $m/e = 412.2$

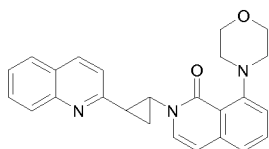
5 Examples 245 to 253 were prepared in analogy to the method described in example 244.

EXAMPLE 245: anti 8-(3-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (2E)-but-2-enedioate



10 LC-MS: $m/e = 426.2$

EXAMPLE 246: anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



15

LC-MS: $m/e = 398.2 (M+H)^+$

Separation of anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one:

20 246 mg of anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one were subjected to a chromatography on a Chiralpak IC column, eluent: 500 parts of n-heptane, 450 parts of DCM, 50 parts of methanol and 1 part of triethylamine to give 95 mg of compound 246 a (R_t : 8.1), 90.2% ee and 74 mg of compound 246b (R_t : 9.4), 90.2% ee.

25 Compound 246a: anti (+) 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

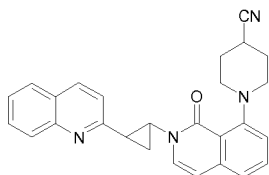
$[\alpha] = + 141.4^\circ$ (methanol)

Compound 246b: anti (-) 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

$[\alpha] = -142.0^\circ$ (methanol)

5

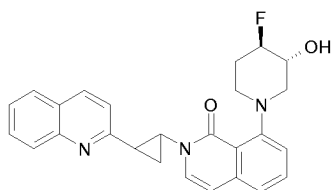
Examples 247: anti 1-(1-oxo-2-(2-(quinolin-2-yl)cyclopropyl)-1,2-dihydroisoquinolin-8-yl)piperidine-4-carbonitrile



LC-MS: $m/e = 421.2$ ($M+H$)⁺

10

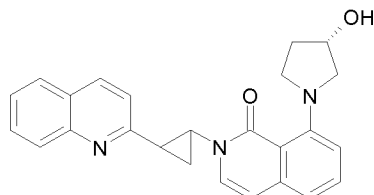
EXAMPLE 248: anti 8-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



LC-MS: $m/e = 430.2$ ($M+H$)⁺

15

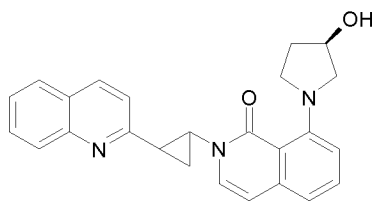
EXAMPLE 249: anti 8-((3S)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one di[(2E)-but-2-enedioate]



LC-MS: $m/e = 398.2$ ($M+H$)⁺

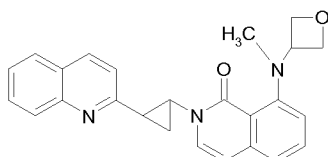
20

EXAMPLE 250: anti 8-((3R)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (2E)-but-2-enedioate



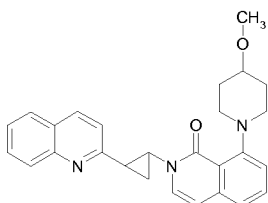
LC-MS: $m/e = 398.2 (M+H)^+$

EXAMPLE 251: anti 8-(methyl(oxetan-3-yl)amino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



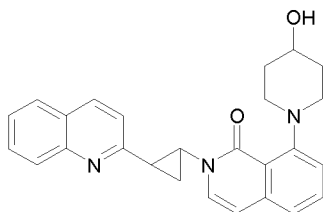
LC-MS: $m/e = 398.1 (M+H)^+$

EXAMPLE 252: anti 8-(4-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (2E)-but-2-enedioate



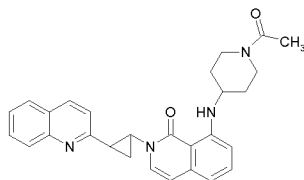
LC-MS: $m/e = 426.2 (M+H)^+$

EXAMPLE 253: anti 8-(4-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one (2E)-but-2-enedioate



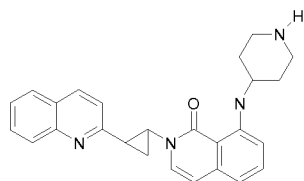
LC-MS: $m/e = 412.2 (M+H)^+$

EXAMPLE 254: anti 8-(1-acetylpiperidin-4-ylamino)-2-(2-quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one



The title compound was prepared in analogy to the method described in example 235.

- 5 EXAMPLE 255: anti 8-(piperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one hydrochloride



The title compound was prepared in analogy to the method described in example 213 but heating for 3 h under reflux and the solvent used was ethanol.

- 10 LC-MS: $m/e = 411.2 (M+H)^+$.

EXAMPLE 256: syn 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one hydrochloride

- 15 256.1 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

The title compound was prepared as described in example 222.

LC-MS: $390.1 (M+H)^+$

- 20 256.2 Separation of 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one:

2.8 g of 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one were dissolved in 50 mL of EA and separated by column chromatography, normal phase, eluent: DCM/methanol to give compound 222 and compound 256..

- 25 Compound 222: anti 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one, yield: 80%; LC-MS: $390.1 (M+H)^+$, R_t : 1.128 min

217

Compound 256: syn 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one, yield: 4.3%; LC-MS: 390.1 (M+H)⁺, R_t: 1.127 min.

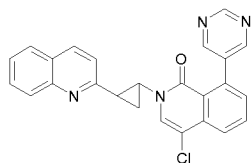
Examples 257 to 275 were prepared in analogy to the methods described above.

5

Ex.	Name	LC-MS: m/e (M+H) ⁺ / [α]
257	anti 2-(2-(quinolin-2-yl)cyclopropyl)-8-(tetrahydro-2H-pyran-4-yl)isoquinolin-1(2H)-one	397.1
258	anti (-) 2-(2-(quinolin-2-yl)cyclopropyl)-8-(2-oxa-6-azaspiro[3.4]octan-6-yl)isoquinolin-1(2H)-one	424.2 / [α] = -194°
259	anti (-) 8-(dihydro-1H-furo[3,4-c]pyrrol-5(3H,6H,6aH)-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	424.2 / [α] = -193°
260	anti (-) 8-(4,4-difluoropiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	432.2 / [α] = -162°
261	anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one, dimethanesulfonate	398.1
262	anti 8-(3-(difluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one, trifluoroacetate	432.2
263	anti 8-((1R,5S)-3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	424.2
264	anti 8-(4-methylpiperazin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one,	411.2
265	anti 8-(3-(fluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one, trifluoroacetate	414.2
266	8-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one,	424.2

Ex.	Name	LC-MS: m/e (M+H) ⁺ / [α]
267	anti 8-(4-fluorophenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one,	407.2
268	anti 8-(furan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	379.1
269	anti 8-(4,5-dihydrofuran-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	381.2
270	anti (-) 8-(4-methoxyphenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	419.2 / [α] = -68°
271	anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-morpholinoisoquinolin-1(2H)-one	416.2
272	anti 2-((2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-3-yl)isoquinolin-1(2H)-one	408.1
273	anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyrimidin-5-yl)isoquinolin-1(2H)-one	409.1
274	anti 2-((2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)isoquinolin-1(2H)-one	408.1
275	anti 4-fluoro-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	408.1

EXAMPLE 276: anti (-)-4-chloro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one

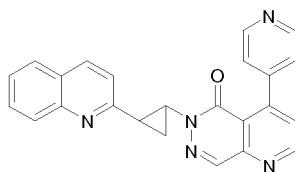


5 Anti (-)-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one hydrochloride from example 240b was mixed with sodium hydrogencarbonate solution and DCM. The phases were separated and the organic phase dried. Purification by column chromatography (DCM/methanol) gave the title compound (7.89% yield) as white solid. LC-MS: m/e = 425.1

10 Example 276a: anti (-)-4-chloro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one hydrochloride

$[\alpha] = +217.7^\circ$ (methanol)

EXAMPLE 277: anti 4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)cyclopropyl)pyrido[2,3-d]pyridazin-5(6H)-one



5 4-(pyridin-4-yl)pyrido[2,3-d]pyridazin-5(6H)-one (19 mg, 0.085 mmol) was suspended in 1 mL of DMF under argon. Then, cesium carbonate carbonate (55.2 mg, 0.169 mmol) and syn 2-(2-bromocyclopropyl)quinoline (22,08 mg, 0,089 mmol) from example c1 were added. The reaction mixture was heated at 110 °C for 3 h min. Water and EA were added. The aqueous phase was extracted twice with EA. The organic phases were combined, washed with HCl, dried (MgSO₄) and evaporated. The residue was purified by chromatography to give 12 mg (yield: 36.2%) of the title compound as bright beige solid. LC-MS: m/e 392.1 (M+H)⁺

15 Examples 278 to 300 were prepared in analogy to the methods described above.

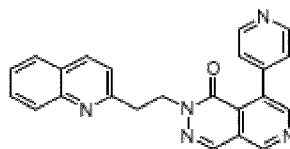
Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min] / [α]
278	anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)phthalazin-1(2H)-one	409.1
279	anti 7-fluoro-3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one	414.1
280	anti 3-(2-fluoropyridin-4-yl)-5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one	432.1
281	anti 5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	414
282	anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one	397.1
282a	anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one,	397.1

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min / [α]
	hydrochloride, enantiomer 1	
282b	anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one, hydrochloride, enantiomer 2	397.1
283	anti 3-(6-fluoropyridin-3-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one hydrochloride	414.1
284	anti 3-(2-methylpyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one	411.1
285	anti 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one	397.1
286	anti 3-(2-fluoropyridin-4-yl)-5-[(2-(quinolin-2-yl)cyclopropyl)]thieno[3,2-c]pyridin-4(5H)-one	414.1
287	anti 3-(morpholin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	404.1
288	anti 3-(pyridin-3-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	401.5
289	anti 3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	396.1
290	anti 3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one, hydrochloride	398.1
291	anti 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one	
292	anti 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	402.0
293	anti 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	396.1
293a	anti (+) 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	396.1

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min] / [α]
293b	anti (-) 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one	396.1/ [α] = -301.7° (methanol)
294	anti 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	397.1/ R _t = 1.084
295	syn 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one	397.4 / R _t = 0.998
296	anti 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one	391.1
297	anti 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one	390.1
298	anti 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one	390.2
299	anti 5-(morpholin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one	398.2
300	anti (-) 4-fluoro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one	396.1

II.20 Preparation of compounds of the formula I in which A is A¹, Y¹-Cyc¹ and X³ is N=C(R⁹)

- 5 EXAMPLE 301: 8-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]pyrido[3,4-d]pyridazin-1(2H)-one



301.1 Ethyl 3-chloro-5-formylisonicotinate

- 10 To a solution of diethyl 5-chloropyridine-3,4-dicarboxylate (2.43 g, 9.43 mmol) in 100 mL of toluene was added diisobutylaluminiumhydride (2.68 g, 18.86 mL, 1 molar) in hexane at -70°C. The reaction mixture was stirred for 2 h at this temperature. The

reaction mixture was poured into an 5% aqueous acetic acid solution followed by the addition of EA. The phases were separated and the organic phase was washed with aq. NaHCO_3 solution. The organic phase was dried and concentrated to give 2.02 g (100%) of the title compound as brown oil.

5

301.2 (E)-ethyl 3-((2-acetylhydrazono)methyl)-5-chloroisonicotinate

To ethyl 3-chloro-5-formylisonicotinate (2 g, 9.36 mmol) in 60 mL of ethanol was added acetohydrazide (0.832 g, 11.24 mmol) at room temperature. The reaction mixture was stirred for 2 h. Then, the reaction mixture was mixed with DCM and water. The
10 organic phase was washed with brine, dried and concentrated. The crude title compound was purified by chromatography (eluent: DCM/methanol) to give 220 mg (8.7%) of the title compound as orange oil.

301.3 8-chloropyrido[4,3-d]pyridazin-1(2H)-one

15 (E)-ethyl 3-((2-acetylhydrazono)methyl)-5-chloroisonicotinate (220 mg, 0.816 mmol) and aq. NaOH solution (3.26 mg, 0.082 mmol, 2 molar) in 5 mL of dioxane were stirred in a microwave at 165°C for 60 min. Then the reaction mixture was basified by addition of aq. NaHCO_3 and extracted with DCM. The organic phase was washed with brine, dried and concentrated. The crude title compound was purified by
20 chromatography (eluent: DCM/methanol) to give 25 mg (16.88%) of the title compound as beige solid.

301.4 8-chloro-2-(2-(quinolin-2-yl)ethyl)pyrido[4,3-d]pyridazin-1(2H)-one

To 69.3 mg (0.264 mmol) in THF was added diisopropylazodicarboxylate (94 mg, 0.463 mmol) in THF under ice-cooling and under nitrogen. Then, the resulting solution was stirred for 30 min at room temperature to give a suspension. 8-Chloropyrido[4,3-d]pyridazin-1(2H)-one (24 mg, 0.132 mmol) in THF and then 2-(quinolin-2-yl)ethanol (22.89 mg, 0.132 mmol) in THF were added and the reaction mixture was stirred overnight at room temperature. The total amount of THF was 60 mL. Then, the reaction
25 mixture was mixed with DCM and water. The organic phase was washed with 1N HCl and the organic phase was discharged. The aqueous phase was basified by 1N NaOH
30

and extracted with DCM. The organic phase was dried and concentrated to give 34 mg (76%) of the title compound as bright beige solid. LC-MS: m/e 337.1 (M+H)⁺.

301.5 8-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]pyrido[3,4-d]pyridazin-1(2H)-one
 5 8-chloro-2-(2-(quinolin-2-yl)ethyl)pyrido[4,3-d]pyridazin-1(2H)-one (34 mg, 0.101 mmol) was suspended in 2 mL of toluene and 2 mL of methanol under argon. Then, an aqueous solution of sodium carbonate (16.5 mg, 0.15 mmol, 2 M) was added. To the suspension, pyridin-4-boronic acid (13.79 mg, 0.101 mmol) and then tetrakis(triphenylphosphine)palladium(0) (11.67 mg, 10.10 μmol) were added. The
 10 reaction mixture was heated in a CEM microwave at 130 °C for 30 min. Water and EA were added. The organic phase was extracted with water, dried (MgSO₄) and evaporated. The residue was purified by chromatography (eluent: DCM/methanol) and then recrystallized from EA/diisopropyl ether (1:1) to give 2.6 mg (yield: 6.79%) of the title compound as off-white solid. LC-MS: m/e 380.1 (M+H)⁺

15

II.21 Preparation of compounds of the formula I in which A is A¹

The compounds of example 302 to 409 were prepared in analogy to the methods described above.

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
302	5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(1-methyl-1H-imidazol-4-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	454.0 / 1.69
303	5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(1-methyl-1H-pyrazol-4-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	
304	5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(pyridin-3-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	451.2 / 1.74
305	5-[2-(6-chloroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	418.1
306	5-[2-(3-methylquinolin-2-yl)ethyl]-3-(pyridin-4-	398.1

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
	yl)thieno[3,2-c]pyridin-4(5H)-one	
307	5-[2-(8-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	402.1
308	5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-3-yl)thieno[3,2-c]pyridin-4(5H)-one hydrochloride	402.1
309	5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	402.1
310	5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-3-yl)thieno[3,2-c]pyridin-4(5H)-one	373.3
311	3-(pyridin-4-yl)-5-[2-(quinoxalin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	386.1
312	5-[2-(1,5-naphthyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	386.1
313	5-[2-(1H-indazol-1-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	374.1
314	3-(1-methyl-1H-pyrazol-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	388.1
315	3-(1H-pyrazol-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one	374.1
316	5-[2-(1H-benzimidazol-1-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	374.1
317	5-[2-(1H-benzimidazol-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	374.1
318	5-[2-(6-chloroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	419.1
319	3-(pyridin-3-ylethynyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	409.1
320	3-(pyridin-4-ylethynyl)-5-[2-(quinolin-2-	409.1

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
	yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one hydrochloride	
321	5-[2-(3,5-dimethylpyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	363.1
322	5-[2-(7-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	403.1
323	5-[2-(pyrazin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one	336.1
324	2-[2-(1,6-naphthyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one	379.1
325	2-[2-(8-fluoroquinolin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one	396.1
326	8-(pyridin-4-yl)-2-[1-(quinolin-2-yl)propan-2-yl]isoquinolin-1(2H)-one	392.1
327	2-[2-(3-methylquinolin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one	392.2
328	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1H-pyrazol-3-yl)phthalazin-1(2H)-one	357.1
329	8-(morpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	387.1
330	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-oxa-4,9-diazaspiro[5.6]dodec-9-yl)phthalazin-1(2H)-one dihydrochloride	459.2
331	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-7-azaspiro[3.5]non-7-yl)phthalazin-1(2H)-one (2E)-but-2-enedioate	
332	8-[(3R)-3-hydroxypiperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one (2E)-but-2-enedioate (salt)	390.2
333	8-[(3S)-3-hydroxypiperidin-1-yl]-2-[2-(imidazo[1,2-	390.2

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
	a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one (2E)-but-2-enedioate (salt)	
334	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-6-azaspiro[3.3]hept-6-yl)phthalazin-1(2H)-one	388.1
335	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,2-oxazolidin-2-yl)phthalazin-1(2H)-one	362.1
336	8-(hexahydrocyclopenta[b][1,4]oxazin-4(4aH)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	416.2
337	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydrofuran-3-yl)phthalazin-1(2H)-one	361.2
338	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)phthalazin-1(2H)-one	402.2
339	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-6-azaspiro[3.4]oct-6-yl)phthalazin-1(2H)-one	402.2
340	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2,2,6,6-tetrafluoromorpholin-4-yl)phthalazin-1(2H)-one	448.1
341	8-(4-hydroxypiperidin-1-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	390.1
342	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-methylpyrimidin-5-yl)phthalazin-1(2H)-one	383.2
343	8-(2-cyclopropylpyrimidin-5-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	409.1
344	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridazin-4-yl)phthalazin-1(2H)-one	369.1
345	8-(5-fluoropyridin-3-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	386.2
346	8-[2-(3-fluorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	470.2
347	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-	399.1

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
	methoxypyrimidin-5-yl)phthalazin-1(2H)-one	
348	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[2-(trifluoromethyl)pyridin-4-yl]phthalazin-1(2H)-one	436.1
349	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)phthalazin-1(2H)-one	402.2
350	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[2-(trifluoromethyl)morpholin-4-yl]phthalazin-1(2H)-one hydrochloride	444.2
351	8-(2,2-dimethylmorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	404.2
352	8-[2-(4-chlorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	486.2
353	8-[2-(3,4-difluorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	488.2
354	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-4-yl)phthalazin-1(2H)-one hydrochloride	374.2
355	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-4-yl)phthalazin-1(2H)-one	375.2
356	8-(2,6-diazabicyclo[3.2.1]oct-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one dihydrochloride	401.2
357	8-[(1S,5S)-3,6-diazabicyclo[3.2.0]hept-3-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	387.2
358	8-(furan-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	357.1
359	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-methyl-1H-pyrazol-4-yl)phthalazin-1(2H)-one hydrochloride	371.2

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
360	8-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one dihydrochloride	401.2
361	8-(2,7-diazaspiro[4.4]non-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one dihydrochloride	415.2
362	8-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one trifluoroacetate	387.2
363	8-(2,7-diazaspiro[3.5]non-7-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	415.2
364	8-(2,6-diazaspiro[3.5]non-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	415.2
365	8-(piperidin-4-yl)-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	378.2
366	8-[2-(aminomethyl)-4-chloropyrrolidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one trifluoroacetate	423.2
367	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4,8-di(pyridin-4-yl)phthalazin-1(2H)-one	445.2
368	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aR,4S,7R,7aS)-octahydro-1H-4,7-epiminoisoindol-8-yl]phthalazin-1(2H)-one dihydrochloride	427.2
369	8-[5-(4-chlorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	497.2
370	4-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-	448

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
	(pyridin-4-yl)phthalazin-1(2H)-one	
371	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aS,8aS)-octahydropyrrolo[3,4-c]azepin-2(1H)-yl]phthalazin-1(2H)-one dihydrochloride	429.2
372	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aS,8aR)-octahydropyrrolo[3,4-c]azepin-2(1H)-yl]phthalazin-1(2H)-one dihydrochloride	429.2
373	tert-butyl (3aR,4S,7R,7aS)-8-{3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl}octahydro-2H-4,7-epiminoisoindole-2-carboxylate	527.3
374	8-(hexahydro-5H-furo[2,3-c]pyrrol-5-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	402.2
375	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,2,3,6-tetrahydropyridin-4-yl)phthalazin-1(2H)-one hydrochloride	372.2
376	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3S)-tetrahydrofuran-3-ylamino]phthalazin-1(2H)-one	
377	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3R)-tetrahydrofuran-3-ylamino]phthalazin-1(2H)-one	
378	8-{[5-(hydroxymethyl)-1,4-dioxan-2-yl]methoxy}-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	437.1
379	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(oxetan-3-yloxy)phthalazin-1(2H)-one	363.1
380	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-ylmethoxy)phthalazin-1(2H)-one	398.1
381	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(morpholin-4-ylmethyl)phthalazin-1(2H)-one	390.2
382	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yloxy)phthalazin-1(2H)-one	384.1

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
383	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(oxetan-3-ylmethyl)amino]phthalazin-1(2H)-one	376.2
384	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-4-ylamino)phthalazin-1(2H)-one	390.2
385	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(1-methylazetidin-3-yl)amino]phthalazin-1(2H)-one	375.2
386	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,3-oxazol-2-ylamino)phthalazin-1(2H)-one	372.3
387	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[methyl(oxetan-3-yl)amino]phthalazin-1(2H)-one	376.2
388	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-4-ylamino)phthalazin-1(2H)-one dihydrochloride	389.2
389	8-[(1-acetylpiperidin-3-yl)amino]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	431.2
390	8-[(1-acetylpiperidin-4-yl)amino]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one	431.2
391	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydrofuran-3-ylamino)phthalazin-1(2H)-one	376.2
392	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-3-ylamino)phthalazin-1(2H)-one hydrochloride	390.2
393	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-3-ylamino)phthalazin-1(2H)-one dihydrochloride	389.2
394	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-{methyl[(3-methyloxetan-3-yl)methyl]amino}phthalazin-1(2H)-one	404.2
395	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(oxetan-3-ylamino)phthalazin-1(2H)-one	362.2
396	8-{[(3aS,4S,6aS)-octahydrocyclopenta[c]pyrrol-4-ylmethyl]amino}-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-	433.3

Ex.	Name	LC-MS: m/e (M+H) ⁺ / R _t [min]
	a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	
397	5-(morpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one hydrochloride	387.2
398	2-[2-(1H-benzimidazol-2-yl)ethyl]-5-(pyridin-4-yl)phthalazin-1(2H)-one	368.1
399	4-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	379.1
400	5-(1,4-dihydropyrimidin-5-yl)-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one dihydrochloride	375.2
401	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-4-yl)phthalazin-1(2H)-one	368.1
402	5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one	379.2
403	2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3-methyloxetan-3-yl)methyl]amino} phthalazin-1(2H)-one	390.2
404	4-(pyridin-4-yl)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one	380.1
405	4-(morpholin-4-yl)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one	388.2
406	4-(oxetan-3-ylamino)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one	374.1
407	2-[2-(6-methoxypyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one	358.1
408	2-[2-(1,3-benzothiazol-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one	384.1
409	2-[2-(5-methylpyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one	342.1

II.22 Preparation of compounds of the formula I in which A is A³

The compounds of example 410 to 415 were prepared in analogy to the methods described above.

5

Ex.	Name	LC-MS: m/e (M+H) ⁺
410	5-[(E)-2-(6-methoxyquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	412.8
411	8-(pyridin-4-yl)-2-[(E)-2-(quinazolin-2-yl)ethenyl]isoquinolin-1(2H)-one	377.1
412	5-[(E)-2-(6-chloroquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	416.1
413	5-[(E)-2-(3-methylquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	396.1
414	8-(pyridin-4-yl)-2-[(E)-2-(quinolin-2-yl)ethenyl]isoquinolin-1(2H)-one	376.1
415	5-[(E)-2-(1,3-benzothiazol-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one	388
416	3-(pyridin-4-yl)-5-[(E)-2-(quinolin-2-yl)ethenyl]thieno[3,2-c]pyridin-4(5H)-one	382.1

Biological Tests

a) Measurement of PDE activity

10 The recombinant PDE proteins are used in in vitro enzymatic reaction for measurement of PDE activity. These recombinant proteins, including PDE10A (human, rat and mouse PDE10) and isoforms of PDEs 1, 3, 4, and 5, were purchased from commercial vendor BPS Bioscience. The enzymatic activity of PDEs was determined by cAMP measurement kit from CisBio (IBA) using HTRF technology.

15 The PDE enzymatic reaction was carried out in assay buffer (20mM Tris-HCl pH7.5, 10mM MgCl₂, 0.1% bovine serum albumin) containing enzyme and substrate. The PDE enzymes concentration ranged from 10pM – 250pM, depending on each

enzyme's specific activity. The substrate cyclic nucleotide (cAMP or cGMP) concentration used in the assay was 20nM for PDE10, and 100nM for other PDEs. The inhibitory effect of compound was determined by incubating various concentration of inhibitor in the enzymatic assay. Typically, compound was serially diluted in DMSO then further diluted in assay buffer. Next, the compound at varying concentration was mixed with PDE enzyme. The reaction was initiated by addition of cyclic nucleotide substrate, and incubated for 60 minutes at 29°C. The reaction was stopped by addition of lysis buffer from assay kit. The cAMP-d2 and anti-cAMP cryptate in the lysis buffer detected the level of cAMP left from the PDE hydrolysis reaction. The PDE activity is reversely correlated with the amount of cAMP left in the reaction and can be converted to the percent activity of an uninhibited control (100%). Thus, IC₅₀ value of inhibitor can be obtained by plotting inhibitor concentration against PDE activity at that concentration. The results are shown in Table 1.

Table 1:

Ex.	IC ₅₀ ¹⁾
1	+++
2	+++
3	+++
5	+++
7	+
8	+++
10	+++
11	++
12	+++
15	+
16	+++
17	++
18	+
20	+++
23	+++
26	+
29	+++
30	++
31	++
32	+
34	++
36	+++
37	+++

Ex.	IC ₅₀ ¹⁾
38	+
39	+++
41	+++
44	+
45	++
46	+++
47	++
48	+++
49	++
50	+
51	+++
52	++
54	++
55	+++
56	+++
57	+
59	+++
60	+
62	+
64	+
67	++
70	++
71	+

Ex.	IC ₅₀ ¹⁾
72	++
76	++
78	+
79	+
80	++
85	++
87	+++
88	+++
90	+
91	++
93	+++
94	+++
95	+++
96	+++
97	+++
98	+++
100	+
103	+++
104	++
105	++
106	+++
107	+++
108	+

Ex.	IC ₅₀ ¹⁾
109	+
111	+++
113	++
114	++
115	+++
116	+++
117	++
119	+
121	++
122	+
123	+
124	+++
125	+
126	+++
127	+++
130	+
133	+++
135	+++
136	+++
137	+++
138	+
139	+++
140	+
143	+
147	+++
148	++
149	+
152	+
153	++
154	+
156	++
157	+
159	+++
161	+++
163	+
164	++
165	+
166	+++
167	+
168	+++
169	+
170	+++
171	+++
173	+++
174	+++
175	++

Ex.	IC ₅₀ ¹⁾
176	+++
179	++
181	+
190	++
191	+
192	+++
193	+++
194	+++
195	++
196	+++
197	+++
198	+++
199	+++
200	+++
201	+
203	+
204	+++
205	+++
206	+++
207	+++
208	+++
209	+
210	+++
211	+
213	+
215	++
216	+++
219	+++
220	+++
221	+++
222	+++
222a	+++
222b	+++
223	+++
224	+++
225	+++
226	+++
228	+++
229	+++
230	++
231	+++
232	+++
233	+++
234	+++
235	+++
235a	+++

Ex.	IC ₅₀ ¹⁾
235b	+++
236	+++
237	+++
238	+++
239	+++
239a	++
239b	+++
240	+++
240a	+++
240b	+++
241	+++
242	+++
243	+++
244	+++
246	+++
246a	+++
246b	+++
247	+++
249	+
250	++
252	+++
253	+++
256	+++
257	+++
258	+++
259	+++
260	+++
262	++
263	+++
266	+++
267	+++
268	+++
269	+++
270	+++
271	+++
272	+++
273	+++
274	+++
275	+++
276	+++
277	+++
278	+++
279	+++
280	+++
281	+++
282	+++

235

Ex.	IC ₅₀ ¹⁾
282a	+++
282b	+++
283	+++
284	+++
285	+++
286	+++
287	+++
288	+++
289	+++
290	+++
291	+++
292	+++
293	+++
293a	+++
293b	+++
295	+++
296	++
297	+++
298	++
299	+++
300	+++
301	+++
302	+++
303	+++
304	+++
306	+++
307	+
308	+++
309	+++
310	+++
311	++
312	+++
315	+++
317	+++

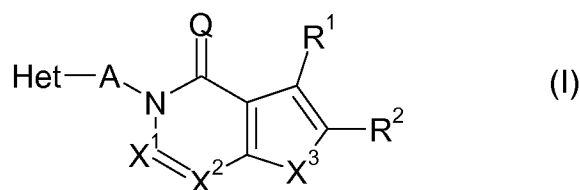
Ex.	IC ₅₀ ¹⁾
318	+
319	+++
320	+
321	++
322	+
327	+++
328	+
329	+++
330	+
332	+
333	+++
334	++
337	+++
338	+++
339	+++
341	+++
342	++
343	+
344	++
345	++
347	++
348	++
349	+++
354	+++
355	+++
358	++
359	+++
365	+++
366	+++
367	+++
370	+++
374	+
375	+++
376	+++

Ex.	IC ₅₀ ¹⁾
377	+++
378	+
380	++
382	+++
383	+++
384	++
385	+
387	+++
388	+++
389	++
390	+
391	+++
392	+++
393	+++
394	+
395	+++
397	+++
398	++
399	+++
401	+++
402	+++
403	+++
404	+++
405	+++
406	+++
410	+++
411	++
412	+++
413	+++
414	+++
415	+++
416	+++

- 1) +++: IC₅₀ < 100 nM
 ++: 100 nM ≤ IC₅₀ ≤ 200 nM
 +: 200 nM < IC₅₀ < 500 nM

We claim:

1. Compound of formula I



wherein

Q is O or S;

X¹ is N or CH;

X² is N or C-R⁷;

X³ is O, S, -X⁴=C(R⁸)-, where C(R⁸) is bound to the carbon atom which carries R², or

-X⁵=C(R⁹)-, where X⁵ is bound to the carbon atom which carries R²;

X⁴ is N or C-R⁹;

X⁵ is N;

Het is selected from

- i. monocyclic hetaryl having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, which is unsubstituted or may carry 1, 2, 3 or 4 identical or different substituents R^x,
- ii. fused bicyclic hetaryl having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, benzothienyl or benzofuryl, where bicyclic hetaryl, benzothienyl and benzofuryl are, independently of each other, unsubstituted or may carry 1, 2, 3 or 4 identical or different substituents R^x, and
- iii. phenyl, which carries a monocyclic hetaryl radical having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, which in addition

to monocyclic hetaryl, may carry 1, 2 or 3 identical or different substituents R^x ,

where

5 R^x is selected from the group consisting of H, halogen, C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, C_3 - C_6 -cycloalkyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, OH, hydroxy- C_1 - C_4 -alkyl, O- C_3 - C_6 -cycloalkyl, benzyloxy, C(O)O-(C_1 - C_4 -alkyl), O-(C_1 - C_4 -alkyl)-CO₂H, N(R^{x1})(R^{x2}), C(O)N(R^{x1})(R^{x2}), C_1 - C_4 -alkyl-N(R^{x1})(R^{x2}),
10 -NR^{x3}-C(O)-N(R^{x1})(R^{x2}), NR^{x3}-C(O)O-(C_1 - C_4 -alkyl), -N(R^{x3})-SO₂-R^{x4}, phenyl, CN, -SF₅, -OSF₅, -SO₂R^{x4}, -SR^{x4} and trimethylsilyl, where R^{x1} , R^{x2} , R^{x3} and R^{x4} , independently of each other are selected from the group consisting of hydrogen, C_1 - C_4 -alkyl, C_1 - C_4 -fluoroalkyl and C_3 - C_6 -cycloalkyl or R^{x1} and
15 R^{x2} form together with the N atom to which they are attached a 3- to 7-membered, nitrogen heterocycle which may have 1, 2 or 3 further different or identical heteroatoms or heteroatom containing groups selected from the group of O, N, S, SO and SO₂ as ring members and which may carry 1, 2, 3, 4, 5 or 6
20 substituents selected from C_1 - C_4 -alkyl; or two radicals R^x which are bound at adjacent carbon atoms may form a fused 5- or 6-membered saturated carbocyclic radical or a fused 5- or 6-membered heterocyclic radical having 1, 2 or 3 heteroatoms as ring members, which are selected from
25 O, S and N;

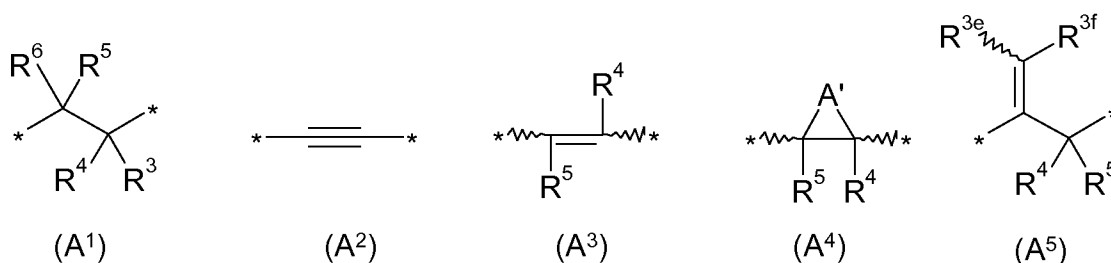
R^1 is selected from the group consisting of hydrogen, halogen, OH, C_1 - C_4 -alkyl, trimethylsilyl, C_1 - C_4 -alkylsulfanyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_1 - C_4 -alkylsulfanyl-
30 C_1 - C_4 -alkoxy, C_2 - C_4 -alkenyloxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl

238

groups, fluorinated cyclopropyl, CN, $\text{NR}^{\text{x1}}\text{R}^{\text{x2}}$, $\text{NR}^{\text{x1}}\text{R}^{\text{x2}}\text{-C}_1\text{-C}_4\text{-alkoxy}$ and the moiety $\text{Y}^1\text{-Cyc}^1$;

R^2 is selected from the group consisting of hydrogen, halogen, OH, $\text{C}_1\text{-C}_4\text{-alkyl}$, trimethylsilyl, $\text{C}_1\text{-C}_4\text{-alkoxy-C}_1\text{-C}_4\text{-alkyl}$, $\text{C}_1\text{-C}_4\text{-alkoxy}$, $\text{C}_1\text{-C}_4\text{-alkoxy-C}_1\text{-C}_4\text{-alkoxy}$, $\text{C}_2\text{-C}_4\text{-alkenyloxy}$, $\text{C}_1\text{-C}_4\text{-fluoroalkyl}$, $\text{C}_1\text{-C}_4\text{-fluoroalkoxy}$, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN and $\text{NR}^{\text{x1}}\text{R}^{\text{x2}}$;

A represents one of the following groups A^1 , A^2 , A^3 , A^4 or A^5 :



where * indicates the points of attachment to Het and to the nitrogen atom, respectively,

R^3 , R^4 , R^5 , R^6 independently of each other are selected from the group consisting of hydrogen, halogen, $\text{C}_1\text{-C}_4\text{-alkyl}$, trimethylsilyl, $\text{C}_1\text{-C}_4\text{-fluoroalkyl}$, $\text{C}_1\text{-C}_4\text{-fluoroalkoxy}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, or the radicals together with the carbon atoms to which they are bound form a saturated 3- to 6-membered carbocycle or a saturated 3- to 6-membered heterocycle having 1 or 2 non-adjacent heteroatoms as ring members, where the carbocycle and the heterocycle are unsubstituted or may carry 1, 2, 3 or 4 substituents selected from fluorine and methyl or either the radicals R^3 , R^4 or the radicals R^5 , R^6 together with the carbon atom to which they are bound form a saturated 3- to 6-membered carbocycle or a saturated 3- to 6-membered heterocycle having 1 or 2 non-adjacent heteroatoms as ring members, where the carbocycle and the heterocycle are unsubstituted or may carry 1, 2, 3 or 4 substituents selected from fluorine and methyl;

- A' is a O, NR^{3a}, CR^{3b}R^{3c} or linear C₂-C₃-alkandiyl, where one of the CH₂-moieties of C₂-C₃-alkandiyl may be replaced by oxygen or NR^{3a}, and where 1, 2, 3, or 4 of the hydrogen atoms of C₂-C₃-alkandiyl may be replaced by a radical R^{3d}, where
 5 R^{3a} is hydrogen or C₁-C₄-alkyl,
 R^{3b}, R^{3c} independently of each other are selected from the group consisting of hydrogen, halogen, C₁-C₄-alkyl or R^{3b} and R^{3c} together form C₂-C₃-alkandiyl;
 10 R^{3d} is selected from the group consisting of halogen and C₁-C₄-alkyl;

 R^{3e}, R^{3f} independently of each other are selected from the group consisting of hydrogen and C₁-C₄-alkyl;
 15
 R⁷ is selected from the group consisting of hydrogen, halogen, OH, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkylsulfanyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkylsulfanyl-C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN, NR^{x1}R^{x2}, NR^{x1}R^{x2}-C₁-C₄-alkoxy and the moiety Y²-Cyc²;
 20
 R⁸ is selected from the group consisting of hydrogen, halogen, OH, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN and NR^{x1}R^{x2};
 25
 R⁹ is selected from the group consisting of hydrogen, halogen, OH, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkylsulfanyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkylsulfanyl-

240

C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN, NR^{x1}R^{x2}, NR^{x1}R^{x2}-C₁-C₄-alkoxy and the moiety Y³-Cyc³;

5

Y¹, Y², Y³ independently of each other are selected from a chemical bond, CH₂, O, O-CH₂, NR^y, NR^y-CH₂, NR^y-S(O)₂, S, S(O), S(O)₂, 1,2-ethandiyl, 1,2-ethendiyl or 1,2-ethyndiyl, where R^y is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl, C₁-C₄-alkylsulfonyl, C₁-C₄-fluoroalkylsulfonyl;

10

Cyc¹, Cyc², Cyc³ independently of each other are selected from the group consisting of phenyl, naphthyl, 4- to 8-membered saturated or partially unsaturated heteromonocyclic radicals, saturated or partially unsaturated 7- to 10 membered heterobicyclic radicals, 5- or 6-membered monocyclic hetaryl, and 8- to 10 membered bicyclic hetaryl, where the saturated or partially unsaturated heteromonocyclic and heterobicyclic radicals have 1, 2, 3 or 4 heteroatoms or heteroatom containing groups as ring members, which are selected from O, S, SO, SO₂ and N, and where the 5- or 6-membered monocyclic hetaryl and the 8- to 10-membered bicyclic hetaryl have 1, 2, 3 or 4 heteroatoms as ring members, which are selected from O, S and N, where phenyl, naphthyl, the saturated or partially unsaturated heteromonocyclic and heterobicyclic radicals and the mono and bicyclic heteroaromatic radicals are unsubstituted or carry 1, 2, 3, 4 or 5 radicals R^{C1} or one radical Y¹-R^{C2} and 0, 1, 2, 3 or 4 radicals R^{C1};

15

20

25

30

R^{C1} is selected from hydrogen, halogen, OH, CN, NO₂, C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkylsulfonyl, hydroxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkoxy, cyano-C₁-C₄-

241

alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, C₁-C₄-alkylsulfonyl, C(O)R^a, Z-C(O)OR^b, Z-C(O)NR^cR^d, S(O)₂NR^cR^d and Z-NR^eR^f, where

5 R^a is selected from the group consisting of C₁-C₄-alkyl and C₁-C₄-fluoroalkyl,

R^b is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₂-C₄-alkenyl and C₁-C₄-fluoroalkyl,

10 R^c, R^d is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-alkoxy and C₁-C₄-fluoroalkoxy,

R^e, R^f is selected from the group consisting of hydrogen, C₁-C₄-alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-alkoxy and C₁-C₄-fluoroalkoxy,

15 Z is a covalent bond or C₁-C₄-alkandiyl, or two radicals R^{C1} which are bound at adjacent carbon atoms may form a fused 5- or 6-membered carbocyclic radical or a fused 5- or 6-membered heterocyclic radical having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N;

20 or two radicals R^{C1} which are bound at the same carbon atom may form a spiro 5- or 6-membered carbocyclic radical or a spiro 5- or 6-membered heterocyclic radical having 1 or 2 heteroatoms as ring members, which are selected from O, S and N,

25 or two radicals R^{C1} which are bound at the same carbon atom may form an oxygen atom, where the fused and the spiro radicals are unsubstituted or carry 1, 2, 3 or 4 radicals R^{C3};

30 Y' is a chemical bond, CH₂, O, O-CH₂, S(O)₂, NR^{Y'}, NR^{Y'}-CH₂ or NR^{Y'}-S(O)₂, where R^{Y'} is selected from the group consisting of

hydrogen, C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl, C₁-C₄-alkylsulfonyl, C₁-C₄-fluoroalkylsulfonyl;

5 R^{C2} is a carbocyclic or heterocyclic radical selected from the group consisting of phenyl, 3- to 7-membered saturated or partially unsaturated monocarbocyclic radicals, 3- to 7-membered saturated or partially unsaturated heteromonocyclic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, and 5- or 6-membered heteroaromatic radicals, having 1, 2 or 3 heteroatoms as ring members, which are selected from O, S and N, where the carbocyclic and the heterocyclic radical is unsubstituted or carries 1, 2, 3, 4 or 5 radicals R^{C3} ;

15 R^{C3} is selected from hydrogen, halogen, OH, CN, C₁-C₄-alkyl, C₁-C₄-alkoxy, hydroxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, cyano-C₁-C₄-alkyl, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, C₂-C₆-alkenyl, C(O)R^a, benzyl, Z-C(O)OR^b, Z-C(O)NR^cR^d, S(O)₂NR^eR^d and Z-NR^eR^f, where, Z, R^a, R^b, R^c, R^d, R^e and R^f are as defined above or two radicals R^{C3} which are bound at the same atom may form an oxygen atom;

provided that for X³ being O or S, at least one of the radicals R¹ and R⁷ is a moiety Y¹-Cyc¹ or Y²-Cyc², respectively;

25 further provided that for X³ being X⁴=C(R⁸), one or two of the radicals R¹, R⁷ and R⁹ are a moiety Y¹-Cyc¹, Y²-Cyc² or Y³-Cyc³, respectively;

30 further provided that for X³ being X⁵=C(R⁹), one or two of the radicals R¹, R⁷ and R⁹ are a moiety Y¹-Cyc¹, Y²-Cyc² or Y³-Cyc³, respectively;

and the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

2. The compound as claimed in claim 1,

5

wherein

X^3 is O, S or $-X^4=C(R^8)-$, where $C(R^8)$ is bound to the carbon atom which carries R^2 ;

X^4 is N or $C-R^9$;

10

Het is selected from

15

- i. monocyclic hetaryl having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, which is unsubstituted or may carry 1, 2, 3 or 4 identical or different substituents R^x ,
- ii. fused bicyclic hetaryl having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, benzothienyl or benzofuryl, where bicyclic hetaryl, benzothienyl and benzofuryl are, independently of each other, unsubstituted or may carry 1, 2, 3 or 4 identical or different substituents R^x , and
- iii. phenyl, which carries a monocyclic hetaryl radical having 1 or 2 nitrogen atoms and optionally a further heteroatom selected from O, S and N as ring members, which in addition to monocyclic hetaryl, may carry 1, 2 or 3 identical or different substituents R^x ,

20

25

where

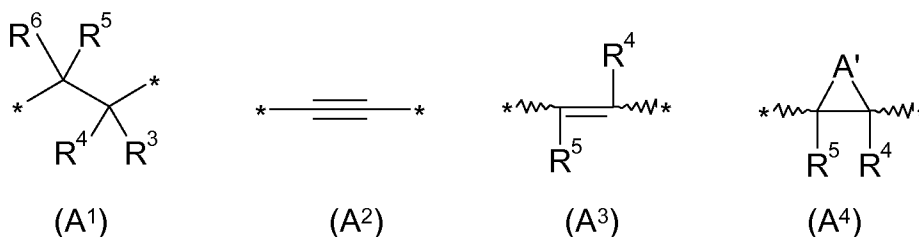
30

R^x is selected from the group consisting of H, halogen, C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, C_1 - C_4 -fluoroalkyl, C_1 - C_4 -fluoroalkoxy, C_3 - C_6 -cycloalkyl, C_1 - C_4 -alkoxy- C_1 - C_4 -alkoxy, C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, OH, hydroxy- C_1 - C_4 -alkyl, O- C_3 - C_6 -cycloalkyl, benzyloxy, $C(O)O-(C_1-C_4-alkyl)$, O- $(C_1-C_4-alkyl)-CO_2H$,

244

$N(R^{x1})(R^{x2})$, $C(O)N(R^{x1})(R^{x2})$, C_1 - C_4 -alkyl- $N(R^{x1})(R^{x2})$,
 $-NR^{x3}-C(O)-N(R^{x1})(R^{x2})$, $NR^{x3}-C(O)O-(C_1-C_4\text{-alkyl})$,
 $-N(R^{x3})-SO_2-R^{x4}$, phenyl, CN, $-SF_5$, $-OSF_5$, $-SO_2R^{x4}$, $-SR^{x4}$ and
 trimethylsilyl, where R^{x1} , R^{x2} , R^{x3} and R^{x4} , independently of
 each other are selected from the group consisting of hydrogen,
 C_1 - C_4 -alkyl, C_1 - C_4 -fluoroalkyl and C_3 - C_6 -cycloalkyl or R^{x1} and
 R^{x2} form together with the N atom to which they are attached a
 3- to 7-membered, nitrogen heterocycle which may have 1, 2 or
 3 further different or identical heteroatoms or heteroatom
 containing groups selected from the group of O, N, S, SO and
 SO_2 as ring members and which may carry 1, 2, 3, 4, 5 or 6
 substituents selected from C_1 - C_4 -alkyl;

A represents one of the following groups A^1 , A^2 , A^3 or A^4 :



where * indicates the points of attachment to Het and to the nitrogen atom, respectively,

R^3 , R^4 , R^5 , R^6 independently of each other are selected from the group consisting
 of hydrogen, halogen, C_1 - C_4 -alkyl, trimethylsilyl, C_1 - C_4 -fluoroalkyl,
 C_1 - C_4 -fluoroalkoxy, C_3 - C_6 -cycloalkyl, or the radicals together with the
 carbon atoms to which they are bound form a saturated 3- to 6-
 membered carbocycle or a saturated 3- to 6-membered heterocycle
 having 1 or 2 non-adjacent heteroatoms as ring members, where the
 carbocycle and the heterocycle are unsubstituted or may carry 1, 2, 3
 or 4 substituents selected from fluorine and methyl or either the
 radicals R^3 , R^4 or the radicals R^5 , R^6 together with the carbon atom to
 which they are bound form a saturated 3- to 6-membered carbocycle

or a saturated 3- to 6-membered heterocycle having 1 or 2 non-adjacent heteroatoms as ring members, where the carbocycle and the heterocycle are unsubstituted or may carry 1, 2, 3 or 4 substituents selected from fluorine and methyl;

5

A' is a O, NR^{3a} , $\text{CR}^{3b}\text{R}^{3c}$ or linear C₂-C₃-alkandiyl, where one of the CH₂-moieties of C₂-C₃-alkandiyl may be replaced by oxygen or NR^{3a} , and where 1, 2, 3, or 4 of the hydrogen atoms of C₂-C₃-alkandiyl may be replaced by a radical R^{3d} , where

10

R^{3a} is hydrogen or C₁-C₄-alkyl,

R^{3b} , R^{3c} independently of each other are selected from the group consisting of hydrogen, halogen, C₁-C₄-alkyl or R^{3b} and R^{3c} together form C₂-C₃-alkandiyl;

R^{3d} is selected from the group consisting of halogen and C₁-C₄-alkyl

15

R^8 is selected from the group consisting of hydrogen, halogen, OH, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN and $\text{NR}^{x1}\text{R}^{x2}$;

20

R^9 is selected from the group consisting of hydrogen, halogen, OH, C₁-C₄-alkyl, trimethylsilyl, C₁-C₄-alkylsulfanyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkoxy-C₁-C₄-alkoxy, C₁-C₄-alkylsulfanyl-C₁-C₄-alkoxy, C₂-C₄-alkenyloxy, C₁-C₄-fluoroalkyl, C₁-C₄-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl, CN, $\text{NR}^{x1}\text{R}^{x2}$, $\text{NR}^{x1}\text{R}^{x2}$ -C₁-C₄-alkoxy and the moiety $\text{Y}^3\text{-Cyc}^3$.

25

30

3. The compound as claimed in claim 1 or 2, where X^3 is selected from O, S, $-\text{X}^4=\text{C}(\text{R}^8)-$, where $\text{C}(\text{R}^8)$ is bound to the carbon atom which carries R^2 .

4. The compound as claimed in any one of claims 1 to 3, where A is selected from A^1 , A^2 , A^3 and A^4 .
- 5 5. The compound as claimed in any of claims 1 to 4, where X^2 is $C-R^7$.
6. The compound as claimed in claim 5, where R^7 is hydrogen or Y^2-Cyc^2 .
7. The compound as claimed in any of claims 1 to 6, where X^1 is N.
- 10 8. The compound as claimed in claim 1 to 6, where X^1 is CH.
9. The compound as claimed in any of claims 1 to 8, where X^3 is S.
- 15 10. The compound as claimed in any of claims 1 to 8, where X^3 is O.
11. The compound as claimed in any one of claims 1 to 8, where X^3 is $C(R^9)=C(R^8)$.
12. The compound as claimed in any one of claims 1 to 8, where X^3 is $N=(CR^9)$.
- 20 13. The compound as claimed in any of claims 11 or 12, where R^9 is hydrogen or Y^3-Cyc^3 .
14. The compound as claimed in any of claims 1 to 8, where X^3 is $N=C(R^8)$.
- 25 15. The compound as claimed in any of claims 11 or 14, where R^8 is hydrogen.
16. The compound as claimed in any one of the preceding claims, where R^1 is a radical Y^1-Cyc^1 .
- 30 17. The compound as claimed in any one of the preceding claims, where R^2 is selected from the group consisting of hydrogen, fluorine, C_1 - C_4 -alkyl, C_1 - C_2 -

fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.

- 5
18. The compound as claimed in claim 17, where R² is hydrogen.
19. The compound as claimed in any one of the preceding claims, where A is A¹.
- 10
20. The compound as claimed in claim 19, where R³, R⁴ are selected from hydrogen and fluorine.
21. The compound as claimed in claim 19 or 20, where R⁵ and R⁶ are, independently of each other, selected from the group consisting of hydrogen, fluorine and methyl.
- 15
22. The compound as claimed in any one of claims 1 to 18, where A is A².
23. The compound as claimed in any one of claims 1 to 18, where A is A³.
- 20
24. The compound as claimed in claim 23, where R⁴, R⁵ are selected from hydrogen and fluorine.
25. The compound as claimed in any one of claims 1 to 18, where A is A⁴.
- 25
26. The compound as claimed in claim 25, where A' is CR^{3b}R^{3c}, where R^{3b} and R^{3c} are independently of each other selected from the group consisting of hydrogen, fluorine and methyl or together form CH₂CH₂.
27. The compound as claimed in claim 26, where R^{3b} and R^{3c} are hydrogen.
- 30
28. The compound as claimed in any one of claims 1 to 18, where A is A⁵.

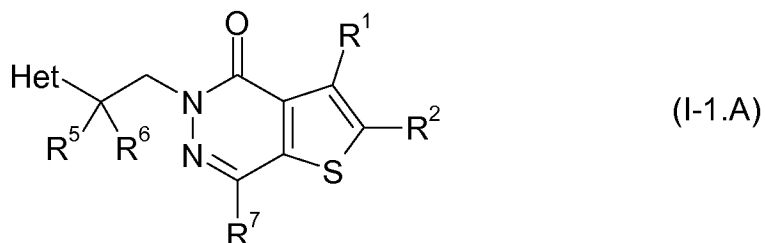
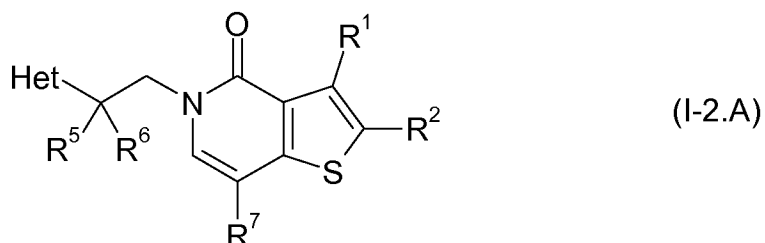
29. The compound as claimed in claim 28, where R^{3e} , R^{3f} , R^4 and R^5 are each hydrogen.
30. The compound as claimed in any one of the preceding claims, where Het is
5 selected from the group consisting of C-bound 6-membered monocyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members, benzofuryl and C-bound, fused bicyclic hetaryl, which has 1 or 2 nitrogen atoms as ring members and optionally a further heteroatom selected from O, S and N as ring member;
where monocyclic hetaryl, benzofuryl and bicyclic hetaryl may be unsubstituted
10 or may carry 1, 2, 3 or 4 substituents R^x .
31. The compound as claimed in claim 30, where Het has at least one imino-nitrogen as ring member, which is located in the position adjacent to the carbon atom which is bound to A.
- 15 32. The compound as claimed in claim 31, where Het is selected from the group consisting of 2-pyridyl, 2-pyrimidinyl, 4-pyrimidinyl, 2-pyrazinyl, 3-pyridazinyl, 2-quinolinyl, 3-isoquinolinyl, 2-quinazolinyl, 2-quinoxalinyl, 1,5-naphthyridin-2-yl, 1,8-naphthyridin-2-yl, benzothiazol-1-yl, benzoxazol-1-yl, benzimidazol-2-yl,
20 1-methylbenzimidazol-2-yl, imidazo[1,2-a]pyridine-2-yl, thieno[3,2-b]pyridine-5-yl, imidazo-[2,1-b]-thiazol-6-yl and 1,2,4-triazolo[1,5-a]pyridine-2-yl, where the aforementioned radicals may carry 1, 2 or 3 radicals selected from fluorine, chlorine, methyl, fluoromethyl, difluoromethyl, trifluoromethyl, methoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, cyclopropyl, optionally
25 substituted by 1, 2 or 3 methyl groups, and fluorinated cyclopropyl.
33. The compound as claimed in any one of the preceding claims, where Y^1 , Y^2 and Y^3 , independently of each other, are selected from the group consisting of a chemical bond, O and NH.

34. The compound as claimed in any one of the preceding claims, where Y^1 , Y^2 and Y^3 are each a chemical bond.

35. The compound as claimed in any one of the preceding claims, where Q is O.

5

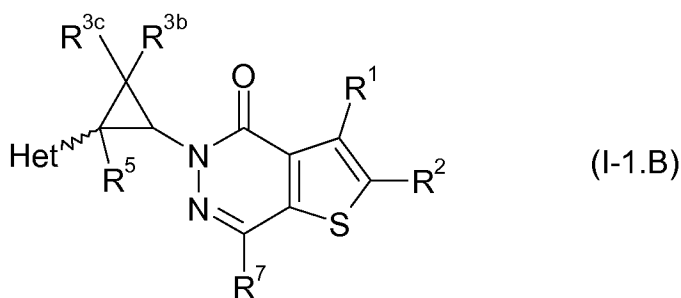
36. The compound as claimed in any one of the preceding claims, which is of the formulae I-1.A or I-2.A



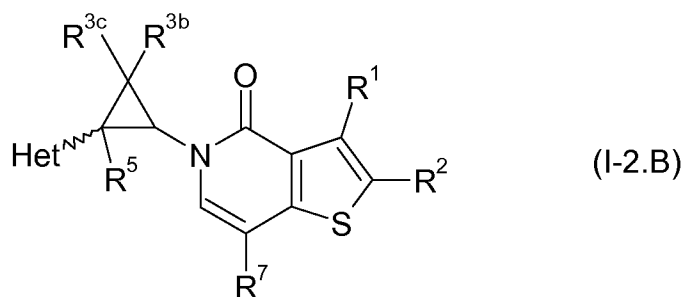
10 where Het, R^1 , R^2 , R^5 , R^6 and R^7 are as defined in any one of the preceding claims.

37. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-1.B or I-2.B

15

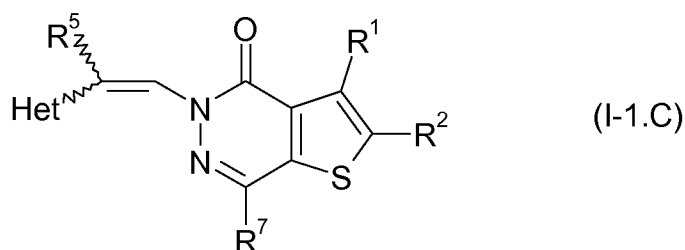
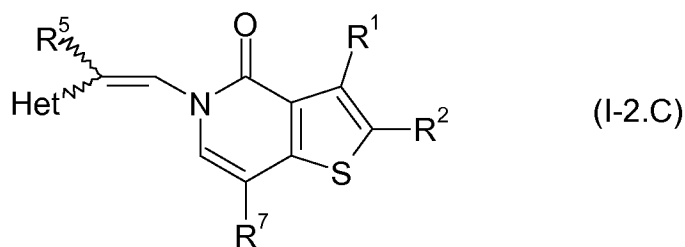


250



where Het, R^1 , R^2 , R^{3b} , R^{3c} and R^7 are as defined in any one of claims 1 to 35 and R^5 is hydrogen.

38. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-1.C or I-2.C



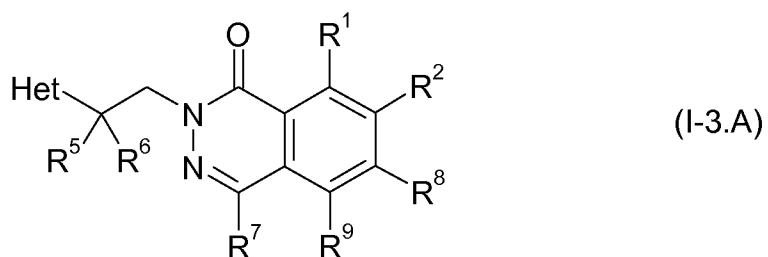
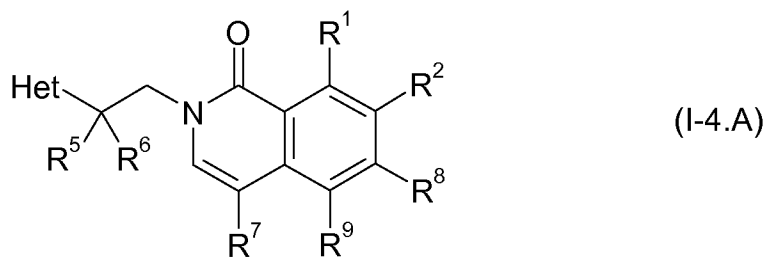
where Het, R^1 , R^2 , R^5 , and R^7 are as defined in any one of claims 1 to 35.

39. The compound as claimed in any of claim 36, 37 or 38, where R^1 is a radical Y^1 -Cyc¹ and R^7 is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y^2 -Cyc².
40. The compound as claimed in any of claim 36, 37 or 38, where R^1 is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-

251

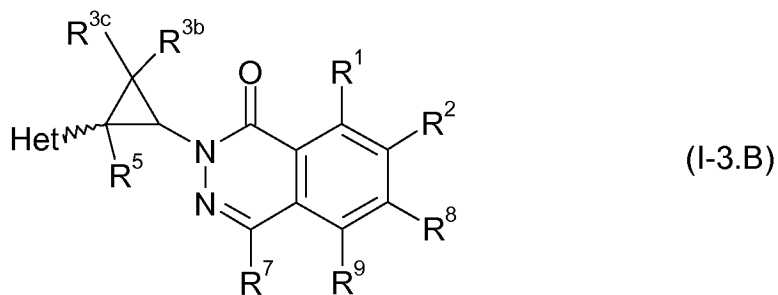
alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and R⁷ is a moiety Y²-Cyc².

41. The compound as claimed in any one of claims 1 to 35, which is of the formulae
5 I-3.A or I-4.A

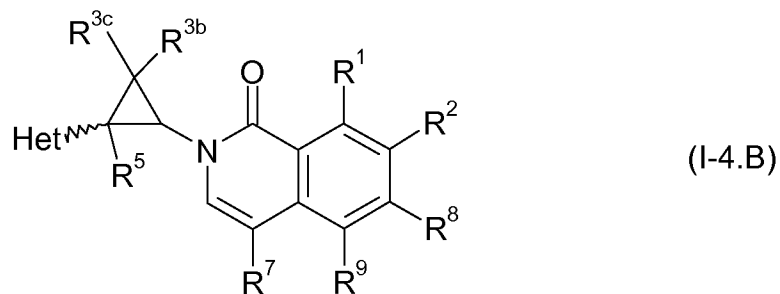


- 10 where Het, R¹, R², R⁵, R⁶, R⁷, R⁸ and R⁹ are as defined in any one of claims 1 to 35.

42. The compound as claimed in any one of claims 1 to 35, which is of the formulae
15 I-3.B or I-4.B

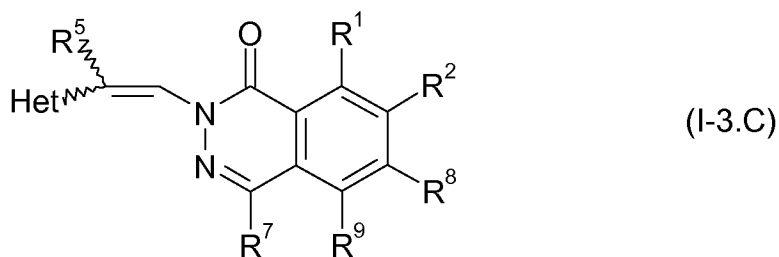
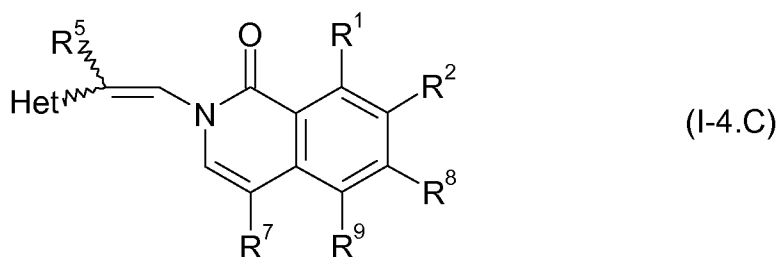


252



where Het, R^1 , R^2 , R^{3b} , R^{3c} , R^7 , R^8 and R^9 are as defined in any one of claims 1 to 35 and R^5 is hydrogen..

- 5 43. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-3.C or I-4.C



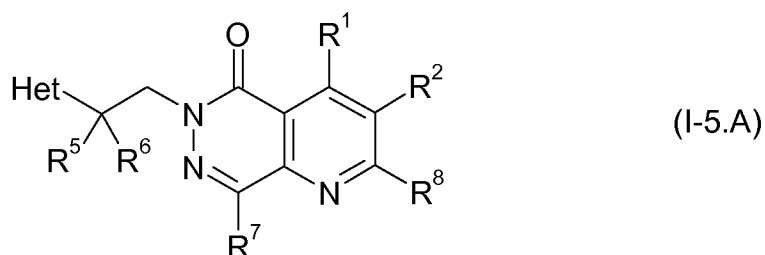
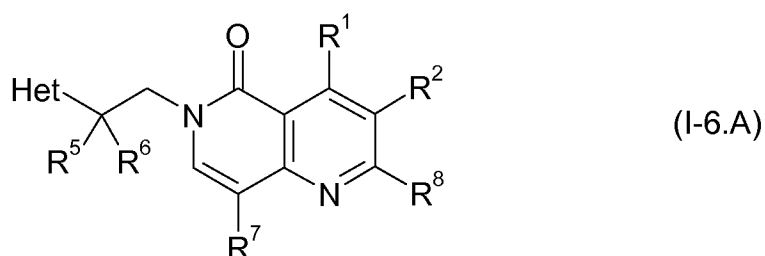
10

where Het, R^1 , R^2 , R^5 , R^7 , R^8 and R^9 are as defined in any one of claims 1 to 35.

- 15 44. The compound as claimed in any one of claims 41, 42 or 43, where R^1 is a radical Y^1 -Cyc¹ and R^7 and R^9 are selected, independently of each other, from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y^2 -Cyc² or Y^3 -Cyc³, respectively.

253

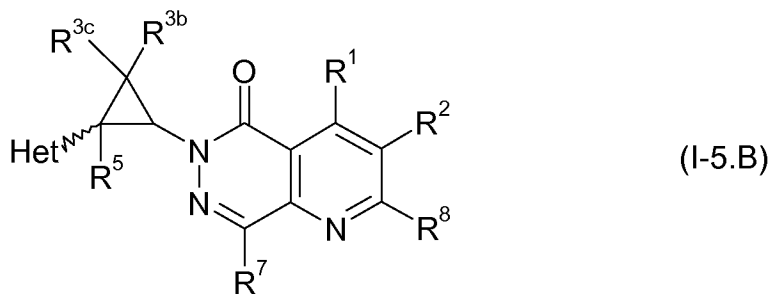
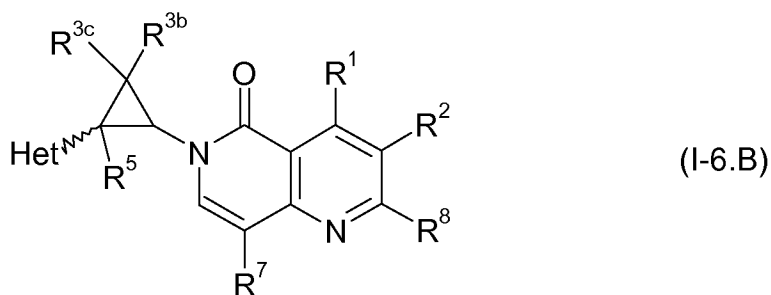
45. The compound as claimed in any one of claims 41, 42 or 43, where R^1 is selected from the group consisting of hydrogen, fluorine, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and R^7 and R^9 are selected, independently of each other, from the group consisting of hydrogen, fluorine, C_1 - C_4 -alkyl, C_1 - C_2 -fluoroalkyl, C_1 - C_4 -alkoxy, C_1 - C_2 -fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y^2 -Cyc² or Y^3 -Cyc³, respectively, provided that either R^7 is Y^2 -Cyc² or R^9 is Y^3 -Cyc³.
46. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-5.A or I-6.A



where Het, R^1 , R^2 , R^5 , R^6 , R^7 and R^8 are as defined in any one of claims 1 to 35.

47. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-5.B or I-6.B

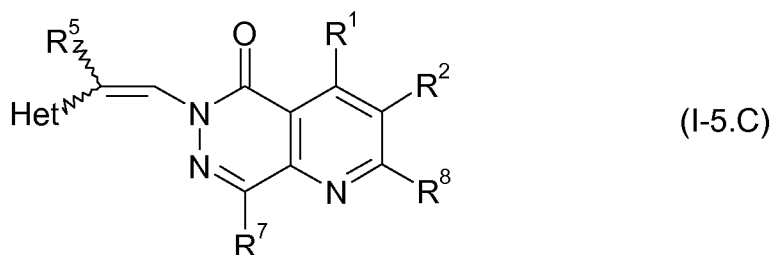
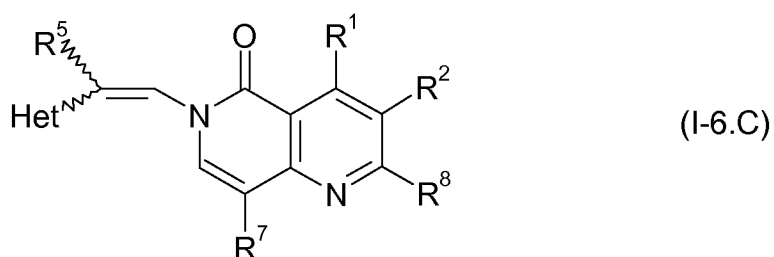
254



where Het, R^1 , R^2 , R^{3b} , R^{3c} , R^7 and R^8 are as defined in any one of claims 1 to 35 and R^5 is hydrogen.

5

48. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-5.C or I-6.C



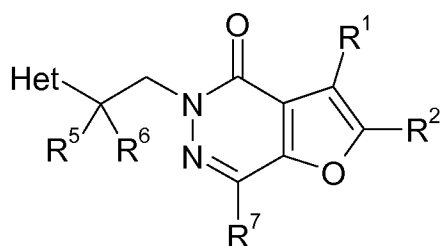
10

where Het, R^1 , R^2 , R^5 , R^7 and R^8 are as defined in any one of claims 1 to 35.

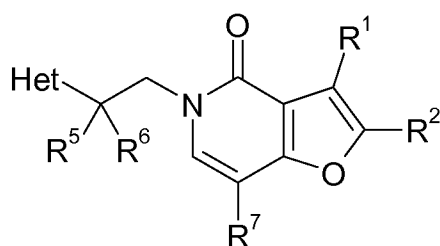
49. The compound as claimed in any one of claims 46, 47 or 48, where R^1 is a radical Y^1 -Cyc¹ and R^7 is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl,

optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc².

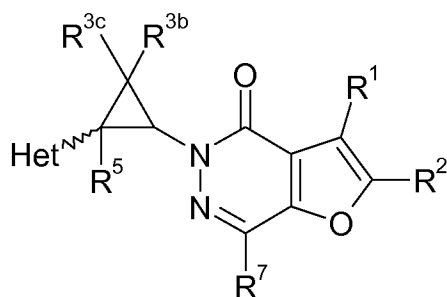
50. The compound as claimed in any one of claims 46, 47 or 48, where R¹ is selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups and fluorinated cyclopropyl and R⁷ is Y²-Cyc².
51. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-7.A, I-8.A, I-7.B, I-8.B, I-7.C, I-8.C,



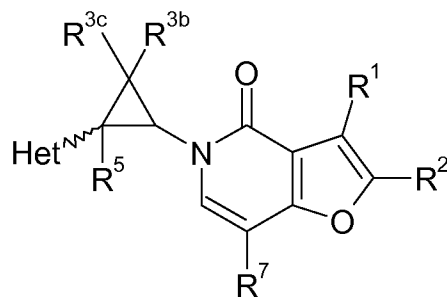
(I-7.A)



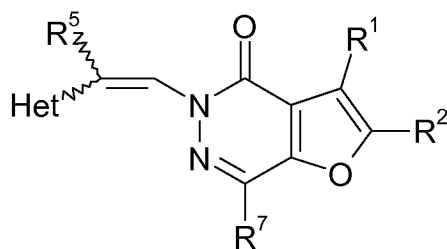
(I-8.A)



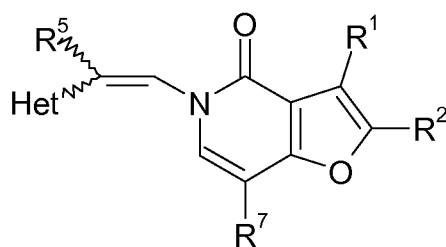
(I-7.B)



(I-8.B)



(I-7.C)



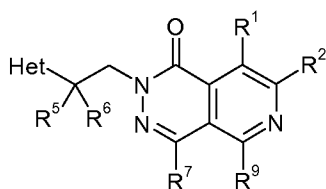
(I-8.C)

- where Het, R¹, R², R^{3b}, R^{3c}, R⁵, R⁶, R⁷ and R⁸ are as defined in any one of claims

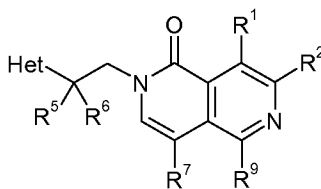
1 to 35.

52. The compound as claimed in claim 51, where R^1 is a radical $Y^1\text{-Cyc}^1$ and R^7 is selected from the group consisting of hydrogen, fluorine, $C_1\text{-C}_4\text{-alkyl}$, $C_1\text{-C}_2\text{-fluoroalkyl}$, $C_1\text{-C}_4\text{-alkoxy}$, $C_1\text{-C}_2\text{-fluoroalkoxy}$, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and $Y^2\text{-Cyc}^2$.

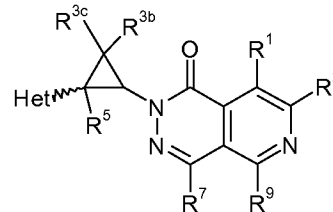
53. The compound as claimed in any one of claims 1 to 35, which is of formulae



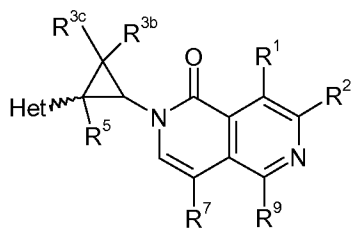
(I-9.A)



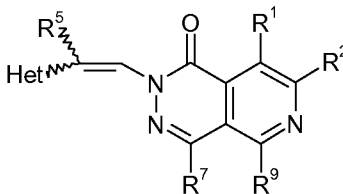
(I-10.A)



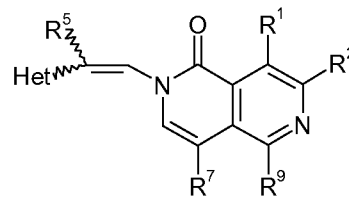
(I-9.B)



(I-10.B)



(I-9.C)



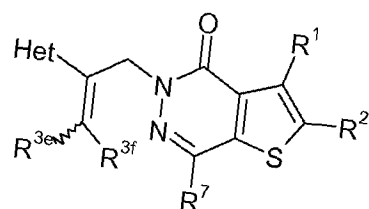
(I-10.C)

where Het, R^1 , R^2 , R^{3b} , R^{3c} , R^5 , R^6 , R^7 , and R^9 are as defined in any one of claims 1 to 35.

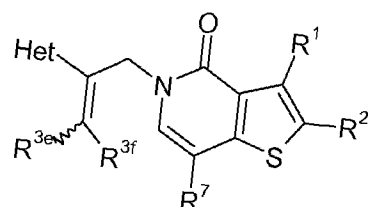
54. The compound as claimed in claim 53, where R^1 is a radical $Y^1\text{-Cyc}^1$ and R^7 and R^9 are selected, independently of each other, from the group consisting of hydrogen, fluorine, $C_1\text{-C}_4\text{-alkyl}$, $C_1\text{-C}_2\text{-fluoroalkyl}$, $C_1\text{-C}_4\text{-alkoxy}$, $C_1\text{-C}_2\text{-fluoroalkoxy}$, cyclopropyl, optionally substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and $Y^2\text{-Cyc}^2$ or $Y^3\text{-Cyc}^3$, respectively.

55. The compound as claimed in any one of claims 1 to 35, which is of the formulae I-1.D, I-2.D, I-3.D, I-4.D, I-5.D, I-6.D, I-7.D, I-8.D, I-9.D, I-10.D

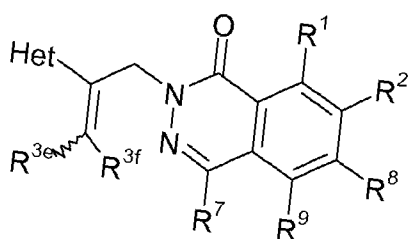
257



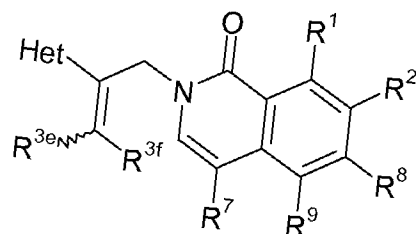
(I-1.D)



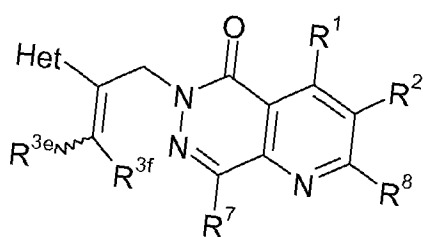
(I-2.D)



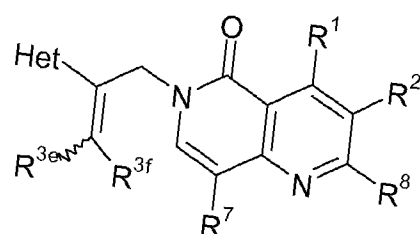
(I-3.D)



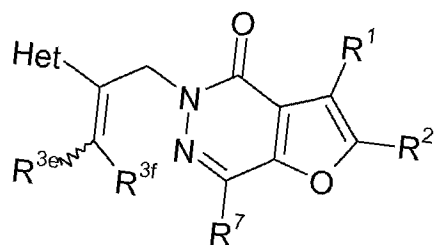
(I-4.D)



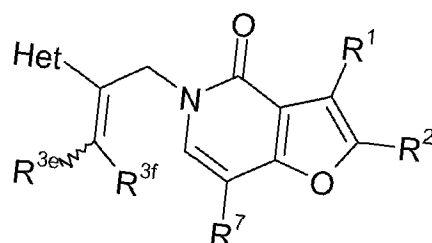
(I-5.D)



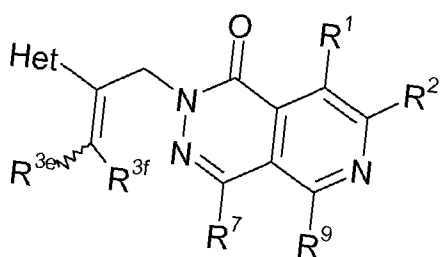
(I-6.D)



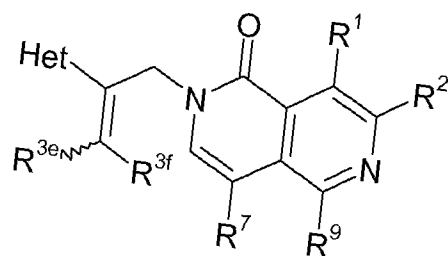
(I-7.D)



(I-8.D)



(I-9.D)



(I-10.D)

258

where Het, R¹, R², R^{3e}, R^{3f}, R⁷, R⁸ and R⁹ are as defined in any one of claims 1 to 35.

56. The compound as claimed in claim 55, where R¹ is a radical Y¹-Cyc¹ and R⁷ is
5 selected from the group consisting of hydrogen, fluorine, C₁-C₄-alkyl, C₁-C₂-
fluoroalkyl, C₁-C₄-alkoxy, C₁-C₂-fluoroalkoxy, cyclopropyl, optionally
substituted by 1, 2 or 3 methyl groups, fluorinated cyclopropyl and Y²-Cyc².
57. The compound as claimed in any one of claims 36 to 56, where R^{3b}, R^{3c}, R⁵, R⁶, if
10 present, are hydrogen.
58. The compound as claimed in any one of the preceding claims, where Cyc¹ is
selected from the group consisting of saturated 4-, 5-, 6-, 7- or 8-membered
heteromonocycles and saturated 7-, 8-, 9- or 10-membered heterobicycles, where
15 the heteromonocycles and the heterobicycles have one nitrogen or oxygen atom as
ring member and may have one further heteroatom or heteroatom group as ring
member, which is selected from the group consisting of O, S, S(=O), S(=O)₂ and
N, where the saturated heteromonocycle and the saturated heterobicycle are
unsubstituted or carry 1, 2, 3, 4 or 5 radicals R^{C1} or one radical Y'-R^{C2} and 0, 1, 2,
20 3 or 4 radicals R^{C1}, where R^{C1}, R^{C2} and Y' are as defined in claim 1.
59. The compound as claimed in any one of the preceding claims, where Y¹-Cyc¹,
is selected from the group consisting of 1-piperidinyl, 4,4-difluoro-1-piperidinyl,
4-piperidinyl, 1-methyl-4-piperidinyl, 1-piperazinyl, 4-methyl-1-piperazinyl,
25 morpholin-4-yl, azepane-1-yl, 1,4-oxazepan-4-yl, hexahydrofuro[3,4-c]pyrrol-5-
yl, 2,5-diazabicyclo[2.2.1]heptan-2-yl, 3,8-diazabicyclo[3.2.1]octan-8-yl,
thiomorpholin-4-yl, 1-oxothiomorpholin-4-yl, N-(oxetan-3-yl)amino, 1,1-
dioxothiomorpholin-4-yl and oxetan-3-ylamino.
- 30 60. The compound as claimed in any one of claims 1 to 57, where Cyc¹ is selected
from the group consisting of phenyl, 5- or 6 membered monocyclic hetaryl, and 9-
or 10 membered bicyclic hetaryl, where hetaryl has one heteroatom, selected from

O, S and N as ring member and optionally one or two further nitrogen atoms as ring members, where phenyl and the hetaryl radical are unsubstituted or either carry, independently of each other, 1, 2, 3, 4 or 5 radicals R^{C1} .

- 5 61. The compound as claimed in claim 60, where Y^1 is a chemical bond and Cyc^1 is selected from the group consisting of phenyl, 5- or 6-membered monocyclic
 10 hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, 9- or 10-membered bicyclic hetaryl selected from the group consisting of indolyl, quinolinyl, isoquinolinyl, quinazolinyl, benzimidazolyl, benzotriazolyl, benzopyrazolyl and benzofuryl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals
 15 R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH_2 , or, if Cyc^1 is phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, benzo-1,3-dioxolan-5-yl, benzo-1,3-dioxolan-6-yl, benzo-1,4-dioxan-5-yl, benzo-1,4-dioxan-6-yl, benzo-1,5-dioxepan-6-yl and benzo-1,4-dioxepan-7-yl.
- 20 62. The compound as claimed in any one of the preceding claims, where Cyc^2 and Cyc^3 , independently of each other, are selected from the group consisting of saturated 4-, 5-, 6-, 7- or 8-membered heteromonocycles and saturated 7-, 8-, 9- or 10-membered heterobicycles, where the heteromonocycles and the heterobicycles
 25 have one nitrogen or oxygen atom as ring member and may have one further heteroatom or heteroatom group as ring member, which is selected from the group consisting of O, S, $S(=O)$, $S(=O)_2$ and N, where the saturated heteromonocycle and the saturated heterobicycle are unsubstituted or carry 1, 2, 3, 4 or 5 radicals R^{C1} or one radical Y^1-R^{C2} and 0, 1, 2, 3 or 4 radicals R^{C1} , where R^{C1} , R^{C2} and Y^1
 30 are as defined in claim 1.

63. The compound as claimed in claim 62, where Y^2 -Cyc² and Y^3 -Cyc³, independently of each other, are selected from the group consisting of phenyl, 5- or 6-membered monocyclic hetaryl selected from the group consisting of pyridyl, pyrimidinyl, furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, oxazolyl and thiazolyl, 9- or 10-membered bicyclic hetaryl selected from the group consisting of indolyl, quinoliny, isoquinoliny, quinazoliny, benzimidazolyl, benzotriazolyl, benzopyrazolyl and benzofuryl, where phenyl and hetaryl are unsubstituted or carry 1, 2 or 3 radicals R^{C1} which are selected from the group consisting of fluorine, chlorine, CN, methyl, difluoromethyl, trifluoromethyl, methoxy and NH₂, or, if Cyc² or Cyc³ are phenyl, two radicals R^{C1} which are bound to adjacent carbon atoms, together with the phenyl ring to which they are bound, form a bicyclic heterocyclic radical, which is selected from 2,3-dihydrobenzofuran-5-yl, 2,3-dihydrobenzofuran-6-yl, 1,3-dihydroindol-2-on-5-yl, 1,3-dihydroindol-2-on-6-yl, benzo-1,3-dioxolan-5-yl, benzo-1,3-dioxolan-6-yl, benzo-1,4-dioxan-5-yl, benzo-1,4-dioxan-6-yl, benzo-1,5-dioxepan-6-yl and benzo-1,4-dioxepan-7-yl.
64. The compound as claimed in claim 1, which is selected from the group consisting of
- 3,7-di(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 7-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 3-(pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 3,7-di(pyridin-4-yl)-5-[2-(pyridin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 5-[2-(quinolin-2-yl)ethyl]-3-[4-(trifluoromethyl)phenyl]thieno[2,3-d]pyridazin-4(5H)-one;
 3-(4-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 3-[4-(propan-2-yl)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 3-(4-ethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
 4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}benzonitrile;

- 3-(4-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(4-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-[4-(dimethylamino)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-
5 4(5H)-one;
(4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}
phenyl)acetonitrile;
3-(4-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-chlorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
10 3-(2-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-ethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(2-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
15 3-(2-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(quinolin-2-yl)ethyl]-3-[2-(trifluoromethyl)phenyl]thieno[2,3-d]pyridazin-
4(5H)-one;
3-[3-(methoxymethyl)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-
4(5H)-one;
20 3-(3-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(3-ethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-[3-(dimethylamino)phenyl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-
4(5H)-one;
3-[4-Oxo-5-(2-quinolin-2-yl-ethyl)-4,5-dihydro-thieno[2,3-d]pyridazin-3-yl}-
25 benzonitrile;
3-(3-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(3-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
N,N-dimethyl-3-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-
d]pyridazin-3-yl}benzamide;
30 3-(3-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(quinolin-2-yl)ethyl]-3-(thiophen-2-yl)thieno[2,3-d]pyridazin-4(5H)-one;

- 3-(1-methyl-1H-indol-5-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one;
- 3-(1H-indol-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5 3-(2-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 10 3-(furan-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(quinolin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(isoquinolin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(isoquinolin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(1H-indol-4-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one;
- 15 3-(2,3-dihydrobenzofuran-5-yl)-5-(2-quinolin-2-yl-ethyl)-5H-thieno[2,3-d]pyridazin-4-one;
- 3-(quinolin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,5-dimethyl-1,2-oxazol-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 3-(6-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,3-dihydro-1,4-benzodioxin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-methylpyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 3-(5-methoxypyridin-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-[6-(morpholin-4-yl)pyridin-3-yl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 30 3-(1,3-benzodioxol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(quinolin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;

263

- 3-(1-methyl-1H-pyrazol-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5 tert-butyl 2-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl}-1H-pyrrole-1-carboxylate;
- 3-(2-methoxypyrimidin-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(quinolin-2-yl)ethyl]-3-(2,3,4-trifluorophenyl)thieno[2,3-d]pyridazin-4(5H)-one;
- 10 3-(4-fluoro-3-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(4-fluoro-2-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 15 3-(3-chloro-4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-chloro-4-fluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,4-dimethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 3-(2,4-dimethylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,4-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 3-(2,4-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,5-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,3-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 30 3-(3,4-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;

- 3-(3,4-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(5-fluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5 3-(4-fluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,5-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,5-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 10 3-(2,3-dimethoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3-fluoro-4-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 15 3-(2-fluoro-3-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3,5-difluorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(3-fluoro-5-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 3-(2-methoxy-5-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2,5-dichlorophenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 25 3-(naphthalen-2-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-phenyl-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(1-benzofuran-2-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(1H-indazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 30 3-(1-methyl-1H-pyrazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;

265

- 3-(4,5-difluoro-2-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(2-fluoro-4-methylphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 5 3-(2-fluoro-5-methoxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 3-methyl-4-{4-oxo-5-[2-(quinolin-2-yl)ethyl]-4,5-dihydrothieno[2,3-d]pyridazin-3-yl} benzonitrile;
- 5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 10 5-[2,2-difluoro-2-(quinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 15 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(7-fluoroimidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 8-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 2-[2-(quinolin-2-yl)ethyl]-8-[4-(trifluoromethyl)phenyl]phthalazin-1(2H)-one;
- 8-(4-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[4-(propan-2-yl)phenyl]-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(4-ethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 4-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl} benzonitrile;
- 25 8-(4-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- (4-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl} phenyl)acetonitrile;
- 8-(4-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 30 8-(2-chlorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(2-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(2-ethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;

- 8-(2-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
3-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl} benzonitrile;
5 8-(3-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
N,N-dimethyl-3-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl} benzamide;
8-(3-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
10 2-[2-(quinolin-2-yl)ethyl]-8-(thiophen-2-yl)phthalazin-1(2H)-one;
8-(1-methyl-1H-indol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,5-dimethyl-1H-pyrazol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1H-indol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1H-indol-6-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
15 8-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(furan-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(quinolin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
20 8-(1H-indol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,3-dihydro-1-benzofuran-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-dihydro-2H-1,5-benzodioxepin-7-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
25 8-(1-benzofuran-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(6-methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,3-dihydro-1,4-benzodioxin-6-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-methylpyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
30 8-(5-methoxypyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(5-fluoropyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1,3-benzodioxol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;

- 8-(1-methyl-1H-pyrazol-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
tert-butyl 2-{4-oxo-3-[2-(quinolin-2-yl)ethyl]-3,4-dihydrophthalazin-5-yl}-1H-pyrrole-1-carboxylate;
5
8-(3-chloro-4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-chloro-4-fluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-dimethylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,4-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
10
8-(2,5-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,3-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,4-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(5-fluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
15
8-(4-fluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3,5-dimethoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2,5-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-fluoro-4-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-fluoro-3-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
20
8-(3,5-difluorophenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(3-fluoro-5-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(naphthalen-2-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-phenyl-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(1-benzofuran-2-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
25
8-(1-methyl-1H-pyrazol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(4,5-difluoro-2-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-fluoro-4-methylphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
8-(2-fluoro-5-methoxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
30
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-yl)phthalazin-1(2H)-one;

- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(3-methoxypyridin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyrimidin-5-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-methyl-1H-pyrazol-3-yl)phthalazin-1(2H)-one;
- 5 8-(furan-3-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxo-2,3-dihydro-1H-indol-6-yl)phthalazin-1(2H)-one;
- 8-(3,4-dihydro-2H-chromen-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 8-(1,1-dioxidothiomorpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(morpholin-4-yl)phthalazin-1(2H)-one;
- 8-(1,1-dioxidothiomorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 15 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)phthalazin-1(2H)-one;
- 8-(5,5-difluorohexahydrocyclopenta[c]pyrrol-2(1H)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperazin-1-yl)phthalazin-1(2H)-one;
- 8-(4,4-difluoropiperidin-1-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[4-(chloromethyl)-4-(hydroxymethyl)piperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 25 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-1-yl)phthalazin-1(2H)-one;
- 8-(2,3-dihydro-4H-1,4-benzoxazin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[4-(trifluoromethyl)piperidin-1-yl]phthalazin-1(2H)-one;
- 30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(4-methylpiperazin-1-yl)phthalazin-1(2H)-one;

- 8-(1,3-dihydro-2H-isoindol-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(7-benzyl-2,7-diazaspiro[4.4]non-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5 8-({[(3aR,4S,6aS)-2-benzyl-octahydrocyclopenta[c]pyrrol-4-yl]methyl}amino)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- tert-butyl (3R)-3-({3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl}amino)pyrrolidine-1-carboxylate;
- 8-(2,6-dimethylmorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,4-oxazepan-4-yl)phthalazin-1(2H)-one;
- tert-butyl 4-{3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl}-3,6-dihydropyridine-1(2H)-carboxylate;
- 15 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(1-methyl-1H-pyrazol-5-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5-(1,1-dioxidothiomorpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-3-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyrimidin-5-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(morpholin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(tetrahydro-1H-furo[3,4-c]pyrrol-5(3H)-yl)phthalazin-1(2H)-one;
- 25 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(pyrimidin-5-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-(morpholin-4-yl)phthalazin-1(2H)-one;
- 3-(3-methoxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 3-(3-hydroxypyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
- 30 3-(1-methyl-1H-pyrazol-5-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;

- 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
3-(pyrimidin-5-yl)-5-(2-quinolin-2-yl)ethylthieno[3,2-c]pyridin-4(5H)-one;
3-(2-oxoindolin-6-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
3-(3-hydroxyphenyl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
5-[2-(5-ethylpyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
3-(morpholin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
tert-butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-5,6-dihydropyridine-1(2H) carboxylate;
5-(2-(quinolin-2-yl)ethyl)-3-(1,2,3,6-tetrahydropyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
tert-butyl-4-(4-oxo-5-(2-quinolin-2-yl)ethyl)-4,5-dihydrothieno[3,2-c]pyridin-3-yl)-piperidine-1 carboxylate;
3-(piperidin-4-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[3,2-c]pyridin-4(5H)-one;
3-methyl-7-(pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)thieno[3,2-c]pyridin-4(5H)-one;
3-(pyridin-4-yl)-5-[2-(5,6,7,8-tetrahydroquinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
(R)-tert-butyl 3-(3-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)-4-oxo-3,4-dihydrophthalazin-5-ylamino)pyrrolidine-1-carboxylate;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3R)-pyrrolidin-3-ylamino]phthalazin-1(2H)-one;
5-(3-hydroxyphenyl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
(E)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)vinyl)isoquinolin-1(2H)-one;
anti (rac) 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti (+)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti (-)-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
8-(pyridin-4-yl)-2-(2-quinolin-2-yl-ethyl)isoquinolin-1(2H)-one;
anti (rac) 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;

- anti (+) 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti (-) 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
5 (E)-8-pyridin-4-yl-2-(2-quinolin-2-yl-vinyl)-2H-phthalazin-1-one;
anti (rac) 8-pyridin-4-yl-2-(2-quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one;
anti (+) 8-pyridin-4-yl-2-(2-quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one;
anti (-) 8-pyridin-4-yl-2-(2-quinolin-2-yl-cyclopropyl)-2H-phthalazin-1-one;
and the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the
10 pharmaceutically acceptable salts thereof.
65. The compound as claimed in claim 1, which is selected from the group consisting of
7-(pyridin-4-yl)-5-[2-(quinolin-2-yl)ethyl]furo[3,2-c]pyridin-4(5H)-one;
15 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one;
5-(2-(1H-benzo[d]imidazol-2-yl)ethyl)-3-(pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one;
5-(2-(imidazo[1,2-a]pyridin-2-yl)ethyl)-3-(pyridin-4-yl)furo[3,2-c]pyridin-4(5H)-one;
20 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)ethyl)furo[3,2-c]pyridin-4(5H)-one;
4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)allyl)pyrido[2,3-d]pyridazin-5(6H)-one;
syn 8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
25 anti 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
syn 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
anti 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;
30 syn 3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)furo[3,2-c]pyridin-4(5H)-one;

- anti 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(oxetan-3-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-(pyridazin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(pyridazin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
5 anti 8-(6-fluoropyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(6-fluoropyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
10 syn 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(pyridin-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
15 anti 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-(1-methyl-1H-pyrazol-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(1-methyl-1H-pyrazol-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
20 anti 8-(3-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(3-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
25 anti 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(2-fluoropyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-((3S)-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
30 syn 8-((3S)-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;

- anti 8-(3-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(3-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 1-(1-oxo-2-(2-(quinolin-2-yl)cyclopropyl)-1,2-dihydroisoquinolin-8-yl)piperidine-4-carbonitrile;
syn 1-(1-oxo-2-(2-(quinolin-2-yl)cyclopropyl)-1,2-dihydroisoquinolin-8-yl)piperidine-4-carbonitrile;
- 10 anti 8-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((3R,4R)-4-fluoro-3-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 15 anti 8-((3S)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((3S)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 20 anti 8-((3R)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((3R)-3-hydroxypyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(methyl(oxetan-3-yl)amino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 25 syn 8-(methyl(oxetan-3-yl)amino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-(4-methoxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 30 anti 8-(4-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;

- syn 8-(4-hydroxypiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(1-acetylpiperidin-4-ylamino)-2-(2-quinolin-2-cyclopropyl)isoquinolin-1(2H)-one;
- 5 syn 8-(1-acetylpiperidin-4-ylamino)-2-(2-quinolin-2-cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(piperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 10 syn 8-(piperidin-4-ylamino)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 2-(2-(quinolin-2-yl)cyclopropyl)-8-(tetrahydro-2H-pyran-4-yl)isoquinolin-1(2H)-one;
- syn 2-(2-(quinolin-2-yl)cyclopropyl)-8-(tetrahydro-2H-pyran-4-yl)isoquinolin-1(2H)-one;
- 15 anti 2-(2-(quinolin-2-yl)cyclopropyl)-8-(2-oxa-6-azaspiro[3.4]octan-6-yl)isoquinolin-1(2H)-one;
- syn 2-(2-(quinolin-2-yl)cyclopropyl)-8-(2-oxa-6-azaspiro[3.4]octan-6-yl)isoquinolin-1(2H)-one;
- anti 8-(dihydro-1H-furo[3,4-c]pyrrol-5(3H,6H,6aH)-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 20 syn 8-(dihydro-1H-furo[3,4-c]pyrrol-5(3H,6H,6aH)-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4,4-difluoropiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 25 syn 8-(4,4-difluoropiperidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 8-morpholino-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(3-(difluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 30 syn 8-(3-(difluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;

- anti 8-((1R,5S)-3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((1R,5S)-3-oxa-8-azabicyclo[3.2.1]octan-8-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 5 anti 8-(4-methylpiperazin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(4-methylpiperazin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 10 anti 8-(3-(fluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(3-(fluoromethyl)pyrrolidin-1-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 15 anti 8-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-((1R,5S)-8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 8-(4-fluorophenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(4-fluorophenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 20 anti 8-(furan-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
anti 8-(4,5-dihydrofuran-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(4,5-dihydrofuran-3-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 25 anti 8-(4-methoxyphenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
syn 8-(4-methoxyphenyl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-morpholinoisoquinolin-1(2H)-one;
syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-morpholinoisoquinolin-1(2H)-one;
- 30 anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-3-yl)isoquinolin-1(2H)-one;

- syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-3-yl)isoquinolin-1(2H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyrimidin-5-yl)isoquinolin-1(2H)-one;
- 5 syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyrimidin-5-yl)isoquinolin-1(2H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 10 anti 4-fluoro-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 4-fluoro-8-(pyridin-4-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- 15 anti 4-chloro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- syn 4-chloro-8-(pyrimidin-5-yl)-2-(2-(quinolin-2-yl)cyclopropyl)isoquinolin-1(2H)-one;
- anti 4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)cyclopropyl)pyrido[2,3-d]pyridazin-5(6H)-one;
- 20 syn 4-(pyridin-4-yl)-6-(2-(quinolin-2-yl)cyclopropyl)pyrido[2,3-d]pyridazin-5(6H)-one;
- anti 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)phthalazin-1(2H)-one;
- 25 syn 2-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-8-(pyridin-4-yl)phthalazin-1(2H)-one;
- anti 7-fluoro-3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- syn 7-fluoro-3-(pyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 30 anti 3-(2-fluoropyridin-4-yl)-5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;

- syn 3-(2-fluoropyridin-4-yl)-5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti 5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 5 syn 5-(2-(6-fluoroquinolin-2-yl)cyclopropyl)-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 10 syn 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 15 syn 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti 3-(pyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 20 syn 3-(6-fluoropyridin-3-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
syn 3-(6-fluoropyridin-3-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti 3-(2-methylpyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 25 syn 3-(2-methylpyrimidin-5-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
- 30 syn 3-(pyridazin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;
anti 3-(2-fluoropyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl)thieno[3,2-c]pyridin-4(5H)-one;

- syn 3-(2-fluoropyridin-4-yl)-5-(2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(morpholin-4-yl)-5[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 5 syn 3-(morpholin-4-yl)-5[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(pyridin-3-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyridin-3-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 10 anti 3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyridin-3-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 15 anti 3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- syn 3-(pyrimidin-5-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- anti 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- 20 syn -(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- anti 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 25 syn 3-(pyridin-4-yl)-5-[2-(thieno[3,2-b]pyridin-5-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- anti 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- syn 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[3,2-c]pyridin-4(5H)-one;
- 30 anti 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;

- syn 3-(pyridin-4-yl)-5-[2-(quinolin-2-yl)cyclopropyl]thieno[2,3-d]pyridazin-4(5H)-one;
- anti 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 5-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- 5 anti 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 5-(pyridin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- anti 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- anti 5-(morpholin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- 10 syn 5-(morpholin-4-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- anti 4-fluoro-8-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- syn 4-fluoro-8-(pyrimidin-5-yl)-2-[2-(quinolin-2-yl)cyclopropyl]isoquinolin-1(2H)-one;
- 15 8-(pyridin-4-yl)-2-[2-(quinolin-2-yl)ethyl]pyrido[3,4-d]pyridazin-1(2H)-one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(1-methyl-1H-imidazol-4-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(1-methyl-1H-pyrazol-4-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 20 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-7-(pyridin-3-yl)-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
- 5-[2-(6-chloroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 5-[2-(3-methylquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 25 one;
- 5-[2-(8-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- one;
- 5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-3-yl)thieno[3,2-c]pyridin-4(5H)-one;
- one;
- 30 5-[2-(6-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- one;
- 5-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-3-(pyridin-3-yl)thieno[3,2-c]pyridin-

- 4(5H)-one;
3-(pyridin-4-yl)-5-[2-(quinoxalin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(1,5-naphthyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5
5-[2-(1H-indazol-1-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
3-(1-methyl-1H-pyrazol-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(1H-pyrazol-3-yl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(1H-benzimidazol-1-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
10 one;
5-[2-(1H-benzimidazol-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(6-chloroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
15 3-(pyridin-3-ylethynyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
3-(pyridin-4-ylethynyl)-5-[2-(quinolin-2-yl)ethyl]thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(3,5-dimethylpyridin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
20 5-[2-(7-fluoroquinolin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
5-[2-(pyrazin-2-yl)ethyl]-3-(pyridin-4-yl)thieno[2,3-d]pyridazin-4(5H)-one;
2-[2-(1,6-naphthyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
25 2-[2-(8-fluoroquinolin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
8-(pyridin-4-yl)-2-[1-(quinolin-2-yl)propan-2-yl]isoquinolin-1(2H)-one;
2-[2-(3-methylquinolin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1H-pyrazol-3-yl)phthalazin-1(2H)-one;
8-(morpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-oxa-4,9-diazaspiro[5.6]dodec-9-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-7-azaspiro[3.5]non-7-

- yl)phthalazin-1(2H)-one;
8-[(3R)-3-hydroxypiperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
8-[(3S)-3-hydroxypiperidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-6-azaspiro[3.3]hept-6-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,2-oxazolidin-2-yl)phthalazin-1(2H)-one;
10 8-(hexahydrocyclopenta[b][1,4]oxazin-4(4aH)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydrofuran-3-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(3-oxa-8-azabicyclo[3.2.1]oct-8-yl)phthalazin-1(2H)-one;
15 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-oxa-6-azaspiro[3.4]oct-6-yl)phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2,2,6,6-tetrafluoromorpholin-4-yl)phthalazin-1(2H)-one;
20 8-(4-hydroxypiperidin-1-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-methylpyrimidin-5-yl)phthalazin-1(2H)-one;
8-(2-cyclopropylpyrimidin-5-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
25 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridazin-4-yl)phthalazin-1(2H)-one;
8-(5-fluoropyridin-3-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
8-[2-(3-fluorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(2-methoxypyrimidin-5-yl)phthalazin-1(2H)-one;

- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[2-(trifluoromethyl)pyridin-4-yl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(8-oxa-3-azabicyclo[3.2.1]oct-3-yl)phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[2-(trifluoromethyl)morpholin-4-yl]phthalazin-1(2H)-one;
- 8-(2,2-dimethylmorpholin-4-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[2-(4-chlorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 8-[2-(3,4-difluorophenyl)morpholin-4-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-4-yl)phthalazin-1(2H)-one;
- 15 8-(2,6-diazabicyclo[3.2.1]oct-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[(1S,5S)-3,6-diazabicyclo[3.2.0]hept-3-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 8-(furan-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1-methyl-1H-pyrazol-4-yl)phthalazin-1(2H)-one;
- 8-(hexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 25 8-(2,7-diazaspiro[4.4]non-2-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[(1S,4S)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-(2,7-diazaspiro[3.5]non-7-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 30 8-(2,6-diazaspiro[3.5]non-6-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;

- 8-(piperidin-4-yl)-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 8-[2-(aminomethyl)-4-chloropyrrolidin-1-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4,8-di(pyridin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aR,4S,7R,7aS)-octahydro-1H-4,7-epiminoisoindol-8-yl]phthalazin-1(2H)-one;
- 8-[5-(4-chlorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 10 4-bromo-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aS,8aS)-octahydropyrrolo[3,4-c]azepin-2(1H)-yl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3aS,8aR)-octahydropyrrolo[3,4-c]azepin-2(1H)-yl]phthalazin-1(2H)-one;
- 15 tert-butyl (3aR,4S,7R,7aS)-8-{3-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-4-oxo-3,4-dihydrophthalazin-5-yl} octahydro-2H-4,7-epiminoisoindole-2-carboxylate;
- 8-(hexahydro-5H-furo[2,3-c]pyrrol-5-yl)-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,2,3,6-tetrahydropyridin-4-yl)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3S)-tetrahydrofuran-3-ylamino]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3R)-tetrahydrofuran-3-ylamino]phthalazin-1(2H)-one;
- 25 8-{[5-(hydroxymethyl)-1,4-dioxan-2-yl]methoxy}-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(oxetan-3-yloxy)phthalazin-1(2H)-one;
- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-4-ylmethoxy)phthalazin-1(2H)-one;
- 30 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(morpholin-4-ylmethyl)phthalazin-1(2H)-one;

- 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(pyridin-3-yloxy)phthalazin-1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(oxetan-3-ylmethyl)amino]phthalazin-
 1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-4-
 5 ylamino)phthalazin-1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(1-methylazetidin-3-
 yl)amino]phthalazin-1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(1,3-oxazol-2-ylamino)phthalazin-
 1(2H)-one;
 10 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[methyl(oxetan-3-yl)amino]phthalazin-
 1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-4-ylamino)phthalazin-1(2H)-
 one;
 8-[(1-acetylpiperidin-3-yl)amino]-2-[2-(imidazo[1,2-a]pyridin-2-
 15 yl)ethyl]phthalazin-1(2H)-one;
 8-[(1-acetylpiperidin-4-yl)amino]-2-[2-(imidazo[1,2-a]pyridin-2-
 yl)ethyl]phthalazin-1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydrofuran-3-ylamino)phthalazin-
 1(2H)-one;
 20 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(tetrahydro-2H-pyran-3-
 ylamino)phthalazin-1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(piperidin-3-ylamino)phthalazin-1(2H)-
 one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-{methyl[(3-methyloxetan-3-
 25 yl)methyl]amino}phthalazin-1(2H)-one;
 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-(oxetan-3-ylamino)phthalazin-1(2H)-
 one;
 8-{[(3aS,4S,6aS)-octahydrocyclopenta[c]pyrrol-4-ylmethyl]amino}-2-[2-(5,6,7,8-
 tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one;
 30 5-(morpholin-4-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
 2-[2-(1H-benzimidazol-2-yl)ethyl]-5-(pyridin-4-yl)phthalazin-1(2H)-one;
 4-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;

285

- 5-(1,4-dihydropyrimidin-5-yl)-2-[2-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)ethyl]phthalazin-1(2H)-one-2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-5-(pyridin-4-yl)phthalazin-1(2H)-one;
- 5-(pyridin-3-yl)-2-[2-(quinolin-2-yl)ethyl]phthalazin-1(2H)-one;
- 5 2-[2-(imidazo[1,2-a]pyridin-2-yl)ethyl]-8-[(3-methyloxetan-3-yl)methyl]amino}-phthalazin-1(2H)-one;
- 4-(pyridin-4-yl)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one;
- 4-(morpholin-4-yl)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one;
- 4-(oxetan-3-ylamino)-6-[2-(quinolin-2-yl)ethyl]pyrido[2,3-d]pyridazin-5(6H)-one;
- 10 2-[2-(6-methoxypyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 2-[2-(1,3-benzothiazol-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 2-[2-(5-methylpyridin-2-yl)ethyl]-8-(pyridin-4-yl)isoquinolin-1(2H)-one;
- 5-[(E)-2-(6-methoxyquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 15 8-(pyridin-4-yl)-2-[(E)-2-(quinazolin-2-yl)ethenyl]isoquinolin-1(2H)-one;
- 5-[(E)-2-(6-chloroquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 5-[(E)-2-(3-methylquinolin-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 20 8-(pyridin-4-yl)-2-[(E)-2-(quinolin-2-yl)ethenyl]isoquinolin-1(2H)-one;
- 5-[(E)-2-(1,3-benzothiazol-2-yl)ethenyl]-3-(pyridin-4-yl)thieno[3,2-c]pyridin-4(5H)-one;
- 3-(pyridin-4-yl)-5-[(E)-2-(quinolin-2-yl)ethenyl]thieno[3,2-c]pyridin-4(5H)-one;
- 25 and the enantiomers, the N-oxides, the prodrugs, the tautomers and the hydrates thereof, and the pharmaceutically acceptable salts thereof.

66. The compound as claimed in any one of the preceding claims for use in therapy.
- 30 67. Pharmaceutical composition which comprises at least one compound as claimed in any one of claims 1 to 65 and at least one excipient.

68. The compounds according to any of claims 1 to 65 for treating a medical disorder, selected from neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A.
- 5
69. The compounds according to any of claims 1 to 65 for treating CNS disorders in a mammalian.
70. The compounds according to any of claims 1 to 65 for treating schizophrenia in a
- 10 mammalian.
71. The compounds according to any of claims 1 to 65 for treating cognitive dysfunction associated with schizophrenia in a mammalian.
- 15 72. The compounds according to any of claims 1 to 65 for treating bipolar disorders in a mammalian.
73. The compounds according to any of claims 1 to 65 for treating depression in a
- 20 mammalian.
74. The compounds according to any of claims 1 to 65 for treating cognitive dysfunction associated with Alzheimer's disease in a mammalian.
75. The compounds according to any of claims 1 to 65 for treating diet-induced
- 25 obesity in a mammalian.
76. The compounds according to any of claims 1 to 65 for treating Huntington's disease in a mammalian.
- 30 77. The compounds according to any of claims 1 to 65 for treating anxiety in a mammalian.

78. A method for treating a medical disorder, selected from neurological and psychiatric disorders which can be treated by inhibition of phosphodiesterase type 10A, said method comprising administering an effective amount of at least one compound as claimed in any of claims 1 to 65 to a subject in need thereof.