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CA 2890356 C 2021/04/06

(11)(21) 2 890 356

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(86) Date de dépôt PCT/PCT Filing Date: 2013/11/04
(87) Date publication PCT/PCT Publication Date: 2014/05/08
(45) Date de délivrance/Issue Date: 2021/04/06
(85) Entrée phase nationale/National Entry: 2015/05/01
(86) N° demande PCT/PCT Application No.: EP 2013/072891
(87) N° publication PCT/PCT Publication No.: 2014/068099
(30) Priorités/Priorities: 2012/11/05 (EP12191201.8); 2013/03/07 (US13/789,655); 2013/07/26 (EP13178248.4)

(51) Cl.Int./Int.Cl. *C07D 471/04* (2006.01), *A61P 9/00* (2006.01), *A61K 31/437* (2006.01)

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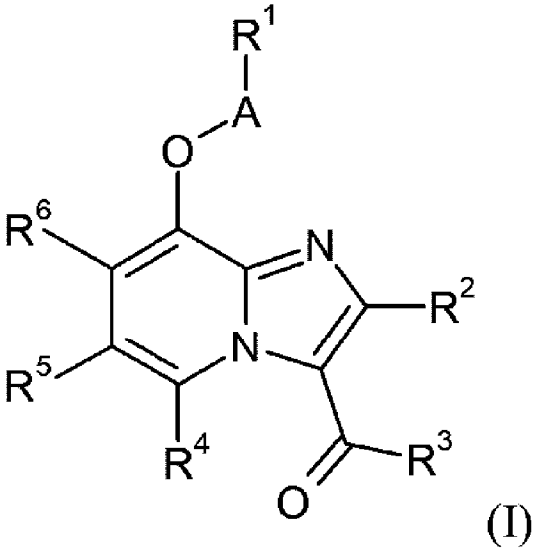
(54) Titre : IMIDAZO[1,2-A]PYRIDINCARBOXAMIDES AMINO-SUBSTITUES ET LEUR UTILISATION
(54) Title: AMINO-SUBSTITUTED IMIDAZO[1,2-A]PYRIDINECARBOXAMIDES AND THEIR USE



(I)

(57) Abrégé/Abstract:
The invention relates to novel substituted imidazo[1,2-aJpyridino-3-carboxamides of Formula (I)

(see formula I),

to methods for their production, their use alone or in combination for the treatment and/or prophylaxis of diseases, and their use for producing medicaments for the treatment and/or prophylaxis of diseases, especially for the treatment and/or prophylaxis of cardiovascular diseases.

CA 2890356 C 2021/04/06

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(13) C

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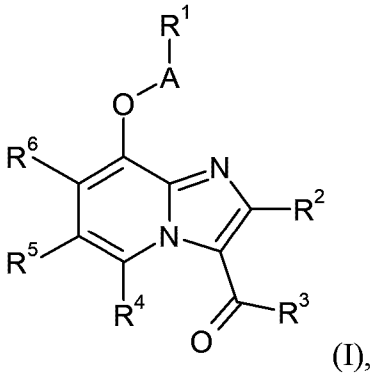
ABSTRACT

The invention relates to novel substituted imidazo[1,2-aJpyridino-3-carboxamides of Formula (I)



(I),

to methods for their production, their use alone or in combination for the treatment and/or prophylaxis of diseases, and their use for producing medicaments for the treatment and/or prophylaxis of diseases, especially for the treatment and/or prophylaxis of cardiovascular diseases.

Date reçu/Date Received 2020-07-09

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JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __3___

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Amino-substituted imidazo[1,2-a]pyridinecarboxamides and their use

The present application relates to novel substituted imidazo[1,2-a]pyridine-3-carboxamides, to processes for their preparation, to their use alone or in combinations for the treatment and/or prophylaxis of diseases and to their use for preparing medicaments for the treatment and/or prophylaxis of diseases, in particular for the treatment and/or prophylaxis of cardiovascular disorders.

One of the most important cellular transmission systems in mammalian cells is cyclic guanosine monophosphate (cGMP). Together with nitric oxide (NO), which is released from the endothelium and transmits hormonal and mechanical signals, it forms the NO/cGMP system. Guanylate cyclases catalyse the biosynthesis of cGMP from guanosine triphosphate (GTP). The representatives of this family disclosed to date can be divided both according to structural features and according to the type of ligands into two groups: the particulate guanylate cyclases which can be stimulated by natriuretic peptides, and the soluble guanylate cyclases which can be stimulated by NO. The soluble guanylate cyclases consist of two subunits and very probably contain one haem per heterodimer, which is part of the regulatory site. The latter is of central importance for the mechanism of activation. NO is able to bind to the iron atom of haem and thus markedly increase the activity of the enzyme. Haem-free preparations cannot, by contrast, be stimulated by NO. Carbon monoxide (CO) is also able to attach to the central iron atom of haem, but the stimulation by CO is distinctly less than that by NO.

Through the production of cGMP and the regulation, resulting therefrom, of phosphodiesterases, ion channels and protein kinases, guanylate cyclase plays a crucial part in various physiological processes, in particular in the relaxation and proliferation of smooth muscle cells, in platelet aggregation and adhesion and in neuronal signal transmission, and in disorders caused by an impairment of the aforementioned processes. Under pathophysiological conditions, the NO/cGMP system may be suppressed, which may lead for example to high blood pressure, platelet activation, increased cellular proliferation, endothelial dysfunction, atherosclerosis, angina pectoris, heart failure, myocardial infarction, thromboses, stroke and sexual dysfunction.

A possible way of treating such disorders which is independent of NO and aims at influencing the cGMP signaling pathway in organisms is a promising approach because of the high efficiency and few side effects which are to be expected.

Compounds, such as organic nitrates, whose effect is based on NO have to date been exclusively used for the therapeutic stimulation of soluble guanylate cyclase. NO is produced by bioconversion and activates soluble guanylate cyclase by attaching to the central iron atom of haem. Besides the

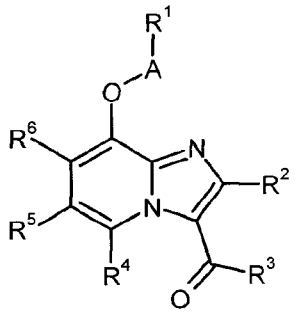
side effects, the development of tolerance is one of the crucial disadvantages of this mode of treatment.

Over the last years, a number of substances which stimulate soluble guanylate cyclase directly, i.e. without prior release of NO, have been described, for example 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole [YC-1; Wu et al., *Blood* 84 (1994), 4226; Mülsch et al., *Brit. J. Pharmacol.* 120 (1997), 681], fatty acids [Goldberg et al., *J. Biol. Chem.* 252 (1977), 1279], diphenyliodonium hexafluorophosphate [Pettibone et al., *Eur. J. Pharmacol.* 116 (1985), 307], isoliquiritigenin [Yu et al., *Brit. J. Pharmacol.* 114 (1995), 1587], and also various substituted pyrazole derivatives (WO 98/16223).

EP 0 266 890-A1, WO 89/03833-A1, JP 01258674-A [cf. *Chem. Abstr.* 112:178986], WO 96/34866-A1, EP 1 277 754-A1, WO 2006/015737-A1, WO 2008/008539-A2, WO 2008/082490-A2, WO 2008/134553-A1, WO 2010/030538-A2, WO 2011/113606-A1 and WO 2012/165399 A1 inter alia, describe various imidazo[1,2-a]pyridine derivatives which can be used for treating disorders.

It was an object of the present invention to provide novel substances which act as stimulators of soluble guanylate cyclase and, as such, are suitable for the treatment and/or prophylaxis of diseases.

The present invention provides compounds of the general formula (I)



(I),

in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

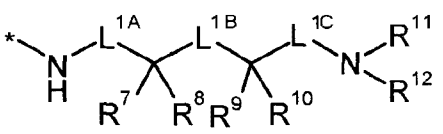
where (C_3-C_7)-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and (C_1-C_4)-alkyl,

and

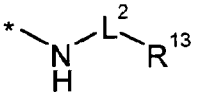
where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, (C_1-C_4)-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula



or



where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

L^{1B} represents a bond or (C_1-C_4)-alkanediyl,

L^{1C} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

R^7 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl,

trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl, (C_1-C_4)-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, trifluoromethyl, (C_1-C_4)-alkyl, (C_1-C_4)-alkylsulphonyl and (C_1-C_4)-alkoxy,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxy-carbonyl, (C_1-C_4)-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, trifluoromethyl, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy and (C_1-C_4)-alkylsulphonyl,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and with the group L^{1B} form a 5- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms a carbo- or heterocycle,

R^{11} represents hydrogen or (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy, (C_1-C_4)-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or (C_1-C_4)-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents selected from the group consisting of halogen, (C_1-C_4)-alkyl and trifluoromethyl,

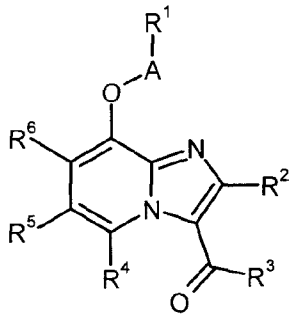
R^4 represents hydrogen,

R^5 represents hydrogen, halogen, cyano, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, (C_2-C_4)-alkynyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

The present invention provides compounds of the general formula (I)



(I),

in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

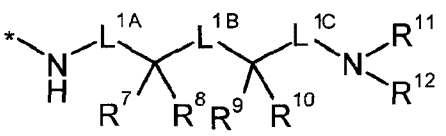
where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and $(C_1$-$C_4)$-alkyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula



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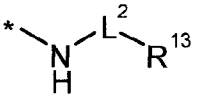


where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

L^{1B} represents a bond or (C_1-C_4)-alkanediyl,

L^{1C} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

R^7 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, cyano, 5- to 10-membered heteroaryl, naphthyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl, (C_1-C_4)-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, nitro, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkenyl, (C_1-C_4)-alkylsulphonyl, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

in which 2 adjacent carbon atoms of the phenyl may be substituted by a difluoromethylenedioxy bridge,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- to 10-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxy-carbonyl, (C_1-C_4)-alkylsulphonyl, 5- or 6-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where 5- or 6-membered heteroaryl may be benzo-fused or substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by (C_1-C_4)-alkyl or trifluoromethyl,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkylsulphonyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where the phenyl may be substituted on two adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_1-C_4)-alkyl, fluorine, hydroxy and (C_1-C_4)-alkoxy,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms a carbo- or heterocycle,

R^{11} represents hydrogen or (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy, (C_1-C_4)-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or (C_1-C_4)-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents

selected from the group consisting of halogen, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy and trifluoromethyl,

or

represents adamantyl,

R^4 represents hydrogen,

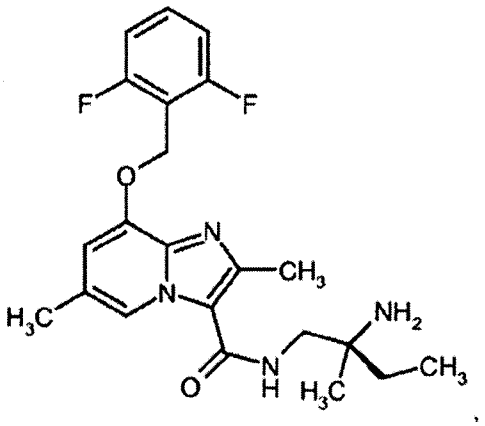
R^5 represents hydrogen, halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, (C_2-C_4)-alkynyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

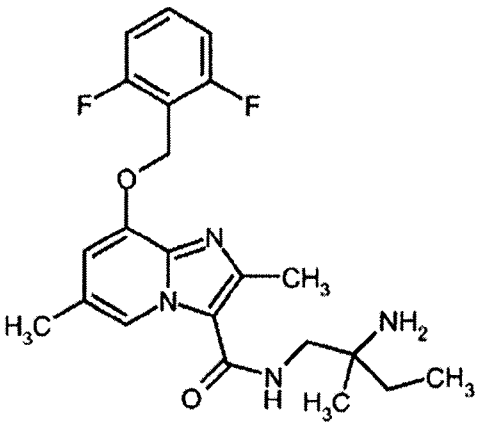
and its *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Specifically, the invention relates to the compound:

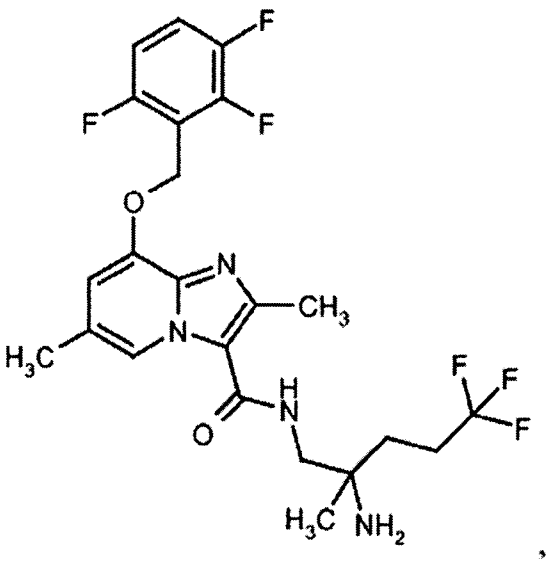
ent-*N*-[(2S)-amino-2-methylbutyl]-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



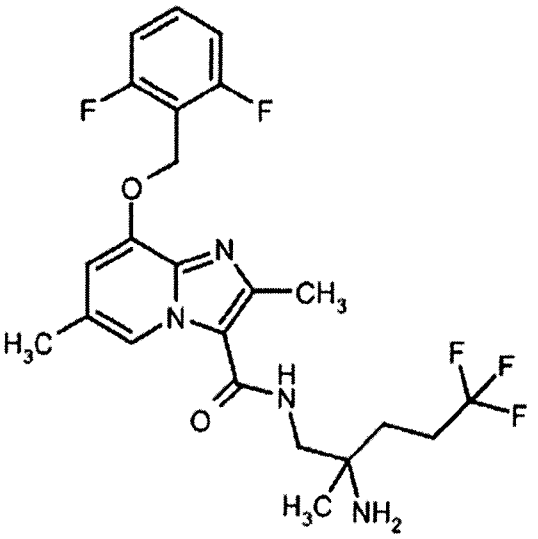
ent-*N*-(2-amino-2-methylbutyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



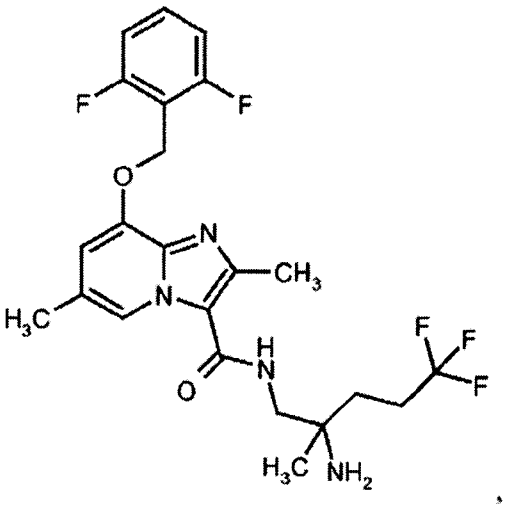
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



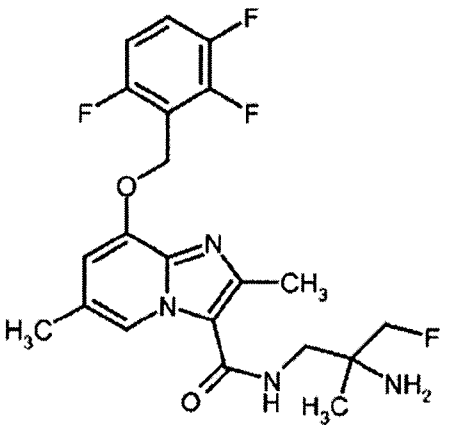
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



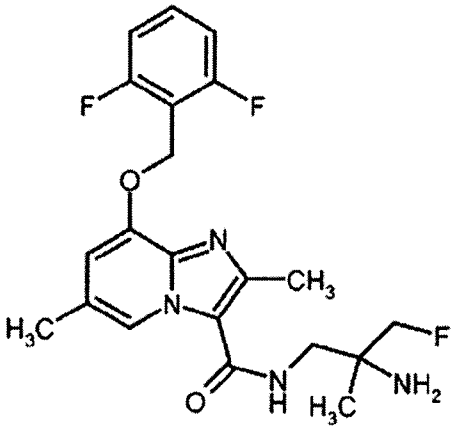
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



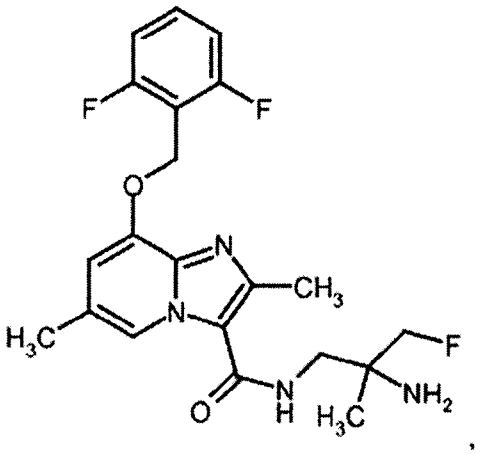
ent-N-(2-amino-3-fluoro-2-methylpropyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



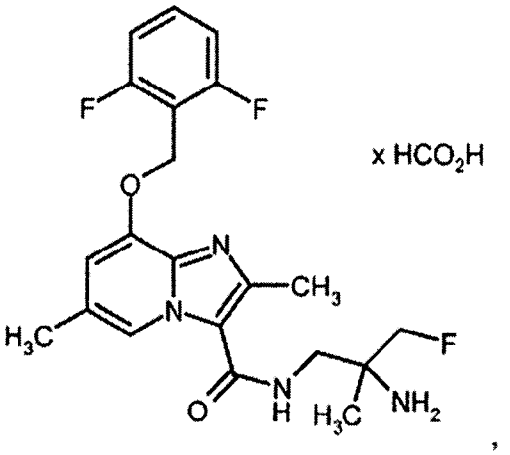
ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamixe (enantiomer B)



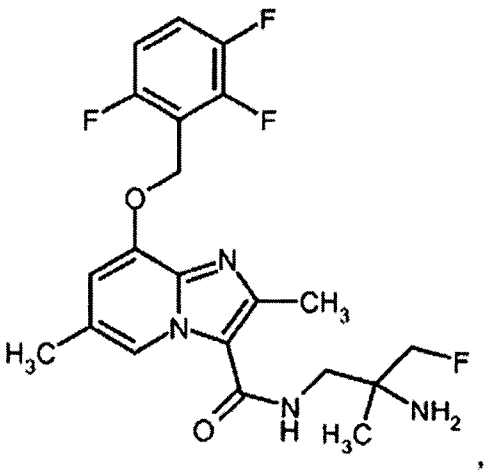
ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-diflurobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-carboxamide (enantiomer A)



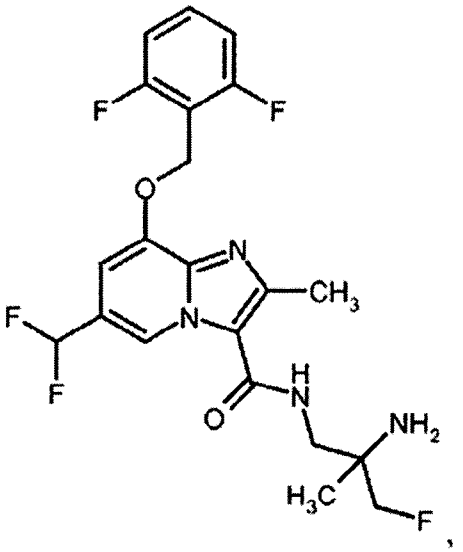
rac-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide formate



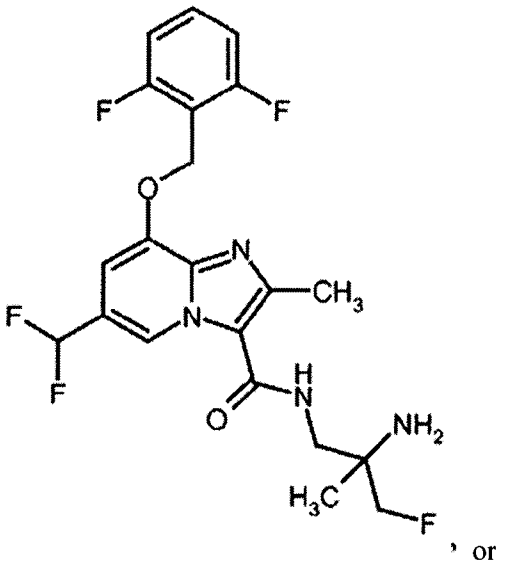
ent-N-(2-amino-3-fluoro-2-methylpropyl)-2,6-dimethyl-8-[(2,3,6-triflurobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(difluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)

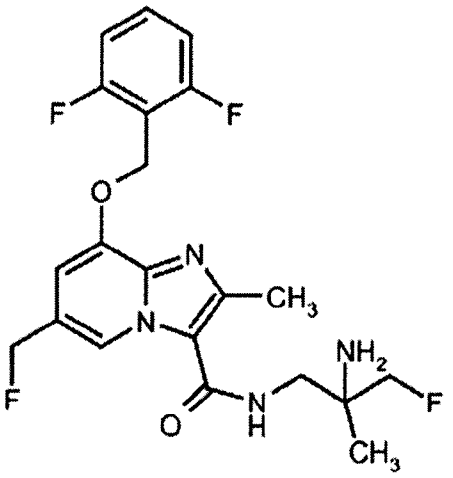


ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(difluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



, or

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(fluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide



Compounds according to the invention are the compounds of the formula (I) and their salts, solvates and solvates of the salts, the compounds included in the formula (I) of the formulae mentioned in the following and their salts, solvates and solvates of the salts, and the compounds included in the formula (I) and mentioned in the following as embodiment examples and their salts, solvates and solvates of the salts, where the compounds included in the formula (I) and mentioned in the following are not already salts, solvates and solvates of the salts.

Preferred salts in the context of the present invention are physiologically acceptable salts of the compounds according to the invention. Salts which are not themselves suitable for pharmaceutical uses but can be used, for example, for isolation or purification of the compounds according to the invention are also included.

Physiologically acceptable salts of the compounds according to the invention include acid addition salts of mineral acids, carboxylic acids and sulphonic acids, e.g. salts of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, ethanesulphonic acid, toluenesulphonic acid, benzenesulphonic acid, naphthalenedisulphonic acid, formic acid, acetic acid, trifluoroacetic acid, propionic acid, lactic acid, tartaric acid, malic acid, citric acid, fumaric acid, maleic acid, and benzoic acid.

Physiologically acceptable salts of the compounds according to the invention also include salts of conventional bases, such as, by way of example and preferably, alkali metal salts (e.g. sodium and potassium salts), alkaline earth metal salts (e.g. calcium and magnesium salts) and ammonium salts derived from ammonia or organic amines having 1 to 16 carbon atoms, such as, by way of example and preferably, ethylamine, diethylamine, triethylamine, ethyldiisopropylamine, monoethanol-

amine, diethanolamine, triethanolamine, dicyclohexylamine, dimethylaminoethanol, procaine, dibenzylamine, N-methylmorpholine, arginine, lysine, ethylenediamine and N-methylpiperidine.

Solvates in the context of the invention are designated as those forms of the compounds according to the invention which form a complex in the solid or liquid state by coordination with solvent molecules. Hydrates are a specific form of solvates, in which the coordination takes place with water. Hydrates are preferred solvates in the context of the present invention.

The compounds according to the invention can exist in different stereoisomeric forms depending on their structure, i.e. in the form of configuration isomers or optionally also as conformation isomers (enantiomers and/or diastereomers, including those in the case of atropisomers). The present invention therefore includes the enantiomers and diastereomers and their particular mixtures. The stereoisomerically uniform constituents can be isolated from such mixtures of enantiomers and/or diastereomers in a known manner; chromatography processes are preferably used for this, in particular HPLC chromatography on an achiral or chiral phase.

Where the compounds according to the invention can occur in tautomeric forms, the present invention includes all the tautomeric forms.

The present invention also encompasses all suitable isotopic variants of the compounds according to the invention. An isotopic variant of a compound according to the invention is understood here to mean a compound in which at least one atom within the compound according to the invention has been exchanged for another atom of the same atomic number, but with a different atomic mass than the atomic mass which usually or predominantly occurs in nature. Examples of isotopes which can be incorporated into a compound according to the invention are those of hydrogen, carbon, nitrogen, oxygen, phosphorus, sulphur, fluorine, chlorine, bromine and iodine, such as ^{2}H (deuterium), ^{3}H (tritium), ^{13}C, ^{14}C, ^{15}N, ^{17}O, ^{18}O, ^{32}P, ^{33}P, ^{33}S, ^{34}S, ^{35}S, ^{36}S, ^{18}F, ^{36}Cl, ^{82}Br, ^{123}I, ^{124}I, ^{129}I and ^{131}I. Particular isotopic variants of a compound according to the invention, especially those in which one or more radioactive isotopes have been incorporated, may be beneficial, for example, for the examination of the mechanism of action or of the active compound distribution in the body; due to comparatively easy preparability and detectability, especially compounds labelled with ^{3}H or ^{14}C isotopes are suitable for this purpose. In addition, the incorporation of isotopes, for example of deuterium, can lead to particular therapeutic benefits as a consequence of greater metabolic stability of the compound, for example an extension of the half-life in the body or a reduction in the active dose required; such modifications of the compounds according to the invention may therefore in some cases also constitute a preferred embodiment of the present invention. Isotopic variants of the compounds according to the invention can be prepared by processes known to those skilled in the art, for example by the methods described below and the methods described in the working examples, by using corresponding isotopic modifications of the particular reagents and/or

starting compounds therein.

The present invention moreover also includes prodrugs of the compounds according to the invention. The term "prodrugs" here designates compounds which themselves can be biologically active or inactive, but are converted (for example metabolically or hydrolytically) into compounds according to the invention during their dwell time in the body.

In the context of the present invention, the substituents have the following meaning, unless specified otherwise:

Alkyl in the context of the invention represents a straight-chain or branched alkyl radical having the number of carbon atoms stated in each case. The following may be mentioned by way of example and by way of preference: methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, 1-methylpropyl, tert-butyl, n-pentyl, isopentyl, 1-ethylpropyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, n-hexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, 3,3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl.

Cycloalkyl or carbocycle in the context of the invention represents a monocyclic saturated alkyl radical having the number of ring carbon atoms stated in each case. The following may be mentioned by way of example and by way of preference: cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

Alkenyl in the context of the invention represents a straight-chain or branched alkenyl radical having 2 to 6 carbon atoms and one or two double bonds. Preference is given to a straight-chain or branched alkenyl radical having 2 to 4 carbon atoms and one double bond. The following may be mentioned by way of example and by way of preference: vinyl, allyl, isopropenyl and n-but-2-en-1-yl.

Alkynyl in the context of the invention represents a straight-chain or branched alkynyl radical having 2 to 6 carbon atoms and one triple bond. The following may be mentioned by way of example and by way of preference: ethynyl, n-prop-1-yn-1-yl, n-prop-2-yn-1-yl, n-but-2-yn-1-yl and n-but-3-yn-1-yl.

Alkanediyl in the context of the invention represents a straight-chain or branched divalent alkyl radical having 1 to 4 carbon atoms. The following may be mentioned by way of example and by way of preference: methylene, 1,2-ethylene, ethane-1,1-diyl, 1,3-propylene, propane-1,1-diyl, propane-1,2-diyl, propane-2,2-diyl, 1,4-butylene, butane-1,2-diyl, butane-1,3-diyl and butane-2,3-diyl.

Alkoxy in the context of the invention represents a straight-chain or branched alkoxy radical having 1 to 4 carbon atoms. The following may be mentioned by way of example and by way of preference: methoxy, ethoxy, n-propoxy, isopropoxy, 1-methylpropoxy, n-butoxy, isobutoxy and tert-butoxy.

Alkoxycarbonyl in the context of the invention represents a straight-chain or branched alkoxy radical having 1 to 4 carbon atoms and a carbonyl group attached at the oxygen atom. The following may be mentioned by way of example and by way of preference: methoxycarbonyl, ethoxycarbonyl, n-propoxycarbonyl, isopropoxycarbonyl and tert-butoxycarbonyl.

Alkylsulphonyl in the context of the invention represents a straight-chain or branched alkyl radical which has 1 to 4 carbon atoms and is attached via a sulphonyl group. The following may be mentioned by way of example and by way of preference: methylsulphonyl, ethylsulphonyl, n-propylsulphonyl, isopropylsulphonyl, n-butylsulphonyl and tert-butylsulphonyl.

A 4- to 7-membered heterocycle in the context of the invention represents a monocyclic saturated heterocycle which has a total of 4 to 7 ring atoms, which contains one or two ring heteroatoms from the group consisting of N, O, S, SO and SO_2 and which is attached via a ring carbon atom or, if appropriate, a ring nitrogen atom. The following may be mentioned by way of example: azetidinyl, oxetanyl, pyrrolidinyl, pyrazolidinyl, tetrahydrofuranyl, thiolanyl, piperidinyl, piperazinyl, tetrahydropyranyl, tetrahydrothiopyranyl, morpholinyl, thiomorpholinyl, hexahydroazepinyl and hexahydro-1,4-diazepinyl. Preference is given to azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl, piperazinyl, tetrahydropyranyl and morpholinyl.

A 4- to 7-membered azaheterocycle in the context of the invention represents a monocyclic saturated heterocycle which has a total of 4 to 7 ring atoms, which contains one nitrogen atom and which may additionally contain a further ring heteroatom from the group consisting of N, O, S, SO and SO_2 and is attached via a ring nitrogen atom. The following may be mentioned by way of example: azetidinyl, pyrrolidinyl, pyrazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,1-dioxothiomorpholinyl, hexahydroazepinyl and hexahydro-1,4-diazepinyl.

5- to 9-membered azaheterocyclyl in the context of the invention represents a monocyclic or bicyclic saturated or partially unsaturated heterocycle which has a total of 5 to 9 ring atoms, which contains a nitrogen atom and which may additionally contain one or two further ring heteroatoms from the group consisting of N, O, S, SO and SO_2 and is attached via a ring carbon atom. The following may be mentioned by way of example: pyrrolidinyl, pyrazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,1-dioxothiomorpholinyl, hexahydroazepinyl, hexahydro-1,4-diazepinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl,

8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl.

Heteroaryl in the context of the invention represents a mono- or optionally bicyclic aromatic heterocycle (heteroaromatic) having a total of 5 to 10 ring atoms which contains up to three identical or different ring heteroatoms from the group consisting of N, O and/or S and is attached via a ring carbon atom or optionally via a ring nitrogen atom. The following may be mentioned by way of example: furyl, pyrrolyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, benzotriazolyl, indolyl, indazolyl, quinolinyl, isoquinolinyl, naphthyridinyl, quinazolinyl, quinoxalinyl, phthalazinyl, pyrazolo[3,4-b]pyridinyl. Heteroaryl in the context of the invention preferably represents a monocyclic aromatic heterocycle (heteroaromatic) which has a total of 5 or 6 ring atoms, which contains up to three identical or different ring heteroatoms from the group consisting of N, O and S and is attached via a ring carbon atom or, if appropriate, a ring nitrogen atom. The following may be mentioned by way of example and by way of preference: furyl, pyrrolyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl and triazinyl.

Halogen in the context of the invention includes fluorine, chlorine, bromine and iodine. Preference is given to chlorine or fluorine.

In the formula of the group which may represent R^3 or R^1, the end point of the line marked by a * or # label does not represent a carbon atom or a CH_2 group but forms part of the bond to the atom which is designated in each case and to which R^3 and R^1, respectively, are attached.

If radicals in the compounds according to the invention are substituted, the radicals may, unless specified otherwise, be mono- or polysubstituted. In the context of the present invention, all radicals which occur more than once are defined independently of one another. Substitution by one, two or three identical or different substituents is preferred.

In the context of the present invention, the term "treatment" or "treat" includes the inhibition, delay, arrest, amelioration, attenuation, limitation, reduction, suppression, reversal or cure of a disease, a condition, a disorder, an injury and a health impairment, of the development, course or the progression of such states and/or the symptoms of such states. Here, the term "therapy" is understood to be synonymous with the term "treatment".

In the context of the present invention, the terms "prevention", "prophylaxis" or "precaution" are used synonymously and refer to the avoidance or reduction of the risk to get, to contract, to suffer

from or to have a disease, a condition, a disorder, an injury or a health impairment, a development or a progression of such states and/or the symptoms of such states.

The treatment or the prevention of a disease, a condition, a disorder, an injury or a health impairment may take place partially or completely.

In the context of the present invention, preference is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

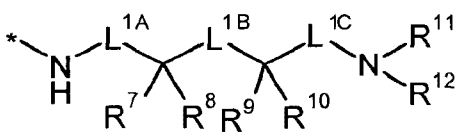
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methoxy, difluoromethyl, trifluoromethyl and methyl,

R^2 represents hydrogen, trifluoromethyl, $(C_1$-$C_4)$-alkyl or cyclopropyl,

R^3 represents a group of the formula



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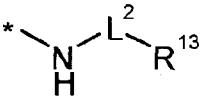


where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1,2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, $(C_1$-$C_4)$-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, $(C_1$-$C_4)$-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where $(C_3$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl and trifluoromethyl,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, 1,1,2,2-tetrafluoroethyl, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl and trifluoromethyl,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and with the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen or (C_1-C_3)-alkyl,

where (C_1-C_3)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, methoxy and ethoxy,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, cyclopropyl, cyclobutyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl or 1,1-dioxothiomorpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl and 1,1-dioxothiomorpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl, azetidinyl, pyrrolidinyl and piperidinyl,

and

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo-[4.1.0]heptanyl and quinuclidinyl attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, bromine, cyano, methyl, ethyl or cyclopropyl,

R^6 represents hydrogen or fluorine,

and to *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts thereof.

In the context of the present invention, preference is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

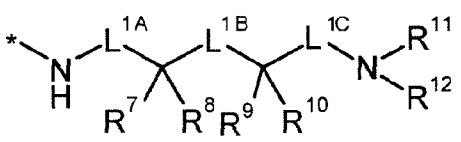
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

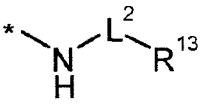
where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, difluoromethyl, trifluoromethyl and methyl,

R^2 represents $(C_1$-$C_3)$-alkyl, trifluoromethyl or cyclopropyl,

R^3 represents a group of the formula



or



where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, $(C_1$-$C_4)$-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where $(C_3$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano and trifluoromethyl,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano and trifluoromethyl,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and with the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen or $(C_1$-$C_3)$-alkyl,

where $(C_1$-$C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl or cyclobutyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl or morpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl and morpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl and cyclobutyl,

and

L^2 represents a bond or methylene,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-aza-bicyclo[4.1.0]heptanyl and quinuclidinyl attached via a ring carbon atom,

or

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo-[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, methyl, ethyl or cyclopropyl,

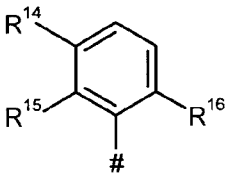
R^6 represents hydrogen,

and to *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts thereof.

In the context of the present invention, particular preference is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



where

represents the point of attachment to A,

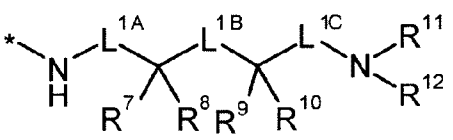
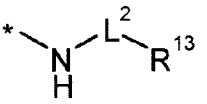
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine or chlorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula

 or 

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and chlorine,

R^8 represents hydrogen, methyl or ethyl,

R^9 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, cyclopropyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and chlorine,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl ring,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl or cyclohexyl ring,

with the proviso that not more than one of the radical pairs R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

and

L^2 represents a bond,

R^{13} represents piperidin-2-yl, piperidin-3-yl, piperidin-4-yl or 1,2,3,4-tetrahydroquinolin-4-yl,

where piperidin-2-yl, piperidin-3-yl and piperidin-4-yl may be substituted by 1 to 5 substituents independently of one another selected from trifluoromethyl and methyl,

and

where 1,2,3,4-tetrahydroquinolin-4-yl may be substituted by fluorine or trifluoromethyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine or methyl,

R^6 represents hydrogen,

and to *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts thereof.

In the context of the present invention, preference is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents phenyl,

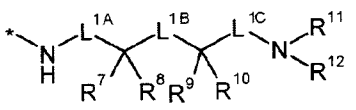
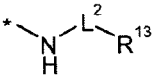
where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl,

and

where phenyl is substituted by 1 to 2 substituents selected from the group consisting of $(C_3$-$C_6)$-cycloalkyl, $(C_1$-$C_4)$-alkoxy, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula

 or 

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

L^{1B} represents a bond or $(C_1$-$C_4)$-alkanediyl,

L^{1C} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

R^7 represents hydrogen, $(C_1$-$C_6)$-alkyl, $(C_2$-$C_6)$-alkenyl, $(C_2$-$C_6)$-alkynyl, $(C_3$-$C_7)$-cycloalkyl, cyano, 5- or 10-membered heteroaryl, naphthyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, $(C_1$-$C_4)$-alkoxy, $(C_1$-$C_4)$-sulphanyl, $(C_1$-$C_4)$-alkoxycarbonyl, $(C_1$-$C_4)$-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, nitro, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, -NH(CO)CH_3, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkenyl, (C_1-C_4)-alkylsulphonyl, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where the phenyl may be substituted on 2 adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- to 10-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy,

(C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl, (C_1-C_4)-alkylsulphonyl, 5- or 6-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where 5- or 6-membered heteroaryl may be benzo-fused or substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by (C_1-C_4)-alkyl or trifluoromethyl,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkylsulphonyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where the phenyl may be substituted on 2 adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of on another selected from the group consisting of fluorine, benzyl and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms which they are attached and the group L^{1B} form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_1-C_4)-alkyl, fluorine, hydroxy and (C_1-C_4)-alkoxy,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms a carbo- or heterocycle,

R^{11} represents hydrogen or (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the

group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy, (C_1-C_4)-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or (C_1-C_4)-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents selected from the group consisting of halogen, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy and trifluoromethyl,

or

represents adamantyl,

R^4 represents hydrogen,

R^5 represents hydrogen, halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, (C_2-C_4)-alkynyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2 or $CH(CH_3)$,

R^1 represents phenyl,

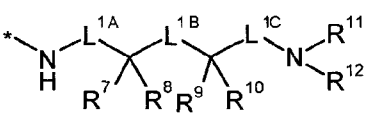
where phenyl may be substituted by 1 to 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl,

and

where phenyl is substituted by a substituent selected from the group consisting of (C_3-C_6)-cycloalkyl, (C_1-C_2)-alkoxy and trifluoromethoxy,

R^2 represents hydrogen, trifluoromethyl, (C_1-C_3)-alkyl or cyclopropyl,

R^3 represents a group of the formula



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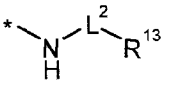


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1,2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, -NH(CO)CH_3, methyl, ethenyl, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, 1,1,2,2-tetrafluoroethyl, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, 5-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where 5-membered heteroaryl may be benzo-fused or substituted by a 5-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by $(C_1$-$C_4)$-alkyl or trifluoromethyl,

where $(C_3$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl, trifluoromethoxy, difluoromethoxy, $(C_1$-$C_4)$-alkoxy and trifluoromethyl,

where $(C_1$-$C_4)$-alkoxy is substituted by hydroxy,

R^{10} represnts hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the abovementioned carbo- or heterocycles,

R^{11} represents hydrogen or (C_1-C_3)-alkyl,

where (C_1-C_3)-alkyl may be substituted by 1 or 2 substituents independnetly of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, methoxy and ethoxy,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, cyclopropyl, cyclobutyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl or 1,1-dioxothiomorpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl and 1,1-dioxothiomorpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl, azetidinyl, pyrrolidinyl and piperidinyl,

and

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabi-

cyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently from one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, bromine, cyano, methyl, ethyl, monofluoromethyl, ethynyl or cyclopropyl,

R^6 represents hydrogen or fluorine,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents phenyl,

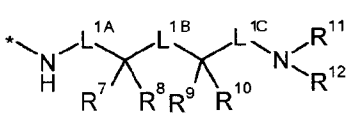
where phenyl is substituted by 1 to 2 fluorine,

and

where phenyl is substituted by a substituent selected from the group consisting of cyclopropyl and methoxy,

R^2 represents trifluoromethyl, methyl, ethyl or cyclopropyl,

R^3 represents a group of the formula



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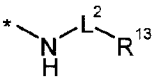


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, $(C_1$-$C_4)$-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where $(C_3$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, ethenyl, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, trifluoromethoxy, difluoromethoxy, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the abovementioned carbo- or heterocycles,

R^{11} represents hydrogen or $(C_1$-$C_3)$-alkyl,

where $(C_1$-$C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl or cyclobutyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl or morpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl and morpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl and cyclobutyl,

and

L^2 represents a bond or methylene,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-aza-bicyclo[4.1.0]heptanyl or quinuclidinyl, attached via a ring carbon atom,

in which pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-

aza-bicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, methyl, ethyl, monofluoromethyl, ethynyl or cyclopropyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents phenyl,

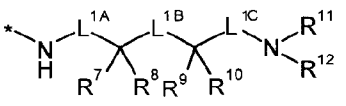
where phenyl is substituted by 1 to 2 fluorine,

and

where phenyl is substituted by a substituent selected from the group consisting of cyclopropyl and methoxy,

R^2 represents methyl,

R^3 represents a group of the formula



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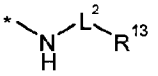


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, difluoromethoxy, trifluoromethoxy, ethenyl, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, cyclopropyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethoxy, difluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl ring,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl or cyclohexyl ring,

with the proviso that not more than one of the radical pairs R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the abovementioned carbo- or heterocycles,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

and

L^2 represents a bond,

R^{13} represents piperidin-2-yl, piperidin-3-yl, piperidin-4-yl or 1,2,3,4-tetrahydroquinolin-4-yl,

where piperidin-2-yl, piperidin-3-yl and piperidin-4-yl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of trifluoromethyl and methyl,

and

where 1,2,3,4-tetrahydroquinolin-4-yl may be substituted by fluorine or trifluoromethyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, monofluoromethyl, ethynyl or methyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

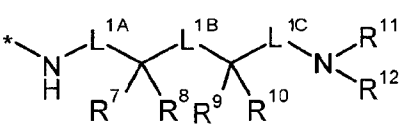
where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and $(C_1$-$C_4)$-alkyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula



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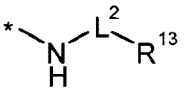


where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

L^{1B} represents a bond or $(C_1$-$C_4)$-alkanediyl,

L^{1C} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

R^7 represents hydrogen, $(C_1$-$C_6)$-alkyl, $(C_2$-$C_6)$-alkenyl, $(C_2$-$C_6)$-alkynyl, $(C_3$-$C_7)$-cycloalkyl, cyano, 5- to 10-membered heteroaryl, naphthyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, $(C_1$-$C_4)$-alkoxy, $(C_1$-$C_4)$-alkoxy-carbonyl, $(C_1$-$C_4)$-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or $(C_1$-$C_4)$-alkoxy substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, nitro, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, -NH(CO)CH_3, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkenyl, (C_1-C_4)-alkylsulphonyl, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

in which 2 adjacent carbon atoms of the phenyl may be substituted by a difluoromethylenedioxy bridge,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents hydrogen, cyano, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- to 10-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, cyano, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxy-carbonyl, (C_1-C_4)-alkylsulphonyl, 5- or 6-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where 5- or 6-membered heteroaryl may be benzo-fused or substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by (C_1-C_4)-alkyl or trifluoromethyl,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkylsulphonyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where the phenyl may be substituted on two adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of $(C_1$-$C_4)$-alkyl, fluorine, hydroxy and $(C_1$-$C_4)$-alkoxy,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms a carbo- or heterocycle,

R^{11} represents hydrogen or $(C_1$-$C_4)$-alkyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

R^{12} represents hydrogen, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, phenyl or benzyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy, $(C_1$-$C_4)$-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or $(C_1$-$C_4)$-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents selected from the group consisting of halogen, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy and trifluoromethyl,

or

represents adamantyl,

R^4 represents hydrogen,

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_2$-$C_4)$-alkenyl, $(C_2$-$C_4)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy, trifluoromethoxy, $(C_1$-$C_4)$-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

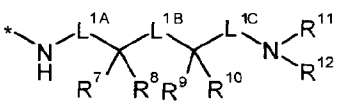
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methoxy, ethoxy, difluoromethyl, trifluoromethyl, (C_3-C_6)-cycloalkyl and methyl,

R^2 represents hydrogen, trifluoromethyl, (C_1-C_3)-alkyl or cyclopropyl,

R^3 represents a group of the formula



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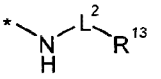


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1,2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, methyl, ethenyl, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, 1,1,2,2-tetrafluoroethyl, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, 5-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where 5-membered heteroaryl may be benzo-fused or substituted by a 5-membered heteroaryl,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the abovementioned carbo- or heterocycles,

R^{11} represents hydrogen or (C_1-C_3)-alkyl,

where (C_1-C_3)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, methoxy and ethoxy,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, cyclopropyl, cyclobutyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl or 1,1-dioxothiomorpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl and 1,1-dioxothiomorpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl, azetidinyl, pyrrolidinyl and piperidinyl,

and

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_2$-$C_4)$-alkenyl, $(C_2$-$C_4)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy, trifluoromethoxy, $(C_1$-$C_4)$-alkoxy, 5- to 6-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen or fluorine,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

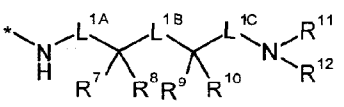
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyclopropyl, methoxy and methyl,

R^2 represents trifluoromethyl, methyl, ethyl or cyclopropyl,

R^3 represents a group of the formula



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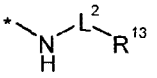


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, ethenyl, difluoromethoxy, trifluoromethoxy, -NH(CO)CH_3, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents

independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, difluoromethoxy, trifluoromethoxy, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen or $(C_1\text{-}C_3)$-alkyl,

where $(C_1\text{-}C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

R^{12} represents hydrogen, $(C_1\text{-}C_4)$-alkyl, cyclopropyl or cyclobutyl,

where $(C_1\text{-}C_4)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl or morpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl and morpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl and cyclobutyl,

and

L^2 represents a bond or methylene,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-

azabicyclo[3.3.1]nonanyl, 3-aza-bicyclo[4.1.0]heptanyl or quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, cyclopropyl, ethynyl, methoxy, morpholino,

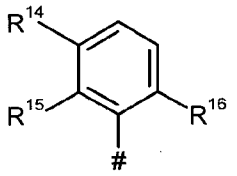
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



where

represents the point of attachment to A,

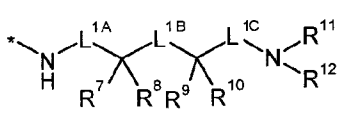
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine, methoxy, cyclopropyl or chlorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula



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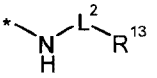


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen, trifluoromethyl, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_6)$-cycloalkyl or phenyl,

where $(C_1\text{-}C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1\text{-}C_4)$-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, ethenyl, difluoromethoxy, trifluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

R^9 represents hydrogen, cyano, trifluoromethyl, $(C_1\text{-}C_6)$-alkyl, cyclopropyl or phenyl,

where $(C_1\text{-}C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, $(C_1\text{-}C_4)$-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, difluoromethoxy, trifluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl ring,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl or cyclohexyl ring,

with the proviso that not more than one of the radical pairs R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

and

L^2 represents a bond,

R^{13} represents piperidin-2-yl, piperidin-3-yl, piperidin-4-yl or 1,2,3,4-tetrahydroquinolin-4-yl,

where piperidin-2-yl, piperidin-3-yl and piperidin-4-yl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of trifluoromethyl and methyl,

and

where 1,2,3,4-tetrahydroquinolin-4-yl may be substituted by fluorine or trifluoromethyl,

R^4 represents hydrogen,

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, cyclopropyl, ethynyl, methoxy, morpholino,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

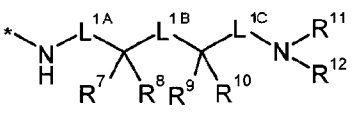
where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and $(C_1$-$C_4)$-alkyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula



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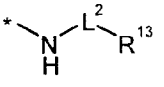


where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

L^{1B} represents a bond or (C_1-C_4)-alkanediyl,

L^{1C} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

R^7 represents (C_1-C_6)-alkyl, (C_2-C_6)-alkynyl, cyano or phenyl,

where (C_1-C_6)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy and phenoxy,

where phenoxy may be substituted by 1 to 3 halogen substituents,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, nitro, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, $-NH(CO)CH_3$ and (C_1-C_4)-alkenyl,

where (C_1-C_4)-alkoxy is substituted by hydroxy,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

R^9 R^9 represents hydrogen, cyano, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- to 10-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, cyano, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxy-

carbonyl, (C_1-C_4)-alkylsulphonyl, 5- or 6-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where 5- or 6-membered heteroaryl may be benzo-fused or substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by (C_1-C_4)-alkyl or trifluoromethyl,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkylsulphonyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where the phenyl may be substituted on two adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

R^{11} represents hydrogen or (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy, (C_1-C_4)-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or (C_1-C_4)-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the

group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents selected from the group consisting of halogen, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy and trifluoromethyl,

or

represents adamantyl,

R^4 represents hydrogen,

R^5 represents hydrogen, halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_2-C_4)-alkenyl, (C_2-C_4)-alkynyl, (C_3-C_6)-cycloalkyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents (C_4-C_6)-alkyl, (C_4-C_6)-cycloalkyl or phenyl,

where (C_4-C_6)-alkyl may be substituted up to six times by fluorine,

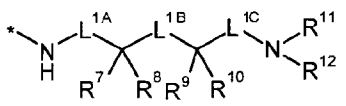
where (C_4-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methoxy, ethoxy, difluoromethyl, trifluoromethyl, (C_3-C_6)-cycloalkyl and methyl,

R^2 represents hydrogen, trifluoromethyl, (C_1-C_3)-alkyl and cyclopropyl,

R^3 represents a group of the formula



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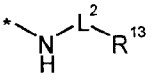


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1,2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents (C_1-C_6)-alkyl, (C_2-C_6)-alkynyl, cyano or phenyl,

where (C_1-C_6)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy and phenoxy,

where phenoxy may be substituted by 1 to 3 fluorine,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, nitro, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, $-NH(CO)CH_3$ and (C_1-C_4)-alkenyl,

where (C_1-C_4)-alkoxy is substituted by hydroxy,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

R^9 represents hydrogen, cyano, 1,1,2,2-tetrafluoroethyl, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, 5-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where 5-membered heteroaryl may be benzo-fused or substituted by a 5-membered heteroaryl,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^{11} represents hydrogen or (C_1-C_3)-alkyl,

where (C_1-C_3)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, methoxy and ethoxy,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, cyclopropyl, cyclobutyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl or 1,1-dioxothiomorpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl and 1,1-dioxothiomorpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl, azetidinyl, pyrrolidinyl and piperidinyl,

and

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, bromine, cyano, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

R^6 represents hydrogen or fluorine,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

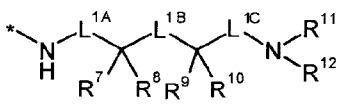
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyclopropyl, methoxy and methyl,

R^2 represents trifluoromethyl, methyl, ethyl or cyclopropyl,

R^3 represents a group of the formula



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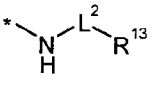


where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents (C_1-C_4)-alkyl, cyano or phenyl,

where (C_1-C_4)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and phenoxy,

where phenoxy may be substituted by 1 to 3 fluorine substituents,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, difluoromethoxy, trifluoromethoxy, ethoxy, -NH(CO)CH_3 and ethenyl,

where ethoxy is substituted by hydroxy,

R^8 represents hydrogen,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently from one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, difluoromethoxy, trifluoromethoxy, ethoxy, cyano and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^{11} represents hydrogen or (C_1-C_3)-alkyl,

where (C_1-C_3)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, cyclopropyl or cyclobutyl,

where (C_1-C_4)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl or morpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl and morpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl and cyclobutyl,

and

L^2 represents a bond or methylene,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl or quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

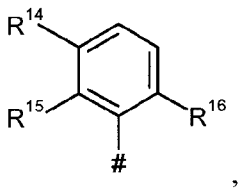
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



,

where

represents the point of attachment to A,

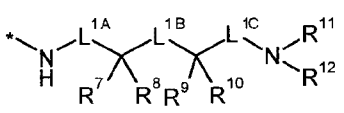
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine, methoxy, cyclopropyl or chlorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula



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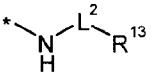


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents (C_1-C_4)-alkyl, cyano or phenyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

and

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy, ethoxy, -NH(CO)CH_3 or ethenyl,

where ethoxy is substituted by hydroxy,

R^8 represents hydrogen,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, cyclopropyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, difluoromethoxy, trifluoromethoxy, ethoxy, and chlorine,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl ring,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

and

L^2 represents a bond,

R^{13} represents piperidin-2-yl, piperidin-3-yl, piperidin-4-yl or 1,2,3,4-tetrahydroquinolin-4-yl,

where piperidin-2-yl, piperidin-3-yl and piperidin-4-yl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of trifluoromethyl and methyl,

and

where 1,2,3,4-tetrahydroquinolin-4-yl may be substituted by fluorine or trifluoromethyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, monofluoromethyl, ethynyl or methyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

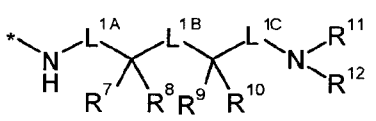
where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and $(C_1$-$C_4)$-alkyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula



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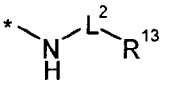


where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

L^{1B} represents a bond or $(C_1$-$C_4)$-alkanediyl,

L^{1C} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

R^7 represents hydrogen, $(C_1$-$C_6)$-alkyl, $(C_2$-$C_6)$-alkenyl, $(C_2$-$C_6)$-alkynyl, $(C_3$-$C_7)$-cycloalkyl, cyano, 5- to 10-membered heteroaryl, naphthyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, $(C_1$-$C_4)$-alkoxy, $(C_1$-$C_4)$-alkoxycarbonyl, $(C_1$-$C_4)$-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or $(C_1$-$C_4)$-alkoxy substituents,

where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl and $(C_1$-$C_4)$-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, nitro, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-

cycloalkyl, (C_1-C_4)-alkenyl, (C_1-C_4)-alkylsulphonyl, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

in which 2 adjacent carbon atoms of the phenyl may be substituted by a difluoromethylenedioxy bridge,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents (C_1-C_6)-alkyl, cyano or phenyl,

where (C_1-C_6)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, 5- or 6-membered heteroaryl, phenoxy and benzyloxy,

where phenoxy is substituted by 1 to 3 halogen substituents,

where benzyloxy may be substituted by 1 to 3 halogen substituents,

where 5- or 6-membered heteroaryl is substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl for its part may be substituted by (C_1-C_4)-alkyl,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, difluoromethoxy, trifluoromethoxy and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy is substituted by hydroxy,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

R^{11} represents hydrogen or (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy, (C_1-C_4)-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or (C_1-C_4)-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the

group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents selected from the group consisting of halogen, (C_1-C_4)-alkyl, (C_1-C_4)-alkoxy and trifluoromethyl,

or

represents adamantyl,

R^4 represents hydrogen,

R^5 represents hydrogen, halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_2-C_4)-alkenyl, (C_2-C_4)-alkynyl, (C_3-C_6)-cycloalkyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents (C_4-C_6)-alkyl, (C_4-C_6)-cycloalkyl or phenyl,

where (C_4-C_6)-alkyl may be substituted up to six times by fluorine,

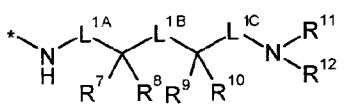
where (C_4-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methoxy, ethoxy, difluoromethyl, trifluoromethyl, (C_3-C_6)-cycloalkyl and methyl,

R^2 represents hydrogen, trifluoromethyl, $(C_1$-$C_3)$-alkyl or cyclopropyl,

R^3 represents a group of the formula



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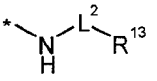


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1-2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, $(C_1$-$C_4)$-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where $(C_3$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl, ethenyl, nitro,

difluoromethoxy, trifluoromethoxy, -NH(CO)CH_3, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently from one another selected from the group consisting of fluorine and methyl,

R^9 represents (C_1-C_4)-alkyl, cyano or phenyl,

where (C_1-C_4)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, 5-membered heteroaryl and benzyloxy,

where benzyloxy may be substituted by 1 to 3 halogen substituents,

where 5-membered heteroaryl is substituted by a 5-membered heteroaryl,

where 5-membered heteroaryl for its part may be substituted by (C_1-C_4)-alkyl,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, difluoromethoxy, trifluoromethoxy and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy is substituted by hydroxy,

R^{10} represents hydrogen or methyl,

R^{11} represents hydrogen or (C_1-C_3)-alkyl,

where $(C_1$-$C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, methoxy and ethoxy,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, cyclobutyl, phenyl or benzyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl or 1,1-dioxothiomorpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl and 1,1-dioxothiomorpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl, azetidinyl, pyrrolidinyl and piperidinyl,

and

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-aza-

bicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, bromine, cyano, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

R^6 represents hydrogen or fluorine,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

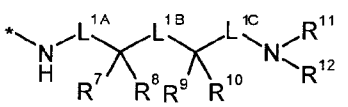
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyclopropyl, methoxy and methyl,

R^2 represents trifluoromethyl, methyl, ethyl or cyclopropyl,

R^3 represents a group of the formula



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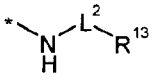


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, difluoromethoxy, trifluoromethoxy, -$NH(CO)CH_3$, ethenyl, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents ethyl, propyl, cyano or phenyl,

where ethyl and propyl are substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and benzyloxy,

where benzyloxy may be substituted by 1 to 3 halogen substituents,

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy or ethoxy,

where ethoxy is substituted by hydroxy,

R^{10} represents hydrogen or methyl,

R^{11} represents hydrogen or $(C_1$-$C_3)$-alkyl,

where $(C_1$-$C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl or cyclobutyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl or morpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl and morpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl and cyclobutyl,

and

L^2 represents a bond or methylene,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo-[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

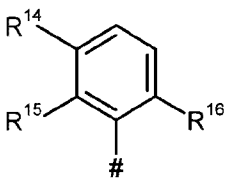
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



,

where

represents the point of attachment to A,

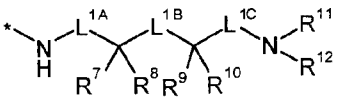
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine, methoxy, cyclopropyl or chlorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula



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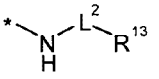


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, difluoromethoxy, trifluoromethoxy, ethenyl, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

R^9 represents ethyl, cyano or phenyl,

where ethyl is substituted up to five times by fluorine,

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy or ethoxy,

where ethoxy is substituted by hydroxy,

R^{10} represents hydrogen or methyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

and

L^2 represents a bond,

R^{13} represents piperidin-2-yl, piperidin-3-yl, piperidin-4-yl or 1,2,3,4-tetrahydroquinolin-4-yl,

where piperidin-2-yl, piperidin-3-yl and piperidin-4-yl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of trifluoromethyl and methyl,

and

where 1,2,3,4-tetrahydroquinolin-4-yl may be substituted by fluorine or trifluoromethyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, monofluoromethyl, methoxy, ethynyl or methyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

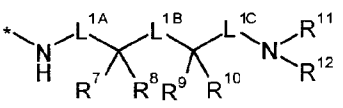
where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and $(C_1$-$C_4)$-alkyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula



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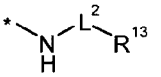


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl, hydroxy and $(C_1$-$C_4)$-alkoxy,

L^{1B} represents a bond or $(C_1$-$C_4)$-alkanediyl,

L^{1C} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where $(C_1$-$C_4)$-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of

fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

R^7 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, cyano, 5- to 10-membered heteroaryl, naphthyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl, (C_1-C_4)-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, nitro, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkenyl, (C_1-C_4)-alkylsulphonyl, (C_1-C_4)-alkoxy-carbonyl and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where phenyl may be substituted on 2 adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents hydrogen, cyano, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- to 10-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, cyano, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl, (C_1-C_4)-alkylsulphonyl, 5- or 6-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where 5- or 6-membered heteroaryl may be benzo-fused or substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by (C_1-C_4)-alkyl or trifluoromethyl,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkylsulphonyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where phenyl may be substituted on 2 adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_1-C_4)-alkyl, fluorine, hydroxy and (C_1-C_4)-alkoxy,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms a carbo- or heterocycle,

R^{11} represents (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle is substituted by 1 or 2 substituents independently of one another selected from the group consisting of $(C_3$-$C_7)$-cycloalkyl and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or $(C_1$-$C_4)$-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_7)$-cycloalkyl and benzyl,

and

where 5- to 9-membered azaheterocyclyl may be fused to a phenyl ring which for its part may be substituted by 1 or 2 substituents selected from the group consisting of halogen, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy and trifluoromethyl,

or

represents adamantyl,

R^4 represents hydrogen,

R^5 represents hydrogen, halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_2$-$C_4)$-alkenyl, $(C_2$-$C_4)$-alkynyl, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy, trifluoromethoxy, $(C_1$-$C_4)$-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

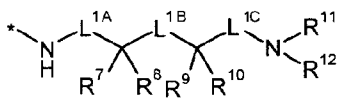
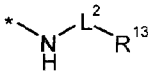
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methoxy, ethoxy, difluoromethyl, trifluoromethyl, $(C_3$-$C_6)$-cycloalkyl and methyl,

R^2 represents hydrogen, trifluoromethyl, $(C_1$-$C_3)$-alkyl and cyclopropyl,

R^3 represents a group of the formula

 or  ,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1,2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, methyl, ethenyl, difluoromethoxy, trifluoromethoxy, -$NH(CO)CH_3$, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and

piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, 1,1,2,2-tetrafluoroethyl, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, 5-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where 5-membered heteroaryl may be benzo-fused or substituted by a 5-membered heteroaryl,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and

piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent methyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously represents one of the carbo- or heterocycles mentioned above,

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{11} represents methyl and ethyl,

where methyl and ethyl are substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and methoxy,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, phenyl or benzyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 6-membered azaheterocycle,

where the 4- to 6-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_3-C_6)-cycloalkyl and 4- to 6-membered heterocyclyl,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, bromine, cyano, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

R^6 represents hydrogen or fluorine,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents (C_4-C_6)-alkyl, (C_4-C_6)-cycloalkyl or phenyl,

where (C_4-C_6)-alkyl may be substituted up to six times by fluorine,

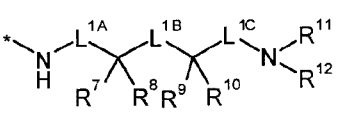
where (C_4-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyclopropyl, methoxy and methyl,

R^2 represents trifluoromethyl, methyl, ethyl and cyclopropyl,

R^3 represents a group of the formula



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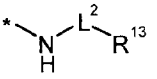


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, ethenyl, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, difluoromethoxy, trifluoromethoxy, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents methyl or ethyl,

where methyl and ethyl are substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and methoxy,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, $(C_3$-$C_6)$-cycloalkyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 6-membered azaheterocycle,

where the 4- to 6-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_3-C_6)-cycloalkyl and 4- to 6-membered heterocyclyl,

and

L^2 represents a bond or methylene,

R^{13} represents pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, indolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl, attached via a ring carbon atom,

where pyrrolidinyl, piperidinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 8-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, 3-azabicyclo[4.1.0]heptanyl and quinuclidinyl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

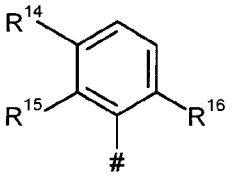
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



where

\# represents the point of attachment to A,

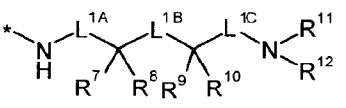
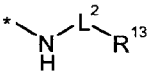
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine, methoxy, cyclopropyl or chlorine,

with the proviso that at two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula

 or  ,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, ethenyl, difluoromethoxy, trifluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, cyclopropyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, difluoromethoxy, trifluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl ring,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

R^{11} represents methyl or ethyl,

where methyl and ethyl are substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and methoxy,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, (C_3-C_6)-cycloalkyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 6-membered azaheterocycle,

where the 4- to 6-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_3-C_6)-cycloalkyl and 4- to 6-membered heterocyclyl,

and

L^2 represents a bond,

R^{13} represents piperidin-2-yl, piperidin-3-yl, piperidin-4-yl or 1,2,3,4-tetrahydroquinolin-4-yl,

where piperidin-2-yl, piperidin-3-yl and piperidin-4-yl may be substituted by 1 to 5 substituents independently of one another selected from the group consisting of trifluoromethyl and methyl,

and

where 1,2,3,4-tetrahydroquinolin-4-yl may be substituted by fluorine or trifluoromethyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, monofluoromethyl, methoxy, ethynyl or methyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_3$-$C_7)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

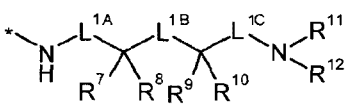
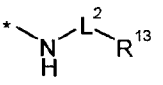
where $(C_3$-$C_7)$-cycloalkyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and $(C_1$-$C_4)$-alkyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl, $(C_1$-$C_4)$-alkoxy, $(C_3$-$C_6)$-cycloalkyl, difluoromethoxy and trifluoromethoxy,

R^2 represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, monofluoromethyl, difluoromethyl or trifluoromethyl,

R^3 represents a group of the formula

 or 

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond or $(C_1$-$C_4)$-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

L^{1B} represents a bond or (C_1-C_4)-alkanediyl,

L^{1C} represents a bond or (C_1-C_4)-alkanediyl,

where (C_1-C_4)-alkanediyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy and (C_1-C_4)-alkoxy,

R^7 represents hydrogen, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, cyano, 5- to 10-membered heteroaryl, naphthyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl, (C_1-C_4)-alkylsulphonyl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, nitro, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, -NH(CO)CH_3, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkenyl, (C_1-C_4)-alkylsulphonyl, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

in which 2 adjacent carbon atoms of the phenyl may be substituted by a difluoromethylenedioxy bridge,

R^8 represents hydrogen or (C_1-C_4)-alkyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and (C_1-C_4)-alkyl,

R^9 represents hydrogen, cyano, (C_1-C_6)-alkyl, (C_2-C_6)-alkenyl, (C_2-C_6)-alkynyl, (C_3-C_7)-cycloalkyl, 5- to 10-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, cyano, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxy-carbonyl, (C_1-C_4)-alkylsulphonyl, 5- or 6-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 to 3 halogen or (C_1-C_4)-alkoxy substituents,

where 5- or 6-membered heteroaryl may be benzo-fused or substituted by a 5- or 6-membered heteroaryl,

where 5- or 6-membered heteroaryl may be substituted by (C_1-C_4)-alkyl or trifluoromethyl,

where (C_3-C_7)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl and (C_1-C_4)-alkoxy,

and

where phenyl and 5- to 10-membered heteroaryl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkyl, (C_1-C_4)-cycloalkyl, (C_1-C_4)-alkoxy, (C_1-C_4)-alkoxycarbonyl and (C_1-C_4)-alkylsulphonyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

and

where the phenyl may be substituted on two adjacent carbon atoms by a difluoromethylenedioxy bridge,

R^{10} represents hydrogen or (C_1-C_4)-alkyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle and the 4- to 7-membered heterocycle for their part may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and (C_1-C_4)-alkyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a 3- to 7-membered carbocycle or a 4- to 7-membered heterocycle,

where the 3- to 7-membered carbocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_1-C_4)-alkyl, fluorine, hydroxy and (C_1-C_4)-alkoxy,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms a carbo- or heterocycle,

R^{11} represents hydrogen or (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and (C_1-C_4)-alkoxy,

R^{12} represents hydrogen, (C_1-C_6)-alkyl, (C_3-C_7)-cycloalkyl, phenyl or benzyl,

where (C_1-C_6)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, (C_3-C_7)-cycloalkyl, hydroxy, (C_1-C_4)-alkoxy and 4- to 7-membered heterocyclyl,

and

L^2 represents a bond or (C_1-C_4)-alkanediyl,

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl is substituted by 1 to 5 substituents independently of one another selected from the group consisting of (C_3-C_7)-cycloalkyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, (C_1-C_4)-alkyl, (C_2-C_4)-alkenyl, (C_2-C_4)-alkynyl, (C_3-C_6)-cycloalkyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

R^6 represents hydrogen, cyano or halogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2, CD_2 or $CH(CH_3)$,

R^1 represents (C_4-C_6)-alkyl, (C_4-C_6)-cycloalkyl or phenyl,

where (C_4-C_6)-alkyl may be substituted up to six times by fluorine,

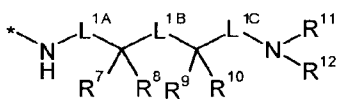
where (C_4-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

where phenyl may be substituted by 1 to 4 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methoxy, ethoxy, difluoromethyl, trifluoromethyl, (C_3-C_6)-cycloalkyl and methyl,

R^2 represents hydrogen, trifluoromethyl, (C_1-C_3)-alkyl or cyclopropyl,

R^3 represents a group of the formula



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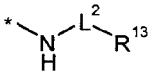


,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond, methylene or 1,2-ethanediyl,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, methyl, ethenyl, difluoromethoxy, trifluoromethoxy, -$NH(CO)CH_3$, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and

piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, 1,1,2,2-tetrafluoroethyl, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl, 5- or 6-membered heteroaryl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy, hydroxy, (C_1-C_4)-alkoxy, 5-membered heteroaryl, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where 5-membered heteroaryl may be benzo-fused or substituted by a 5-membered heteroaryl,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl and 5- or 6-membered heteroaryl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, methyl, difluoromethoxy, trifluoromethoxy, (C_1-C_4)-alkoxy and trifluoromethyl,

where (C_1-C_4)-alkoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and

piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen or $(C_1$-$C_3)$-alkyl,

where $(C_1$-$C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, methoxy and ethoxy,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl, cyclobutyl, phenyl or benzyl,

where $(C_1$-$C_4)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl or 1,1-dioxothiomorpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, thiomorpholinyl and 1,1-dioxothiomorpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl, cyclobutyl, azetidinyl, pyrrolidinyl and piperidinyl,

and

L^2 represents a bond, methylene or 1,1-ethanediyl,

R^{13} represents 5- to 6-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 6-membered azaheterocyclyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of $(C_3$-$C_7)$-cycloalkyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, bromine, cyano, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

R^6 represents hydrogen or fluorine,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents $(C_4$-$C_6)$-alkyl, $(C_4$-$C_6)$-cycloalkyl or phenyl,

where $(C_4$-$C_6)$-alkyl may be substituted up to six times by fluorine,

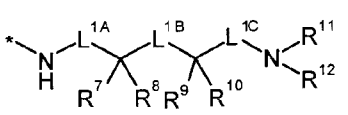
where $(C_4$-$C_6)$-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and methyl,

and

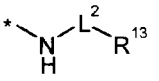
where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyclopropyl, methoxy and methyl,

R^2 represents trifluoromethyl, methyl, ethyl or cyclopropyl,

R^3 represents a group of the formula



or



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, (C_1-C_4)-alkyl, cyclopropyl and cyclobutyl,

R^7 represents hydrogen, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, nitro, ethenyl, difluoromethoxy, trifluoromethoxy, $-NH(CO)CH_3$, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

or

R^7 and R^8 together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and methyl,

R^9 represents hydrogen, cyano, trifluoromethyl, (C_1-C_6)-alkyl, (C_3-C_6)-cycloalkyl or phenyl,

where (C_1-C_6)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy, phenyl, phenoxy and benzyloxy,

where phenyl, phenoxy and benzyloxy for their part may be substituted by 1 or 2 substituents selected from the group consisting of fluorine and chlorine,

where (C_3-C_6)-cycloalkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl and ethyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, difluoromethoxy, trifluoromethoxy, ethoxy and trifluoromethyl,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl or piperidinyl ring,

where the 3- to 6-membered carbocycle and the oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl and piperidinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, benzyl and methyl,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

or

R^7 and R^9 together with the carbon atoms to which they are attached and the group L^{1B} form a cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, piperidinyl or tetrahydropyranyl ring,

with the proviso that not more than one of the radical pairs R^7 and R^8, R^9 and R^{10} and R^7 and R^9, respectively, simultaneously forms one of the carbo- or heterocycles mentioned above,

R^{11} represents hydrogen or $(C_1$-$C_3)$-alkyl,

where $(C_1$-$C_3)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

R^{12} represents hydrogen, $(C_1$-$C_4)$-alkyl, cyclopropyl or cyclobutyl,

where (C_1-C_4)-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form an azetidinyl, pyrrolidinyl, piperidinyl or morpholinyl ring,

where the azetidinyl, pyrrolidinyl, piperidinyl and morpholinyl ring may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, methyl, ethyl, cyclopropyl and cyclobutyl,

and

L^2 represents a bond or methylene,

R^{13} represents 5- to 6-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 6-membered azaheterocyclyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of (C_3-C_7)-cycloalkyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, methyl, ethyl, monofluoromethyl, methoxy, ethynyl or cyclopropyl,

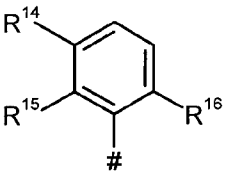
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



where

represents the point of attachment to A,

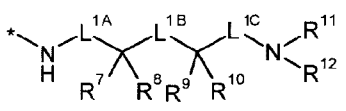
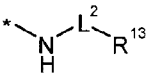
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine, methoxy, cyclopropyl or chlorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula

 or  ,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen, trifluoromethyl, $(C_1$-$C_6)$-alkyl, $(C_3$-$C_6)$-cycloalkyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, ethenyl, difluoromethoxy, trifluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^8 represents hydrogen, methyl or ethyl,

R^9 represents hydrogen, cyano, trifluoromethyl, $(C_1$-$C_6)$-alkyl, cyclopropyl or phenyl,

where $(C_1$-$C_6)$-alkyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of cyano, fluorine, trifluoromethyl, hydroxy, $(C_1$-$C_4)$-alkoxy and phenyl,

and

where phenyl may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of fluorine, difluoromethoxy, trifluoromethoxy, ethoxy and chlorine,

where ethoxy may be substituted by hydroxy,

R^{10} represents hydrogen, methyl or ethyl,

or

R^9 and R^{10} together with the carbon atom to which they are attached form a 3- to 6-membered carbocycle or an oxetanyl ring,

with the proviso that the radicals R^7 and R^9 do not both simultaneously represent phenyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

and

L^2 represents a bond,

R^{13} represents 5- to 6-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 6-membered azaheterocyclyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of (C_3-C_7)-cycloalkyl and benzyl,

R^4 represents hydrogen,

R^5 represents hydrogen, fluorine, chlorine, monofluoromethyl, methoxy, ethynyl or methyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Particular preference in the context of the present invention is given to compounds of the formula (I) in which

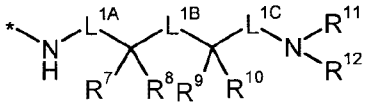
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents hydrogen or $(C_1$-$C_4)$-alkyl,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

R^4 represents hydrogen,

R^5 represents hydrogen or methyl,

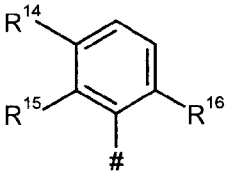
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Particular preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



,

where

represents the point of attachment to A,

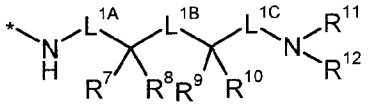
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen or fluorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula



where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents hydrogen or $(C_1$-$C_4)$-alkyl,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

R^4 represents hydrogen,

R^5 represents hydrogen or methyl,

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Particular preference in the context of the present invention is given to compounds of the formula (I) in which

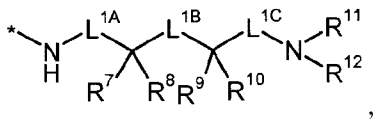
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents $(C_1\text{-}C_4)$-alkyl,

where $(C_1\text{-}C_4)$-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

R^4 represents hydrogen,

R^5 represents hydrogen or methyl,

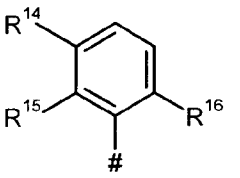
R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Particular preference in the context of the present invention is given to compounds of the formula (I) in which

A represents CH_2,

R^1 represents a phenyl group of the formula



,

where

represents the point of attachment to A,

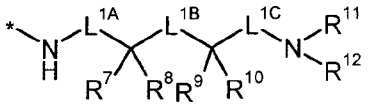
and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen or fluorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

R^2 represents methyl,

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents $(C_1$-$C_4)$-alkyl,

where $(C_1$-$C_4)$-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

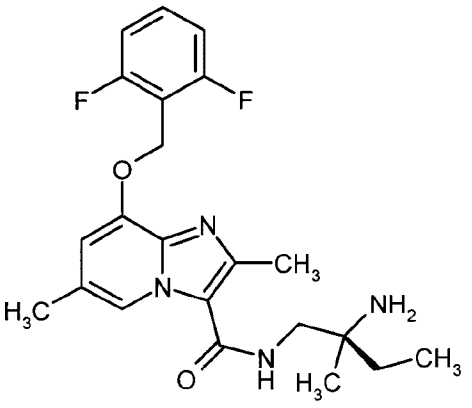
R^4 represents hydrogen,

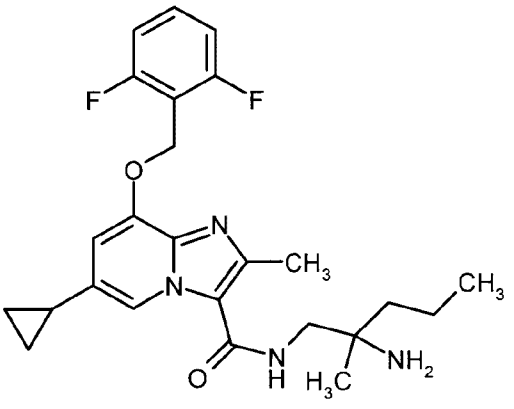
R^5 represents hydrogen or methyl,

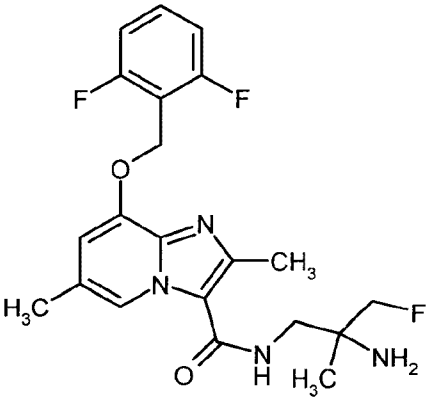
R^6 represents hydrogen,

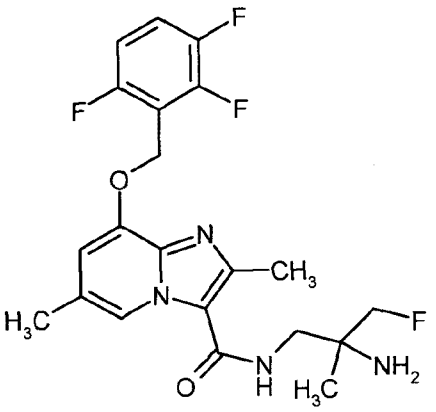
and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

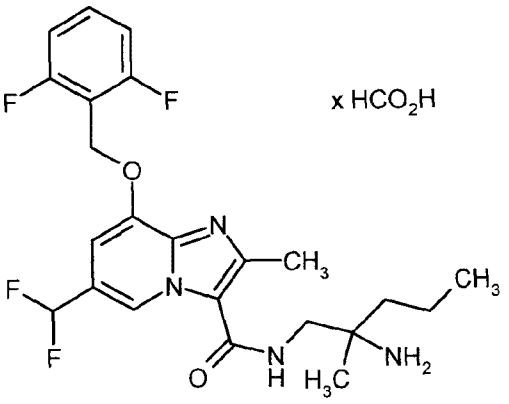
Particular preference is also given to the following compounds

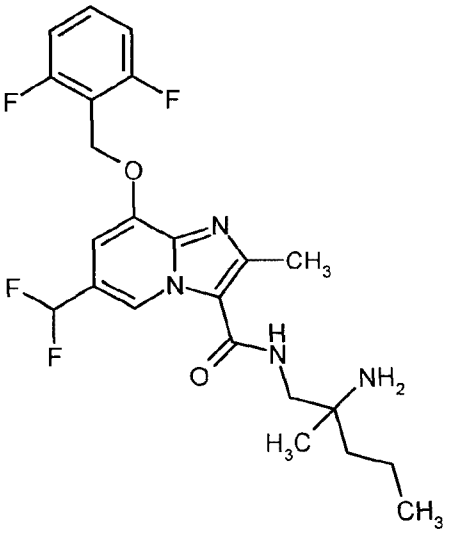


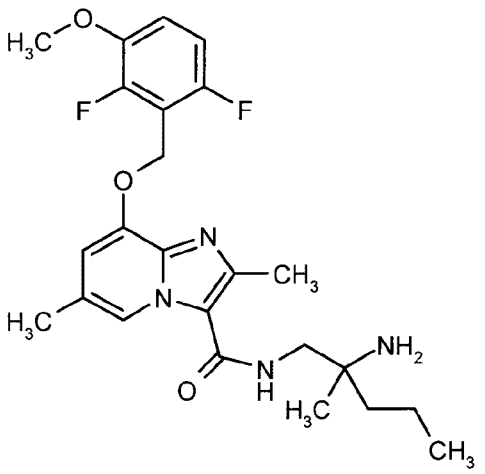


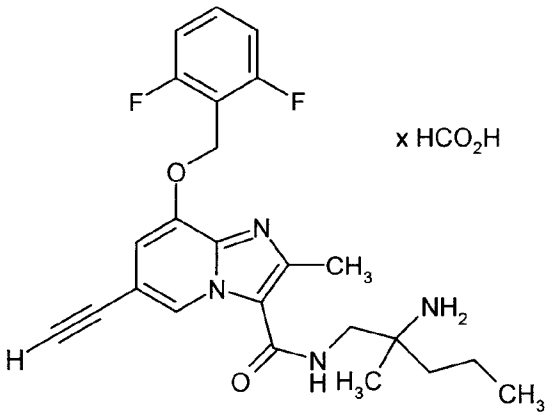


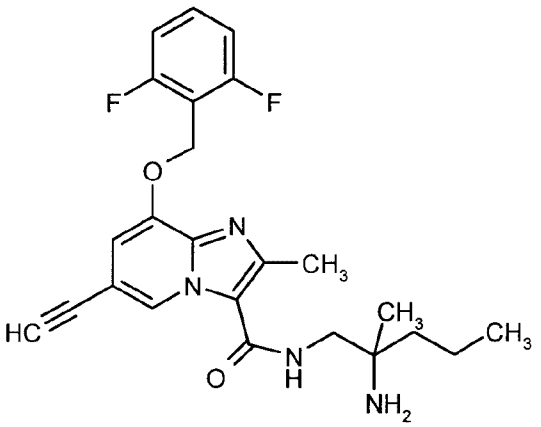


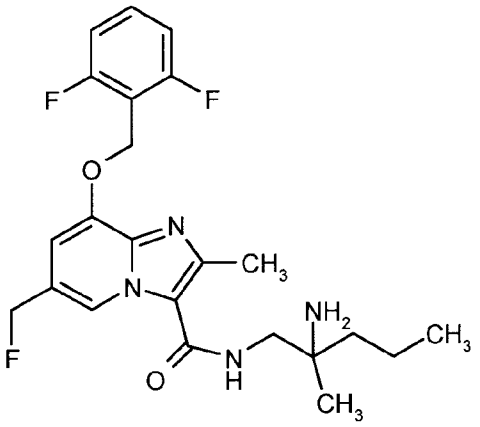

x HCO2H

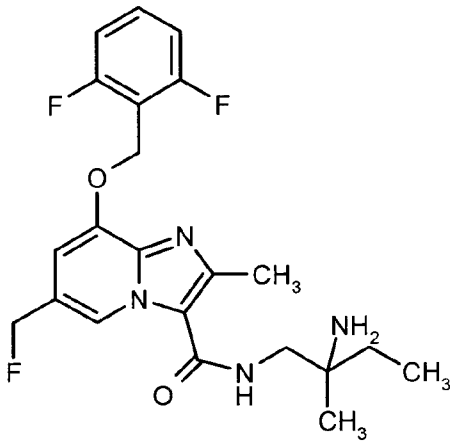


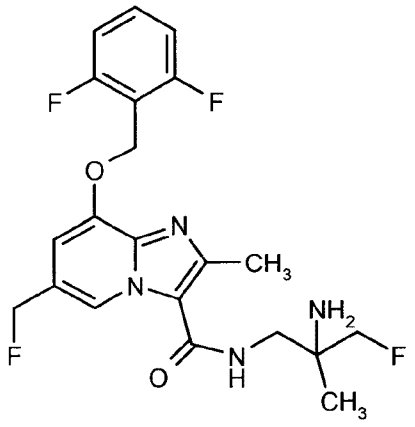


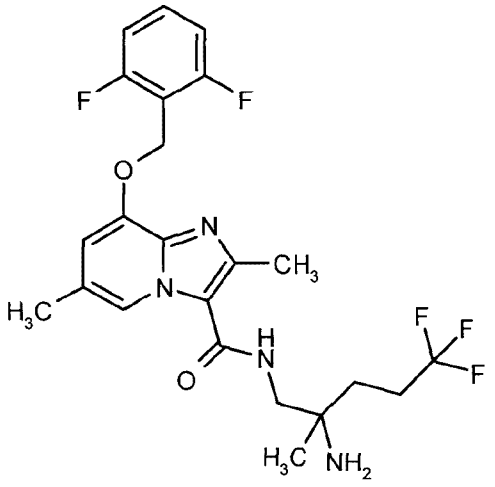


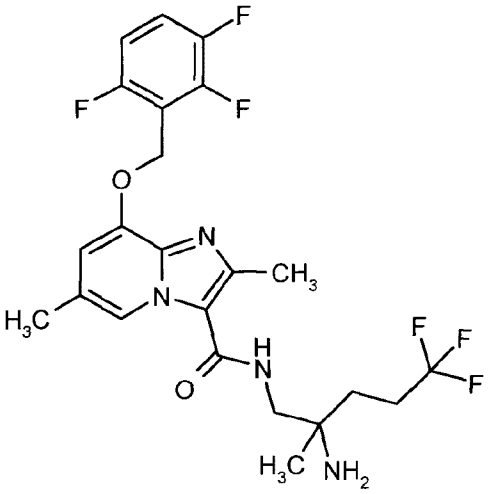






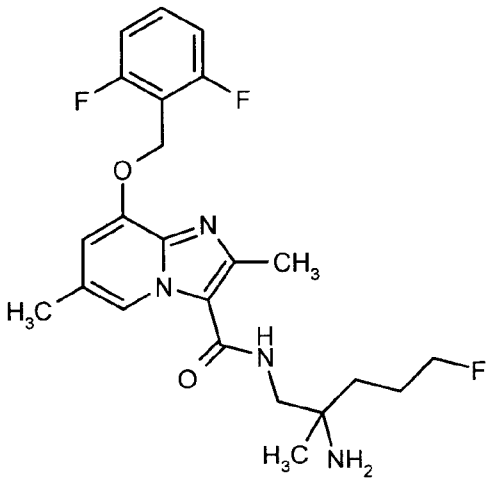


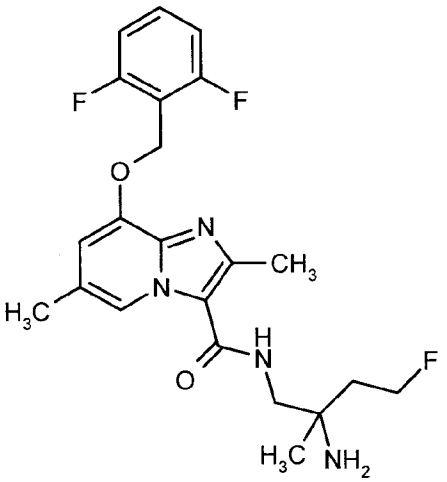


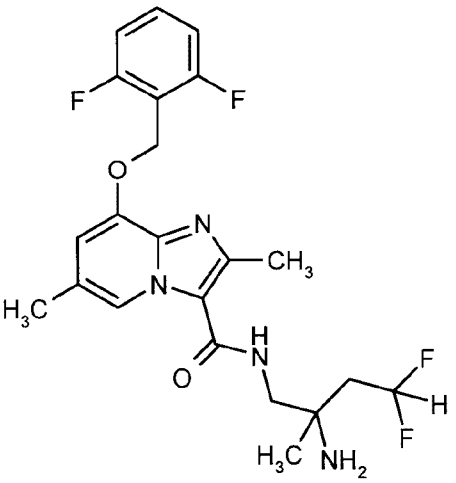


and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Particular preference is also given to the following compounds



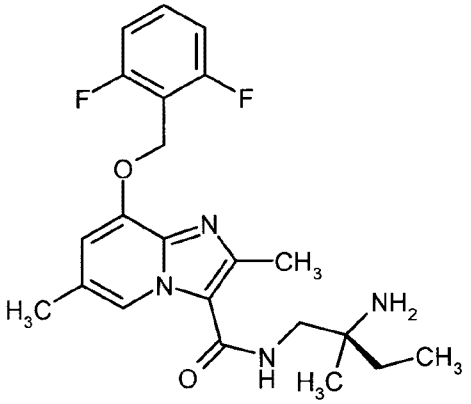


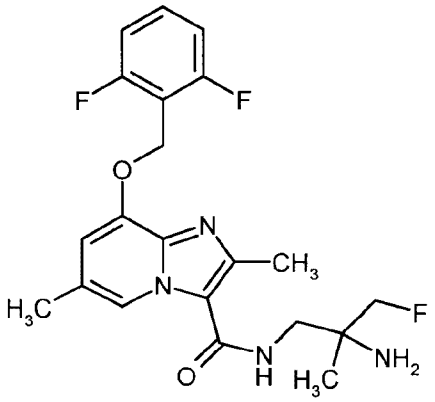


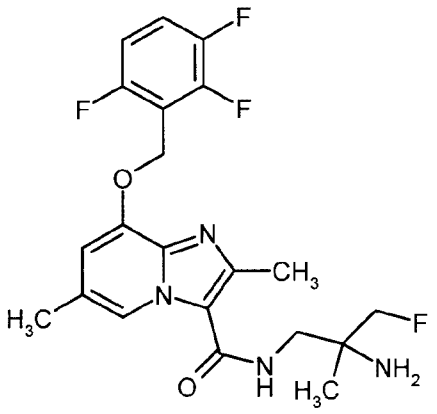
and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

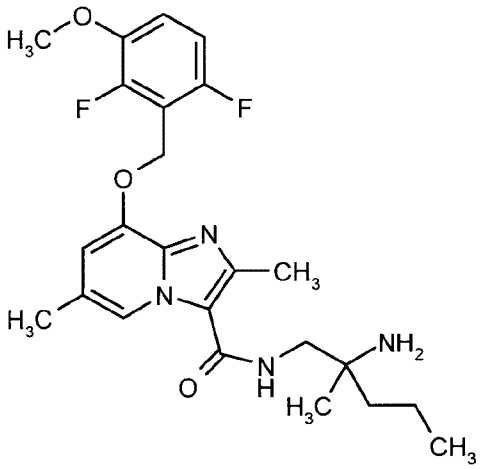
Those three compounds can be prepared by methods known from the literature and familiar to the person skilled in the art (see Schemes 6 -17).

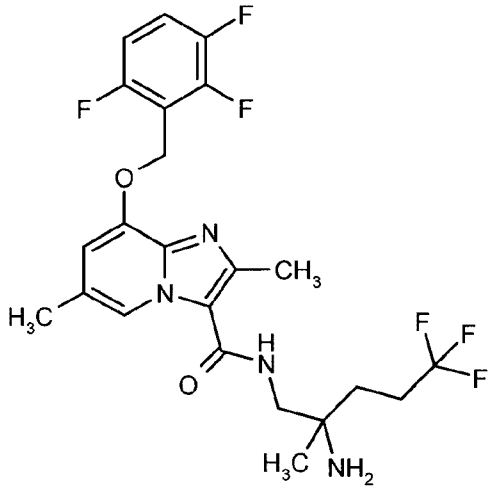
Particular preference is also given to the following compounds

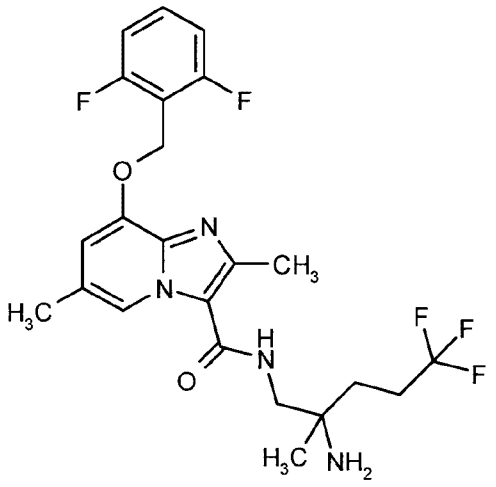








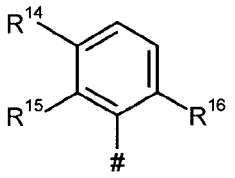




and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^1 represents a phenyl group of the formula



,

where

\# denotes the point of attachment to A,

and

R^{14}, R^{15} and R^{16} independently of one another represent hydrogen, fluorine or chlorine,

with the proviso that at least two of the radicals R^{14}, R^{15}, R^{16} are different from hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

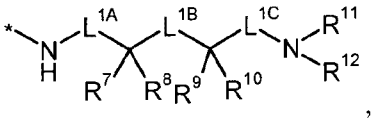
Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^2 represents methyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond or methylene,

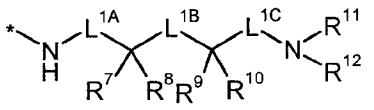
L^{1C} represents a bond or methylene,

where methylene may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of trifluoromethyl, $(C_1$-$C_4)$-alkyl, cyclopropyl and cyclobutyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^3 represents a group of the formula



,

where

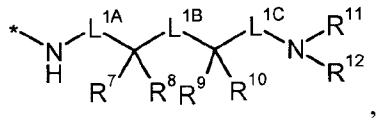
* represents the point of attachment to the carbonyl group,

R^8 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

and

R^{10} represents hydrogen or methyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^5 represents hydrogen, fluorine, chlorine or methyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^6 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^1 represents phenyl,

where phenyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl,

and

where phenyl is substituted by 1 to 2 substituents selected from the group consisting of $(C_3$-$C_7)$-cycloalkyl, $(C_1$-$C_4)$-alkoxy, monofluoromethoxy, difluoromethoxy or trifluoromethoxy,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^1 represents phenyl,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of fluorine, chlorine, cyano, monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_1$-$C_4)$-alkyl,

and

where phenyl is substituted by a substituent selected from the group consisting of $(C_3$-$C_6)$-cycloalkyl, $(C_1$-$C_2)$-alkoxy and trifluoromethoxy,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^1 represents phenyl,

where phenyl is substituted by 1 to 2 fluorine,

and

where phenyl is substituted by a substituent selected from the group consisting of cyclopropyl and methoxy,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_3$-$C_6)$-cycloalkyl, $(C_2$-$C_4)$-alkenyl, $(C_2$-$C_4)$-alkynyl, difluoromethoxy, trifluoromethoxy, $(C_1$-$C_4)$-alkoxy, amino, 4- to 7-membered heterocyclyl or 5- or 6-membered heteroaryl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, $(C_3$-$C_6)$-cycloalkyl, $(C_2$-$C_4)$-alkynyl, difluoromethoxy, trifluoromethoxy, $(C_1$-$C_4)$-alkoxy, 5- to 6-membered heterocyclyl or 5- or 6-membered heteroaryl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^5 represents monofluoromethyl, difluoromethyl, trifluoromethyl, cyclopropyl, $(C_2$-$C_4)$-alkynyl, methoxy, morpholino,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^7 represents $(C_1$-$C_6)$-alkyl, $(C_2$-$C_6)$-alkynyl, cyano or phenyl,

where $(C_1$-$C_6)$-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, difluoromethoxy, trifluoromethoxy and phenoxy,

where phenoxy may be substituted by 1 to 3 fluorine,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, nitro, difluoromethoxy, trifluoromethoxy, $(C_1$-$C_4)$-alkoxy, $-NH(CO)CH_3$ and $(C_1$-$C_4)$-alkenyl,

where $(C_1$-$C_4)$-alkoxy is substituted by hydroxy,

R^8 represents hydrogen or $(C_1$-$C_4)$-alkyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^7 represents (C_1-C_4)-alkyl, cyano or phenyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

and

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy, ethoxy, -NH(CO)CH_3 or ethenyl,

where ethoxy is substituted by hydroxy,

R^8 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^7 represents (C_1-C_4)-alkyl, cyano or phenyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

and

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy, ethoxy, -NH(CO)CH_3 or ethenyl,

where ethoxy is substituted by hydroxy,

R^8 represents hydrogen,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^9 represents (C_1-C_4)-alkyl, cyano or phenyl,

where (C_1-C_4)-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy, 5-membered heteroaryl and benzyloxy,

where benzyloxy may be substituted by 1 to 3 halogen substituents,

where 5-membered heteroaryl is substituted by a 5-membered heteroaryl,

where 5-membered heteroaryl for its part may be substituted by (C_1-C_4)-alkyl,

where phenyl is substituted by 1 to 2 substituents independently of one another selected from the group consisting of cyano, difluoromethoxy, trifluoromethoxy and (C_1-C_4)-alkoxy,

where (C_1-C_4)-alkoxy is substituted by hydroxy,

R^{10} represents hydrogen or methyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^9 represents ethyl, propyl, cyano or phenyl,

where ethyl and propyl are substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl and benzyloxy,

where benzyloxy may be substituted by 1 to 3 halogen substituents,

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy or ethoxy,

where ethoxy is substituted by hydroxy,

R^{10} represents hydrogen or methyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^9 represents ethyl, cyano or phenyl,

where ethyl is substituted up to five times by fluorine,

where phenyl is substituted by cyano, difluoromethoxy, trifluoromethoxy or ethoxy,

where ethoxy is substituted by hydroxy,

R^{10} represents hydrogen or methyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^{11} represents $(C_1\text{-}C_4)$-alkyl,

where $(C_1\text{-}C_4)$-alkyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and $(C_1\text{-}C_4)$-alkoxy,

R^{12} represents hydrogen, $(C_1\text{-}C_6)$-alkyl, $(C_3\text{-}C_7)$-cycloalkyl, phenyl or benzyl,

where $(C_1\text{-}C_6)$-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, $(C_1\text{-}C_4)$-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 7-membered azaheterocycle,

where the 4- to 7-membered azaheterocycle is substituted by 1 or 2 substituents independently of one another selected from the group consisting of $(C_3\text{-}C_7)$-cycloalkyl and 4- to 7-membered heterocyclyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^{11} represents methyl or ethyl,

where methyl and ethyl are substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy and methoxy,

R^{12} represents hydrogen, (C_1-C_4)-alkyl, (C_3-C_6)-cycloalkyl, phenyl or benzyl,

where (C_1-C_4)-alkyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of fluorine, trifluoromethyl, hydroxy, (C_1-C_4)-alkoxy and phenoxy,

and

where phenyl and benzyl may be substituted by 1 to 3 substituents independently of one another selected from the group consisting of halogen and trifluoromethyl,

or

R^{11} and R^{12} together with the nitrogen atom to which they are attached form a 4- to 6-membered azaheterocycle,

where the 4- to 6-membered azaheterocycle may be substituted by 1 or 2 substituents independently of one another selected from the group consisting of (C_3-C_6)-cycloalkyl and 4- to 6-membered heterocyclyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^{13} represents 5- to 9-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 9-membered azaheterocyclyl is substituted by 1 to 5 substituents independently of one another selected from the group consisting of (C_3-C_7)-cycloalkyl and benzyl,

and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

Preference in the context of the present invention is also given to compounds of the formula (I) in which

R^{13} represents 5- to 6-membered azaheterocyclyl which is attached via a ring carbon atom,

where 5- to 6-membered azaheterocyclyl is substituted by 1 to 3 substituents independently of one another selected from the group consisting of $(C_3$-$C_7)$-cycloalkyl and benzyl,

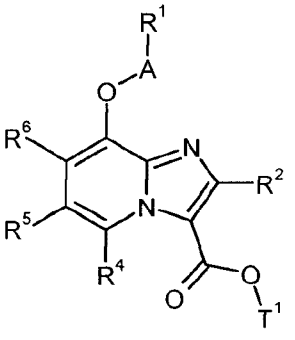
and their *N*-oxides, salts, solvates, salts of the *N*-oxides and solvates of the *N*-oxides and salts.

The definitions of radicals indicated specifically in the respective combinations or preferred combinations of radicals are replaced as desired irrespective of the particular combinations indicated for the radicals also by definitions of radicals of other combinations.

Combinations of two or more of the preferred ranges mentioned above are particularly preferred.

The invention furthermore provides a process for preparing the compounds of the formula (I) according to the invention, characterized in that

[A] a compound of the formula (II)

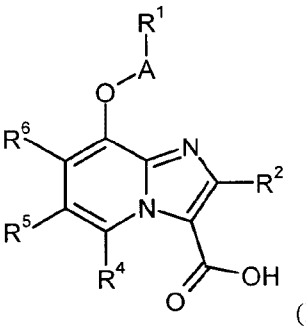


(II),

in which A, R^1, R^2, R^4, R^5 and R^6 each have the meanings given above and

T^1 represents $(C_1$-$C_4)$-alkyl or benzyl,

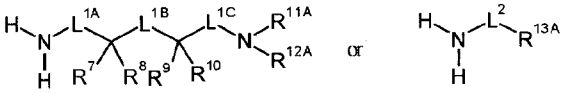
is reacted in an inert solvent in the presence of a suitable base or acid to give a carboxylic acid of the formula (III)



(III),

in which A, R^1, R^2, R^4, R^5 and R^6 each have the meanings given above,

and this is subsequently reacted in an inert solvent under amide coupling conditions with an amine of the formula (IV-A) or (IV-B)



(IV-A) (IV-B),

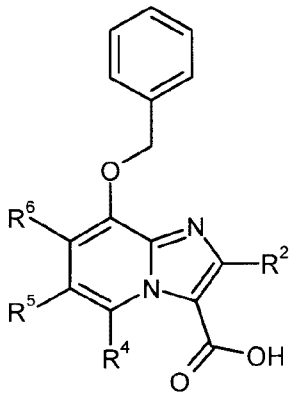
in which L^{1A}, L^{1B}, L^{1C}, L^2, R^7, R^8, R^9, and R^{10} each have the meanings given above

and

R^{11A}, R^{12A} and R^{13A} have the meanings given above for R^{11}, R^{12} and R^{13}, respectively, or represent an amino protective group, for example tert-butoxycarbonyl, benzyloxycarbonyl or benzyl,

or

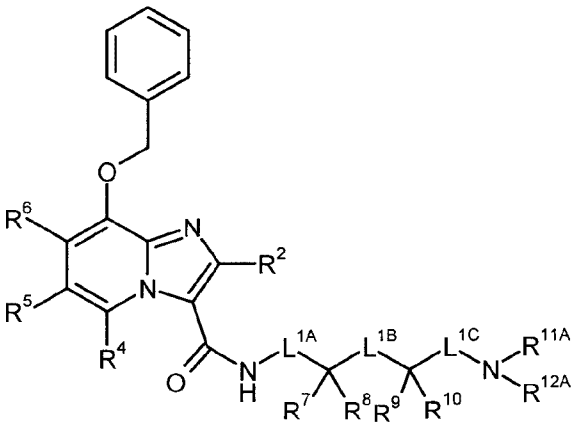
[B] a compound of the formula (III-B)



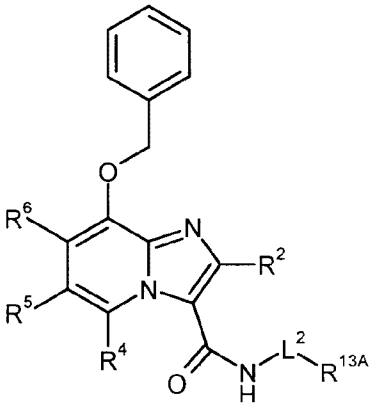
(III-B),

in which R^2, R^4, R^5 and R^6 each have the meanings given above,

is reacted in an inert solvent under amide coupling conditions with an amine of the formula (IV) to give a compound of the formula (I-A) and (I-B),



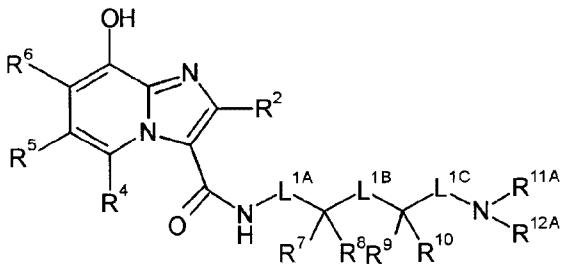
(I-A)



(I-B)

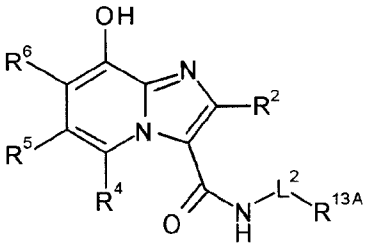
in which R^2, R^4, R^5, R^6, L^{1A}, L^{1B}, L^{1C}, L^2, R^7, R^8, R^9, R^{10}, R^{11A}, R^{12A} and R^{13A} each have the meanings given above,

from this compound, the benzyl group is subsequently removed using methods known to the person skilled in the art and the resulting compound of the formula (V-A) or (V-B)



(V-A)

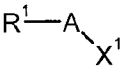
or



(V-B),

in which R^2, R^4, R^5, R^6, L^{1A}, L^{1B}, L^{1C}, L^2, R^7, R^8, R^9, R^{10}, R^{11A}, R^{12A} and R^{13A} each have the meanings given above,

is reacted in an inert solvent in the presence of a suitable base with a compound of the formula (VI)



(VI),

in which A and R^1 have the meanings given above and

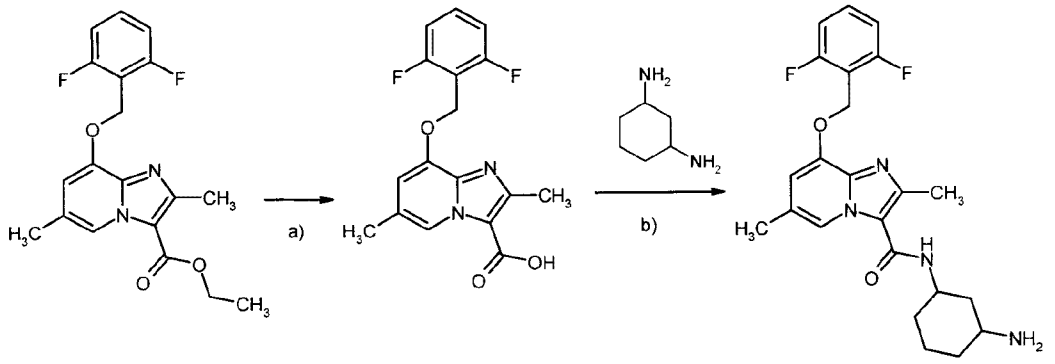
X^1 represents a suitable leaving group, in particular chlorine, bromine, iodine, mesylate, triflate or tosylate,

any protective groups present are subsequently removed, and the resulting compounds of the formula (I) are optionally converted with the appropriate (i) solvents and/or (ii) acids or bases into their solvates, salts and/or solvates of the salts.

The compounds of the formulae (I-A) and (I-B) form a subset of the compounds of the formula (I) according to the invention.

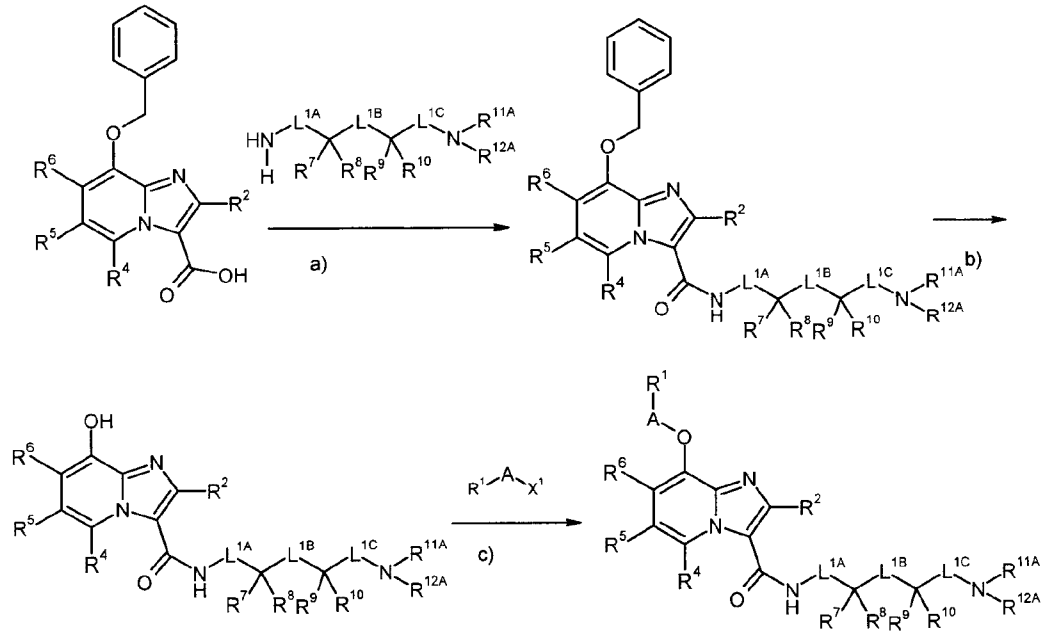
The preparation processes described can be illustrated in an exemplary manner by the synthesis schemes below (Schemes 1 and 2):

Scheme 1:



[a): lithium hydroxide, THF/methanol/ H_2O, RT; b): HATU, *N,N*-diisopropylethylamine, DMF, RT].

Scheme 2:



[a): TBTU, N-methylmorpholine, DMF; b): H_2, Pd/C, ethyl acetate; c): Cs_2CO_3, DMF].

The compounds of the formulae (IV-A), (IV-B) and (VI) are commercially available, known from the literature or can be prepared analogously to processes known from the literature.

The free bases of (IV-A) can be released from the compounds (IV-A) optionally provided with an amino protective group, for example by using acids such as hydrogen chloride and trifluoroacetic acid in suitable solvents such as diethyl ether, dichloromethane, 1,4-dioxane, water, methanol, ethanol and mixtures thereof.

Inert solvents for the process steps (III) + (IV) → (I) and (III-B) + (IV) → (I-B) are, for example, ethers such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether or diethylene glycol dimethyl ether, hydrocarbons such as benzene, toluene, xylene, hexane, cyclohexane or mineral oil fractions, halogenated hydrocarbons such as dichloromethane, trichloromethane, carbon tetrachloride, 1,2-dichloroethane, trichloroethylene or chlorobenzene, or other solvents such as acetone, ethyl acetate, acetonitrile, pyridine, dimethyl sulphoxide, *N,N*-dimethylformamide, *N,N*-dimethylacetamide, *N,N'*-dimethylpropyleneurea (DMPU) or *N*-methylpyrrolidone (NMP). It is also possible to use mixtures of the solvents mentioned. Preference is given to dichloromethane, tetrahydrofuran, dimethylformamide or mixtures of these solvents.

Suitable condensing agents for the amide formation in process steps (III) + (IV) → (I) and (III-B) + (IV) → (I-B) are, for example, carbodiimides such as *N,N'*-diethyl-, *N,N'*-dipropyl-, *N,N'*-diisopropyl-, *N,N'*-dicyclohexylcarbodiimide (DCC) or *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC), phosgene derivatives such as *N,N'*-carbonyldiimidazole (CDI), 1,2-oxazolium compounds such as 2-ethyl-5-phenyl-1,2-oxazolium 3-sulphate or 2-*tert*-butyl-5-methylisoxazolium perchlorate, acylamino compounds such as 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline, or isobutyl chloroformate, propanephosphonic anhydride (T3P), 1-chloro-*N,N*,2-trimethylprop1-ene-1-amine, diethyl cyanophosphonate, bis-(2-oxo-3-oxazolidinyl)phosphoryl chloride, benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate, benzotriazol-1-yloxytris(pyrrolidino)phosphonium hexafluorophosphate (PyBOP), *O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium tetrafluoroborate (TBTU), *O*-(benzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HBTU), 2-(2-oxo-1-(2*H*)-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TPTU), *O*-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU) or *O*-(1*H*-6-chlorobenzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TCTU), if appropriate in combination with further auxiliaries such as 1-hydroxybenzotriazole (HOBt) or *N*-hydroxysuccinimide (HOSu), and also as bases alkali metal carbonates, for example sodium carbonate or potassium carbonate or sodium bicarbonate or potassium bicarbonate, or organic bases such as trialkylamines, for example triethylamine, *N*-methylmorpholine, *N*-methylpiperidine or *N,N*-diisopropylethylamine. Preference is given to using TBTU

in combination with N-methylmorpholine, HATU in combination with *N,N*-diisopropylethylamine or 1-chloro-*N,N*,2-trimethylprop-1-ene-1amine.

The condensations (III) + (IV) → (I) and (III-B) + (IV) → (I-B) are generally carried out in a temperature range of from -20°C to +100°C, preferably at from 0°C to +60°C. The reaction can be performed at atmospheric, elevated or at reduced pressure (for example from 0.5 to 5 bar). In general, the reaction is carried out at atmospheric pressure.

Alternatively, the carboxylic acids of the formula (III) can also initially be converted into the corresponding carbonyl chloride and this can then be reacted directly or in a separate reaction with an amine of the formula (IV) to give the compounds according to the invention. The formation of carbonyl chlorides from carboxylic acids is carried out by methods known to the person skilled in the art, for example by treatment with thionyl chloride, sulphuryl chloride or oxalyl chloride in the presence of a suitable base, for example in the presence of pyridine, and also optionally with addition of dimethylformamide, optionally in a suitable inert solvent.

The hydrolysis of the ester group T^1 of the compounds of the formula (II) is carried out by customary methods by treating the esters in inert solvents with acids or bases, where in the latter case the salts initially formed are converted into the free carboxylic acids by treatment with acid. In the case of the tert-butyl esters the ester cleavage is preferably carried out with acids. In the case of benzyl esters, the ester cleavage is preferably carried out hydrogenolytically using palladium on activated carbon or Raney nickel. Suitable inert solvents for this reaction are water or the organic solvents customary for an ester cleavage. These preferably include alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol or tert-butanol, or ethers such as diethyl ether, tetrahydrofuran, 2-methyltetrahydrofuran, dioxane or glycol dimethyl ether, or other solvents such as acetone, dichloromethane, dimethylformamide or dimethyl sulphoxide. It is also possible to use mixtures of the solvents mentioned. In the case of a basic ester hydrolysis, preference is given to using mixtures of water with dioxane, tetrahydrofuran, methanol and/or ethanol.

Suitable bases for the ester hydrolysis are the customary inorganic bases. These preferably include alkali metal or alkaline earth metal hydroxides, for example sodium hydroxide, lithium hydroxide, potassium hydroxide or barium hydroxide, or alkali metal or alkaline earth metal carbonates such as sodium carbonate, potassium carbonate or calcium carbonate. Particular preference is given to sodium hydroxide or lithium hydroxide.

Suitable acids for the ester cleavage are, in general, sulphuric acid, hydrogen chloride/hydrochloric acid, hydrogen bromide/hydrobromic acid, phosphoric acid, acetic acid, trifluoroacetic acid, toluenesulphonic acid, methanesulphonic acid or trifluoromethanesulphonic acid, or mixtures thereof, if appropriate with addition of water. Preference is given to hydrogen

chloride or trifluoroacetic acid in the case of the tert-butyl esters and hydrochloric acid in the case of the methyl esters.

The ester cleavage is generally carried out in a temperature range of from 0°C to +100°C, preferably at from +0°C to +50°C.

The reactions mentioned can be carried out at atmospheric, elevated or reduced pressure (for example from 0.5 to 5 bar). In general, the reactions are in each case carried out at atmospheric pressure.

Inert solvents for the process step (V) + (VI) → (I) are, for example, halogenated hydrocarbons such as dichloromethane, trichloromethane, carbon tetrachloride, trichloroethylene or chlorobenzene, ethers such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether or diethylene glycol dimethyl ether, hydrocarbons such as benzene, toluene, xylene, hexane, cyclohexane or mineral oil fractions, or other solvents such as acetone, methyl ethyl ketone, ethyl acetate, acetonitrile, *N,N*-dimethylformamide, *N,N*-dimethylacetamide, dimethyl sulphoxide, *N,N'*-dimethylpropyleneurea (DMPU), *N*-methylpyrrolidone (NMP) or pyridine. It is also possible to use mixtures of the solvents mentioned. Preference is given to using dimethylformamide or dimethyl sulphoxide.

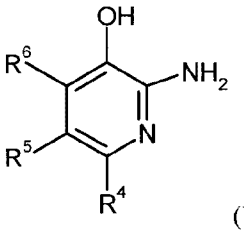
Suitable bases for the process step (V) + (VI) → (I) are the customary inorganic or organic bases. These preferably include alkali metal hydroxides, for example lithium hydroxide, sodium hydroxide or potassium hydroxide, alkali metal or alkaline earth metal carbonates such as lithium carbonate, sodium carbonate, potassium carbonate, calcium carbonate or caesium carbonate, if appropriate with addition of an alkali metal iodide, for example sodium iodide or potassium iodide, alkali alkoxides such as sodium methoxide or potassium methoxide, sodium ethoxide or potassium ethoxide or sodium tert-butoxide or potassium tert-butoxide, alkali metal hydrides such as sodium hydride or potassium hydride, amides such as sodium amide, lithium bis(trimethylsilyl)amide or potassium bis(trimethylsilyl)amide or lithium diisopropylamide, or organic amines such as triethylamine, *N*-methylmorpholine, *N*-methylpiperidine, *N,N*-diisopropylethylamine, pyridine, 4-(*N,N*-dimethylamino)pyridine (DMAP), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 1,4-diazabicyclo[2.2.2]octane (DABCO®). Preference is given to using potassium carbonate, caesium carbonate or sodium methoxide.

The reaction is generally carried out in a temperature range of from 0°C to +120°C, preferably at from +20°C to +80°C, if appropriate in a microwave. The reaction can be carried out at atmospheric, elevated or reduced pressure (for example from 0.5 to 5 bar).

Preferred for use as amino protective group is *tert*-butoxycarbonyl (Boc) or benzyloxycarbonyl (Z). As protective group for a hydroxyl or carboxyl function, preference is given to using *tert*-butyl or benzyl. The removal of these protective groups is carried out by customary methods, preferably by reaction with a strong acid such as hydrogen chloride, hydrogen bromide or trifluoroacetic acid in an inert solvent such as dioxane, diethyl ether, dichloromethane or acetic acid; if appropriate, the removal can also be carried out without any additional inert solvent. In the case of benzyl and benzyloxycarbonyl as protective group, these can also be removed by hydrogenolysis in the presence of a palladium catalyst. If appropriate, the removal of the protective groups mentioned can be performed simultaneously in a one-pot reaction or in separate reaction steps.

Here, the removal of the benzyl group in reaction step (I-B) → (V) is carried out by customary methods known from protective group chemistry, preferably by hydrogenolysis in the presence of a palladium catalyst such as palladium on activated carbon in an inert solvent, for example ethanol or ethyl acetate [see also, for example, T.W. Greene and P.G.M. Wuts, *Protective Groups in Organic Synthesis*, Wiley, New York, 1999].

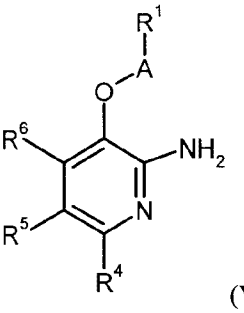
The compounds of the formula (II) are known from the literature or can be prepared by reacting a compound of the formula (VII)



(VII),

in which R^4, R^5 and R^6 have the meanings given above,

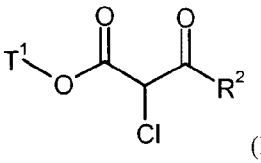
in an inert solvent in the presence of a suitable base with a compound of the formula (VI) to give a compound of the formula (VIII)



(VIII),

in which R^1, R^4, R^5 and R^6 each have the meanings given above,

and this is then reacted in an inert solvent with a compound of the formula (IX)

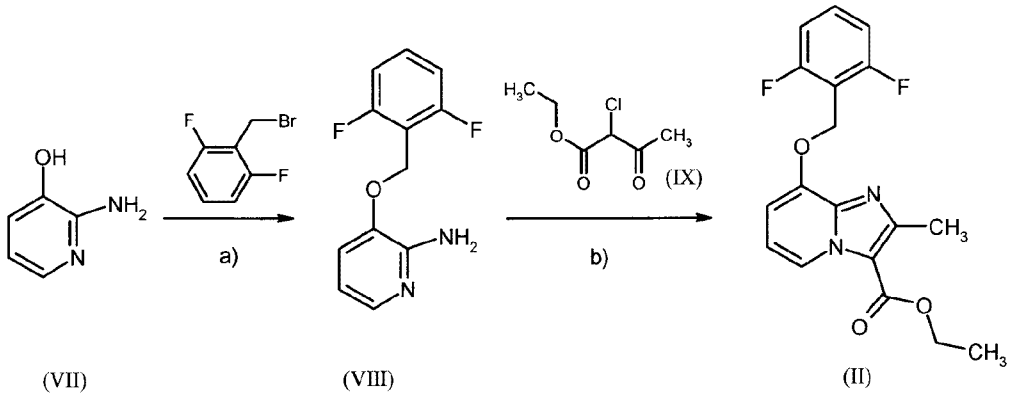


(IX),

in which R^2 and T^1 each have the meanings given above.

The process described is illustrated in an exemplary manner by the scheme below (Scheme 3):

Scheme 3:

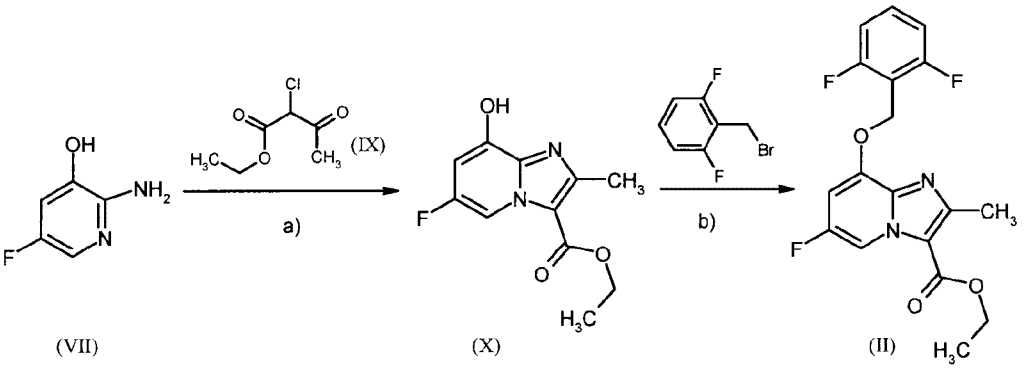


(VII) (VIII) (II)

[a): i) NaOMe, MeOH, RT; ii) DMSO, RT; b): EtOH, molecular sieve, reflux].

The synthesis sequence shown can be modified such that the respective reaction steps are carried out in a different order. An example of such a modified synthesis sequence is shown in Scheme 4.

Scheme 4:



(VII) (X) (II)

[a): EtOH, molecular sieve, reflux; b): b) Cs_2CO_3, DMF, 50°C].

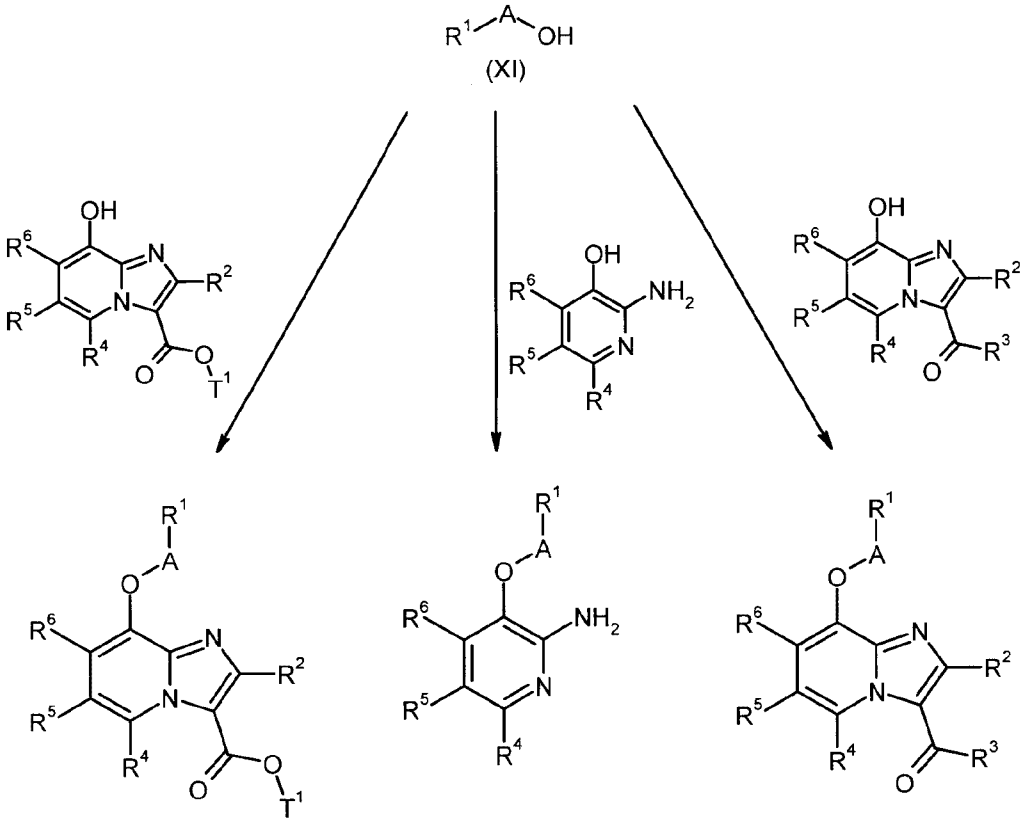
Inert solvents for the ring closure affording the imidazo[1,2-a]pyridine skeleton (VIII) + (IX) → (II) or (VII) + (IX) → (X) are the customary organic solvents. These preferably include alcohols such as methanol, ethanol, n-propanol, isopropanol, n-butanol, n-pentanol or tert-butanol, or ethers such as diethyl ether, tetrahydrofuran, 2-methyltetrahydrofuran, dioxane or glycol dimethyl ether, or other solvents such as acetone, dichloromethane, 1,2-dichloroethane, acetonitrile, dimethylformamide or dimethyl sulphoxide. It is also possible to use mixtures of the solvents mentioned. Preference is given to using ethanol.

The ring closure is usually carried out in a temperature range from +50°C to +150°C, preferably at from +50°C to +100°C, if appropriate in a microwave oven.

The ring closure (VIII) + (IX) → (II) or (VII) + (IX) → (X) is optionally carried out in the presence of dehydrating agents, for example in the presence of molecular sieve (pore size 4Å) or using a water separator. The reaction (VIII) + (IX) → (II) or (VII) + (IX) → (X) is carried out using an excess of the reagent of the formula (IX), for example using 1 to 20 equivalents of reagent (IX), if appropriate with addition of bases (such as sodium bicarbonate), where the addition of this reagent can be carried out once or in several portions.

Alternatively to the introductions of R^1 shown in Schemes 1 to 4 by reaction of the compounds (V), (VII) or (X) with compounds of the formula (VI), it is also possible – as shown in Scheme 5 – to react these intermediates with alcohols of the formula (XI) under the conditions of the Mitsunobu reaction.

Scheme 5:

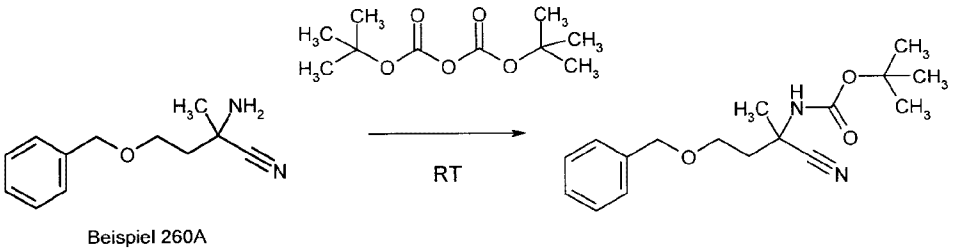


Typical reaction conditions for such Mitsunobu condensations of phenols with alcohols can be found in the relevant literature, for example Hughes, D.L. *Org. React.* **1992**, *42*, 335; Dembinski, R. *Eur. J. Org. Chem.* **2004**, 2763. Typically, the compound is reacted with an activating agent, for example diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD), and a phosphine reagent, for example triphenylphosphine or tributylphosphine, in an inert solvent, for example THF, dichloromethane, toluene or DMF, at a temperature between 0°C and the boiling point of the solvent employed.

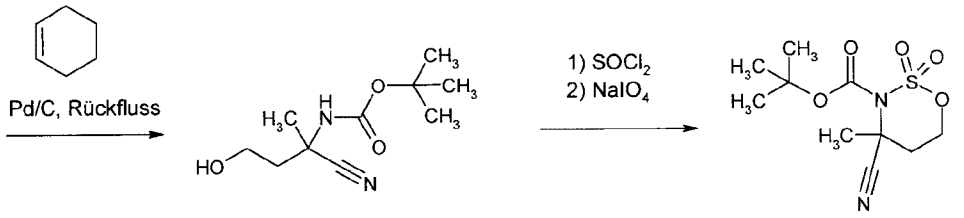
Further Working Examples can be prepared by methods known from the literature and familiar to the person skilled in the art, as shown in Schemes 6 – 17.

Synthesis of the Amines:

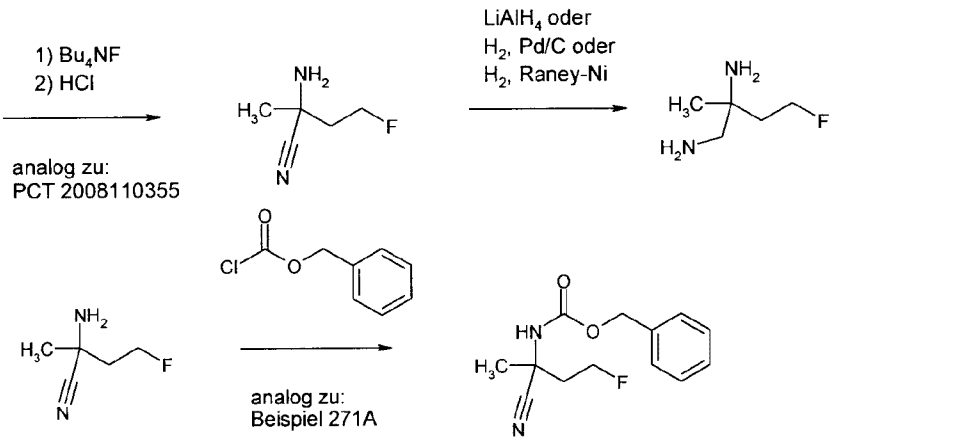
Scheme 6:

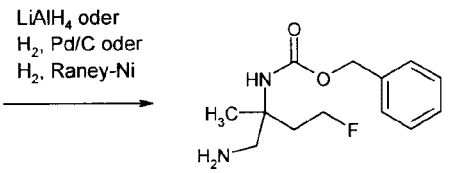


Beispiel 260A

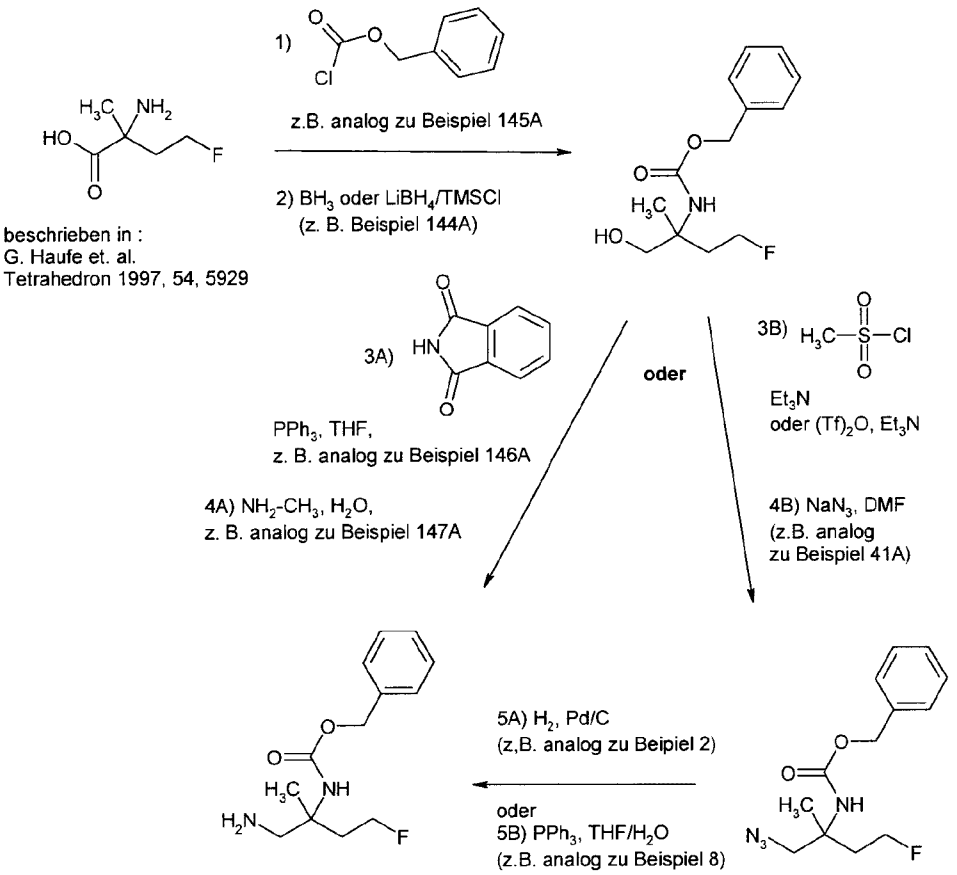


analog zu:
T. A. Moss et al. Angewandte Chemie Int. Ed, 2010, 49, 56
and F. Galaud et al., Heterocycles 2008, Vol. 76, No. 2, 112

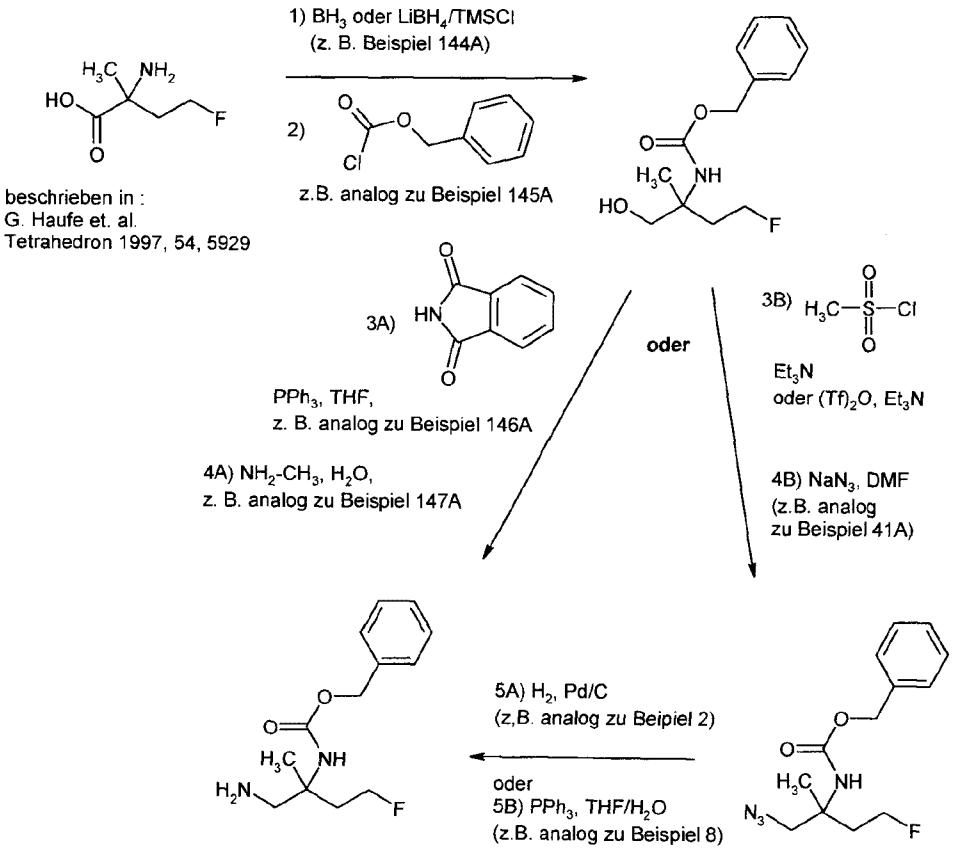




Scheme 7:

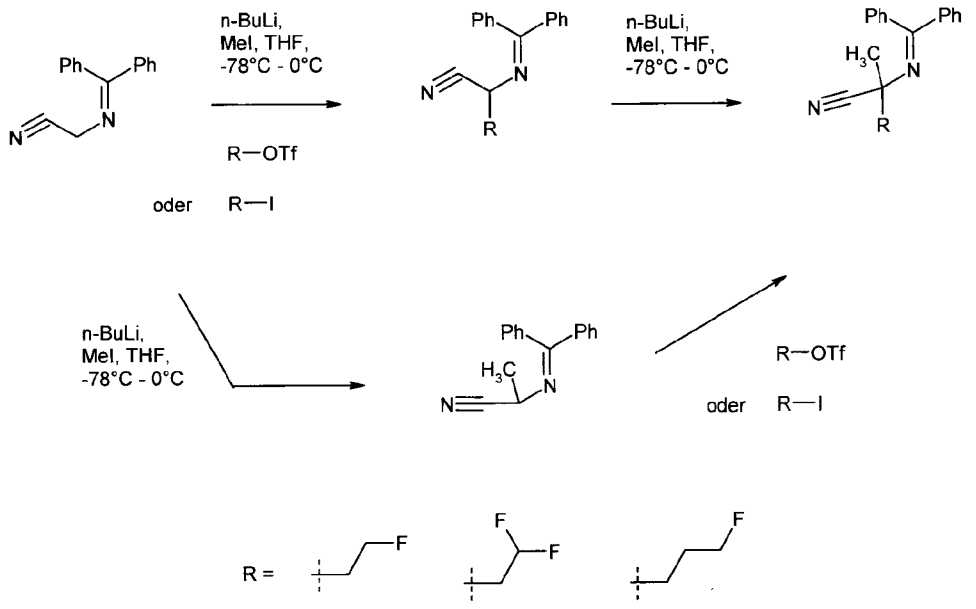

1)
z.B. analog zu Beispiel 145A
2) BH3 oder LiBH4/TMSCl
(z. B. Beispiel 144A)
beschrieben in :
G. Haufe et. al.
Tetrahedron 1997, 54, 5929
3A)
PPh3, THF,
z. B. analog zu Beispiel 146A
4A) NH2-CH3, H2O,
z. B. analog zu Beispiel 147A
oder
3B)
Et3N
oder (Tf)2O, Et3N
4B) NaN3, DMF
(z.B. analog
zu Beispiel 41A)
5A) H2, Pd/C
(z,B. analog zu Beipiel 2)
oder
5B) PPh3, THF/H2O
(z.B. analog zu Beispiel 8)

Scheme 8:

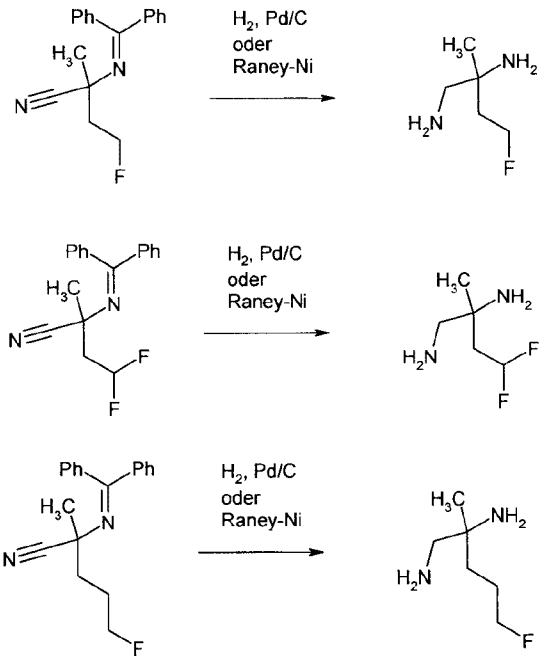

1) BH3 oder LiBH4/TMSCl
(z. B. Beispiel 144A)
2)
z.B. analog zu Beispiel 145A
beschrieben in :
G. Haufe et. al.
Tetrahedron 1997, 54, 5929
3A)
PPh3, THF,
z. B. analog zu Beispiel 146A
oder
3B)
Et3N
oder (Tf)2O, Et3N
4A) NH2-CH3, H2O,
z. B. analog zu Beispiel 147A
4B) NaN3, DMF
(z.B. analog
zu Beispiel 41A)
5A) H2, Pd/C
(z,B. analog zu Beipiel 2)
oder
5B) PPh3, THF/H2O
(z.B. analog zu Beispiel 8)

Scheme 9:

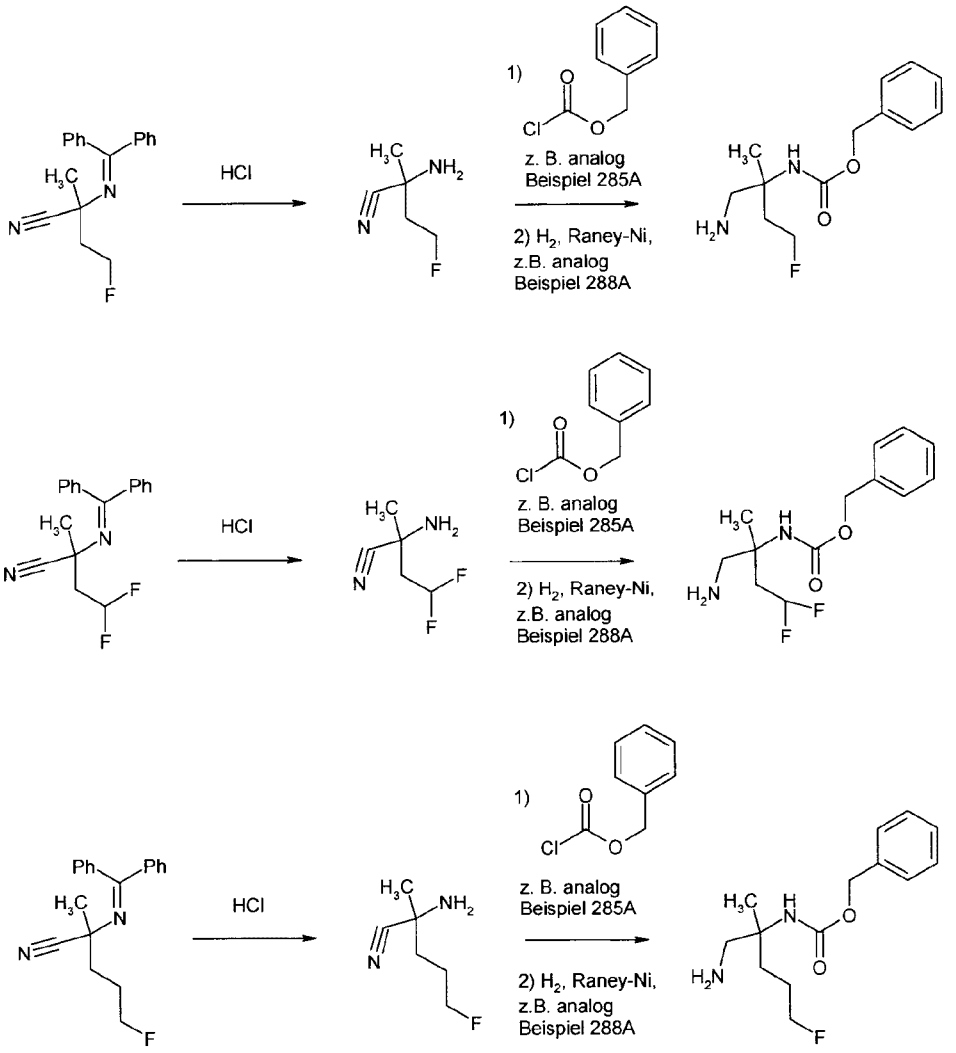
analog zu:
A. Perosa et al. J.Chem. Soc. Perkin Trans 2,1999, 2485 oder
J. O. Opio et al. Synthetic Communications 1991, 21, 1743



Scheme 10:

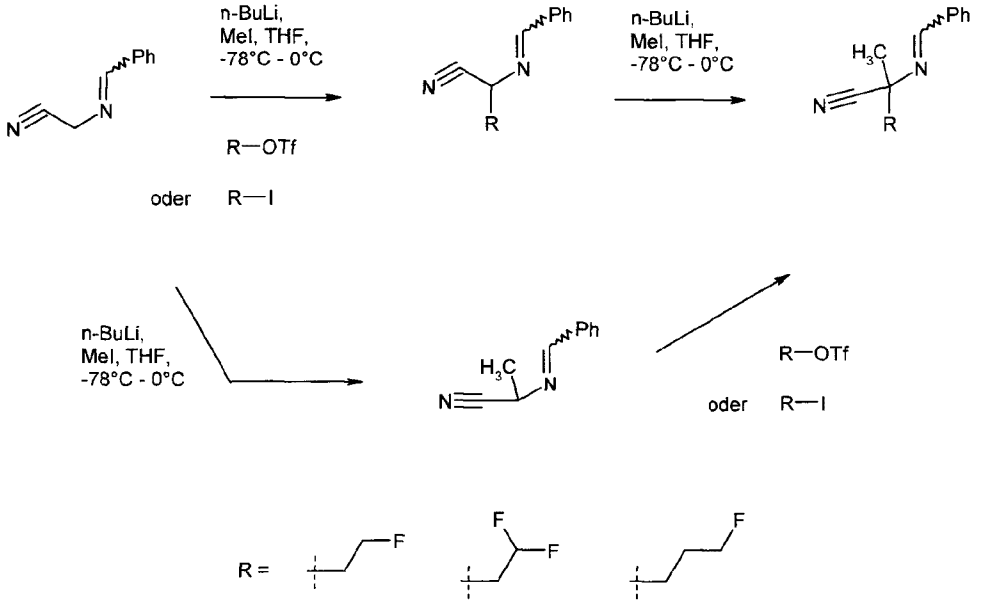


Scheme11:

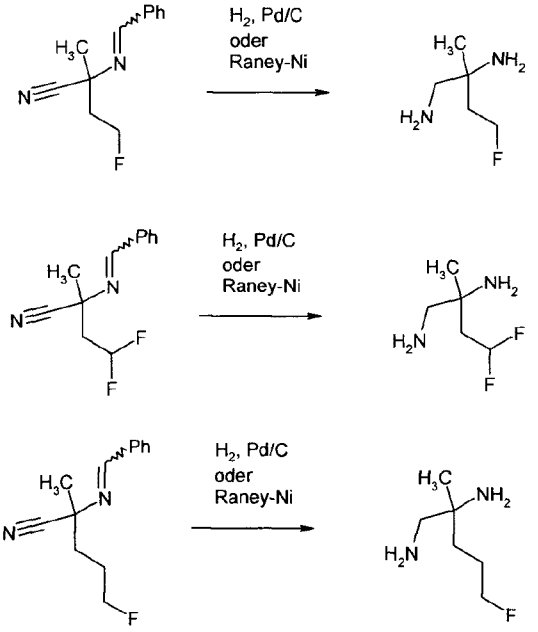

HCl
1)
z. B. analog Beispiel 285A
2) H2, Raney-Ni, z.B. analog Beispiel 288A
HCl
1)
z. B. analog Beispiel 285A
2) H2, Raney-Ni, z.B. analog Beispiel 288A
HCl
1)
z. B. analog Beispiel 285A
2) H2, Raney-Ni, z.B. analog Beispiel 288A

Scheme 12:

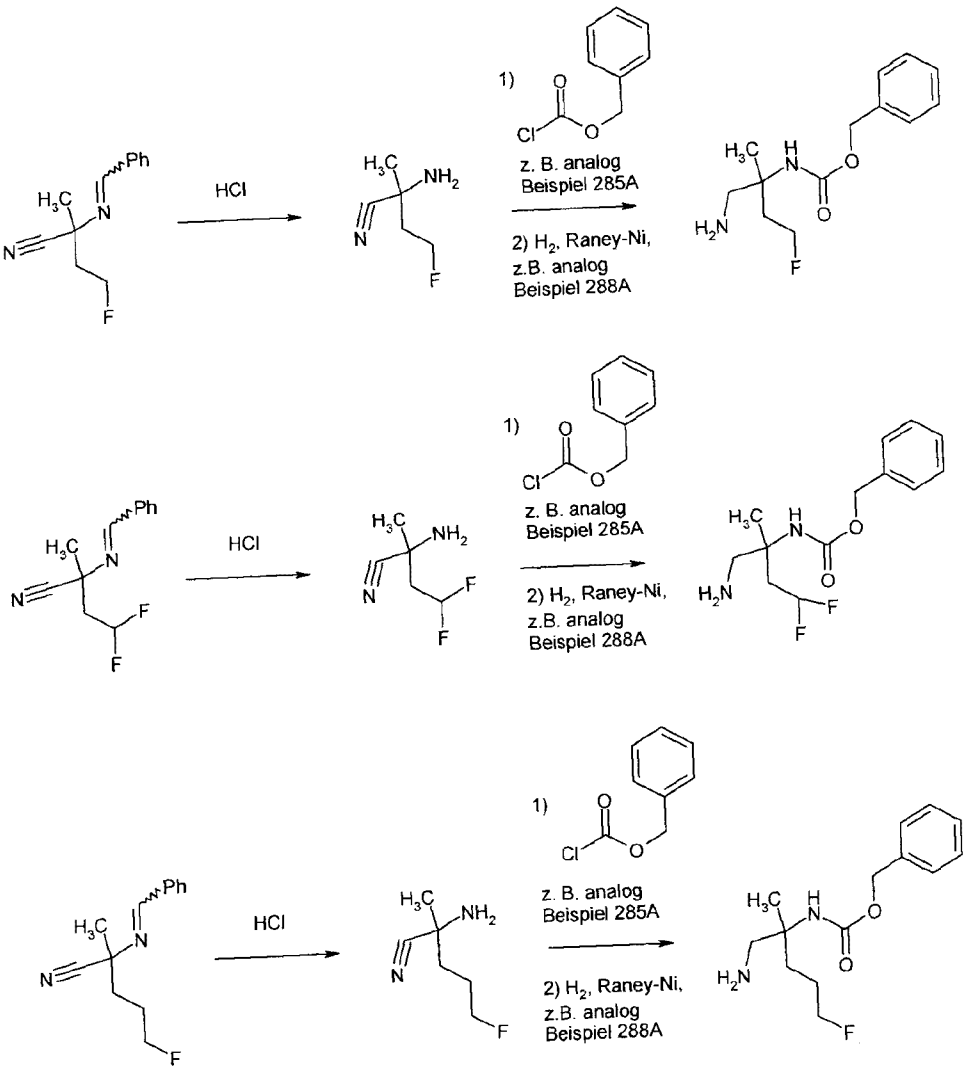
analog zu:
A. Perosa et al. J.Chem. Soc. Perkin Trans 2,1999, 2485 oder
J. O. Opio et al. Synthetic Communications 1991, 21, 1743 oder
O. Tsuge et al. Bulletin of the Chemical Society 1987, 60, 3347



Scheme 13:



Scheme 14:

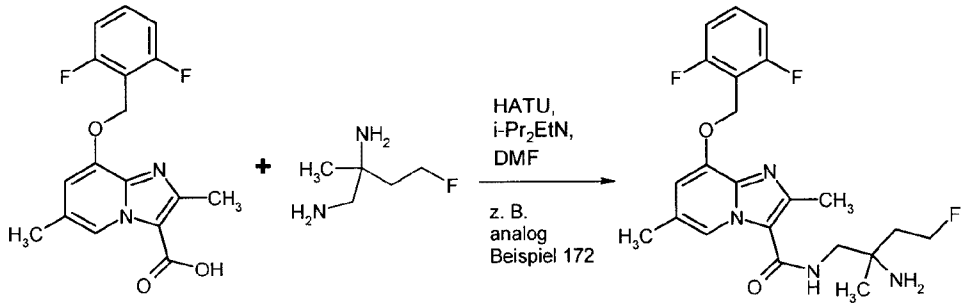


5

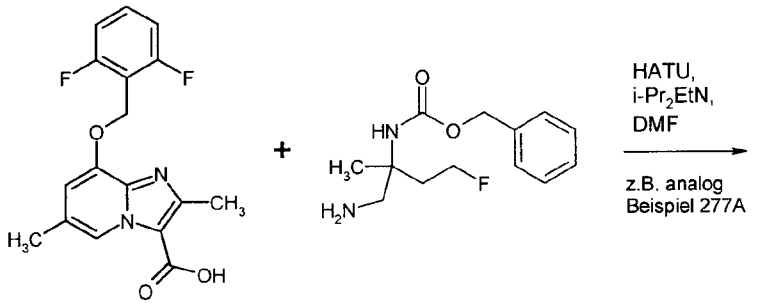
10

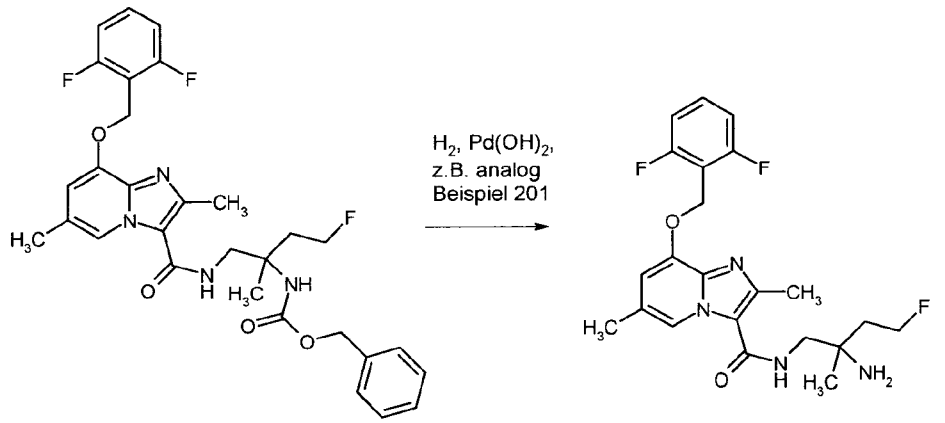
Synthesis oft the Working Examples:

Scheme 15:

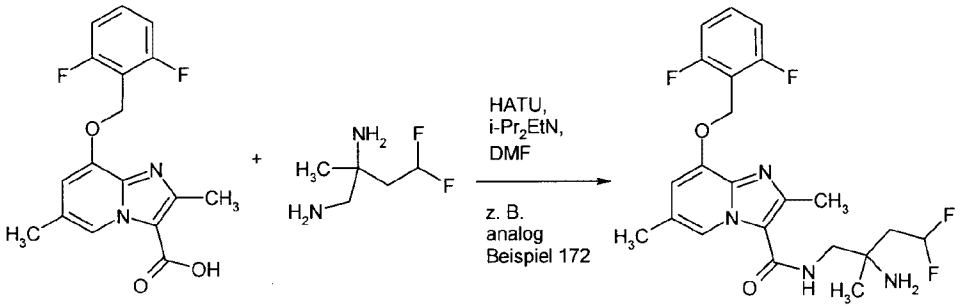


or:

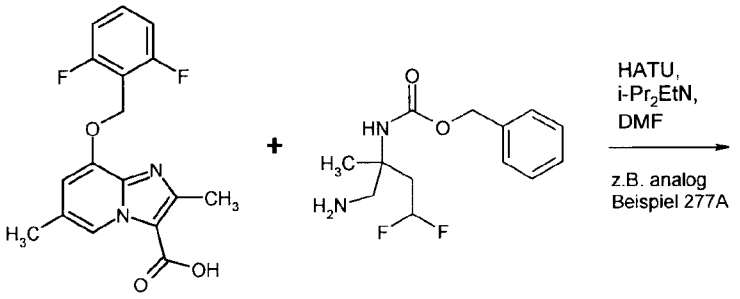


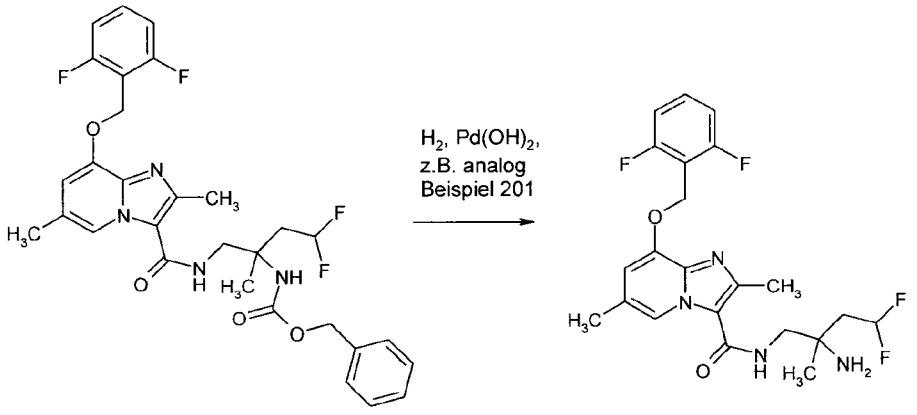


Scheme 16:

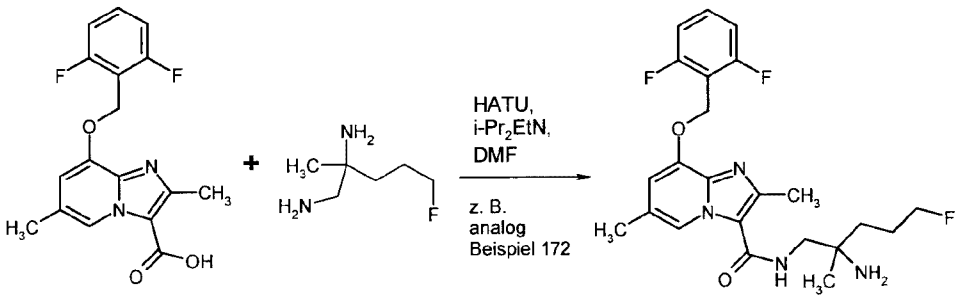

HATU,
i-Pr2EtN,
DMF
z. B.
analog
Beispiel 172

or:

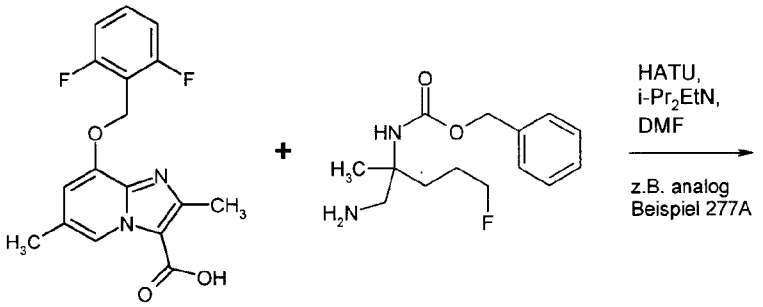

HATU,
i-Pr2EtN,
DMF
z.B. analog
Beispiel 277A

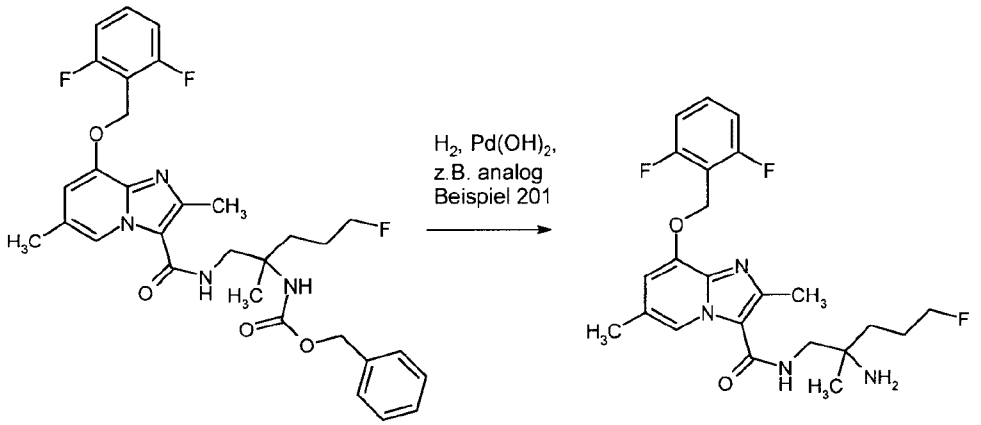

H2, Pd(OH)2,
z.B. analog
Beispiel 201

Scheme 17:



or:





Further compounds according to the invention can optionally also be prepared by converting functional groups of individual substituents, in particular those listed under R^3, starting with the compounds of the formula (I) obtained by the above processes. These conversions are carried out by customary methods known to the person skilled in the art and include, for example, reactions such as nucleophilic and electrophilic substitutions, oxidations, reductions, hydrogenations, transition metal-catalyzed coupling reactions, eliminations, alkylation, amination, esterification,

ester cleavage, etherification, ether cleavage, formation of carboxamides, and also the introduction and removal of temporary protective groups.

The compounds according to the invention have useful pharmacological properties and can be employed for the prevention and treatment of disorders in humans and animals. The compounds according to the invention open up a further treatment alternative and are therefore an enrichment of pharmacy.

The compounds according to the invention bring about vessel relaxation and inhibition of thrombocyte aggregation and lead to a lowering of blood pressure and to an increase in coronary blood flow. These effects are due to direct stimulation of soluble guanylate cyclase and an increase in intracellular cGMP. Moreover, the compounds according to the invention intensify the action of substances that raise the cGMP level, for example EDRF (endothelium-derived relaxing factor), NO donors, protoporphyrin IX, arachidonic acid or phenylhydrazine derivatives.

The compounds according to the invention are suitable for the treatment and/or prophylaxis of cardiovascular, pulmonary, thromboembolic and fibrotic diseases.

The compounds according to the invention can therefore be used in medicinal products for the treatment and/or prophylaxis of cardiovascular diseases, for example high blood pressure (hypertension), resistant hypertension, acute and chronic heart failure, coronary heart disease, stable and unstable angina pectoris, peripheral and cardiac vascular diseases, arrhythmias, disturbances of atrial and ventricular rhythm and conduction disturbances, for example atrioventricular blocks of degree I-III (AVB I-III), supraventricular tachyarrhythmia, atrial fibrillation, atrial flutter, ventricular fibrillation, ventricular flutter, ventricular tachyarrhythmia, torsade-de-pointes tachycardia, atrial and ventricular extrasystoles, AV-junction extrasystoles, sick-sinus syndrome, syncopes, AV-node reentry tachycardia, Wolff-Parkinson-White syndrome, acute coronary syndrome (ACS), autoimmune heart diseases (pericarditis, endocarditis, valvulitis, aortitis, cardiomyopathies), shock such as cardiogenic shock, septic shock and anaphylactic shock, aneurysms, Boxer cardiomyopathy (premature ventricular contraction (PVC)), for the treatment and/or prophylaxis of thromboembolic diseases and ischaemias such as myocardial ischaemia, myocardial infarction, stroke, cardiac hypertrophy, transient ischaemic attacks, preeclampsia, inflammatory cardiovascular diseases, spasms of the coronary arteries and peripheral arteries, development of oedema, for example pulmonary oedema, cerebral oedema, renal oedema or oedema due to heart failure, peripheral perfusion disturbances, reperfusion injury, arterial and venous thromboses, microalbuminuria, myocardial insufficiency, endothelial dysfunction, for preventing restenoses such as after thrombolysis therapies, percutaneous transluminal angioplasty (PTA), transluminal coronary angioplasty (PTCA), heart transplant and bypass operations, and micro- and macrovascular damage (vasculitis), increased level of fibrinogen and of low-density

LDL and increased concentrations of plasminogen activator inhibitor 1 (PAI-1), and for the treatment and/or prophylaxis of erectile dysfunction and female sexual dysfunction.

In the sense of the present invention, the term heart failure comprises both acute and chronic manifestations of heart failure, as well as more specific or related forms of disease such as acute decompensated heart failure, right ventricular failure, left ventricular failure, total heart failure, ischaemic cardiomyopathy, dilatated cardiomyopathy, hypertrophic cardiomyopathy, idiopathic cardiomyopathy, congenital heart defects, heart failure with valvular defects, mitral valve stenosis, mitral valve insufficiency, aortic valve stenosis, aortic valve insufficiency, tricuspid stenosis, tricuspid insufficiency, pulmonary valve stenosis, pulmonary valve insufficiency, combined valvular defects, heart muscle inflammation (myocarditis), chronic myocarditis, acute myocarditis, viral myocarditis, diabetic heart failure, alcoholic cardiomyopathy, storage cardiomyopathies, diastolic heart failure and also systolic heart failure and acute phases of an existing chronic heart failure (worsening heart failure).

In addition, the compounds according to the invention can also be used for the treatment and/or prophylaxis of arteriosclerosis, disturbances of lipid metabolism, hypolipoproteinaemias, dyslipidaemias, hypertriglyceridaemias, hyperlipidaemias, hypercholesterolaemias, abetalipoproteinaemia, sitosterolaemia, xanthomatosis, Tangier disease, adiposity, obesity, and combined hyperlipidaemias and metabolic syndrome.

Moreover, the compounds according to the invention can be used for the treatment and/or prophylaxis of primary and secondary Raynaud phenomenon, microcirculation disturbances, claudication, peripheral and autonomic neuropathies, diabetic microangiopathies, diabetic retinopathy, diabetic limb ulcers, gangrene, CREST syndrome, erythematous disorders, onychomycosis, rheumatic diseases and for promoting wound healing.

Furthermore, the compounds according to the invention are suitable for treating urological diseases, for example benign prostatic syndrome (BPS), benign prostatic hyperplasia (BPH), benign prostatic enlargement (BPE), bladder outlet obstruction (BOO), lower urinary tract syndromes (LUTS, including feline urological syndrome (FUS)), diseases of the urogenital system including neurogenic overactive bladder (OAB) and (IC), urinary incontinence (UI) for example mixed, urge, stress, or overflow incontinence (MUI, UUI, SUI, OUI), pelvic pains, benign and malignant diseases of the organs of the male and female urogenital system.

Furthermore, the compounds according to the invention are suitable for the treatment and/or prophylaxis of kidney diseases, in particular acute and chronic renal insufficiency, and acute and chronic renal failure. In the sense of the present invention, the term renal insufficiency comprises both acute and chronic manifestations of renal insufficiency, as well as underlying or related

kidney diseases such as renal hypoperfusion, intradialytic hypotension, obstructive uropathy, glomerulopathies, glomerulonephritis, acute glomerulonephritis, glomerulosclerosis, tubulointerstitial diseases, nephropathic diseases such as primary and congenital kidney disease, nephritis, immunological kidney diseases such as kidney transplant rejection, immune complex–induced kidney diseases, nephropathy induced by toxic substances, contrast medium–induced nephropathy, diabetic and non-diabetic nephropathy, pyelonephritis, renal cysts, nephrosclerosis, hypertensive nephrosclerosis and nephrotic syndrome, which can be characterized diagnostically for example by abnormally reduced creatinine and/or water excretion, abnormally increased blood concentrations of urea, nitrogen, potassium and/or creatinine, altered activity of renal enzymes such as e.g. glutamyl synthetase, altered urine osmolarity or urine volume, increased microalbuminuria, macroalbuminuria, lesions of glomeruli and arterioles, tubular dilatation, hyperphosphataemia and/or need for dialysis. The present invention also comprises the use of the compounds according to the invention for the treatment and/or prophylaxis of sequelae of renal insufficiency, for example pulmonary oedema, heart failure, uraemia, anaemia, electrolyte disturbances (e.g. hyperkalaemia, hyponatraemia) and disturbances in bone and carbohydrate metabolism.

Furthermore, the compounds according to the invention are also suitable for the treatment and/or prophylaxis of asthmatic diseases, pulmonary arterial hypertension (PAH) and other forms of pulmonary hypertension (PH), comprising pulmonary hypertension associated with left ventricular disease, HIV, sickle cell anaemia, thromboembolism (CTEPH), sarcoidosis, COPD or pulmonary fibrosis, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), acute lung injury (ALI), alpha-1-antitrypsin deficiency (AATD), pulmonary fibrosis, pulmonary emphysema (e.g. smoking-induced pulmonary emphysema) and cystic fibrosis (CF).

The compounds described in the present invention are also active substances for controlling diseases in the central nervous system that are characterized by disturbances of the NO/cGMP system. In particular, they are suitable for improving perception, capacity for concentration, capacity for learning or memory performance after cognitive disturbances, such as occur in particular in situations/diseases/syndromes such as mild cognitive impairment, age-related learning and memory disturbances, age-related memory loss, vascular dementia, head injury, stroke, post-stroke dementia, post-traumatic head injury, general disturbances of concentration, disturbances of concentration in children with learning and memory problems, Alzheimer's disease, Lewy body dementia, dementia with frontal lobe degeneration including Pick's syndrome, Parkinson's disease, progressive nuclear palsy, dementia with corticobasal degeneration, amyotrophic lateral sclerosis (ALS), Huntington's disease, demyelination, multiple sclerosis, thalamic degeneration, Creutzfeldt-Jakob dementia, HIV-dementia, schizophrenia with dementia or Korsakoff psychosis. They are also suitable for the treatment and/or prophylaxis of diseases of the central nervous system such as

anxiety, tension and depression, CNS-related sexual dysfunctions and sleep disturbances and for controlling pathological eating disorders and use of luxury foods and addictive drugs.

Furthermore, the compounds according to the invention are also suitable for controlling cerebral perfusion and are effective agents for combating migraines. They are also suitable for the prophylaxis and control of consequences of cerebral infarctions (apoplexia cerebri) such as stroke, cerebral ischaemias and head injury. The compounds according to the invention can also be used for controlling pain states and tinnitus.

In addition, the compounds according to the invention possess anti-inflammatory action and can therefore be used as anti-inflammatory agents for the treatment and/or prophylaxis of sepsis (SIRS), multiple organ failure (MODS, MOF), inflammatory diseases of the kidney, chronic intestinal inflammations (IBD, Crohn's disease, UC), pancreatitis, peritonitis, rheumatoid diseases, inflammatory skin diseases and inflammatory eye diseases.

Moreover, the compounds according to the invention can also be used for the treatment and/or prophylaxis of autoimmune diseases.

Furthermore, the compounds according to the invention are suitable for the treatment and/or prophylaxis of fibrotic diseases of the internal organs, for example of the lung, heart, kidney, bone marrow and in particular of the liver, and dermatological fibroses and fibrotic diseases of the eye. In the sense of the present invention, the term fibrotic diseases comprises in particular the following terms: hepatic fibrosis, hepatic cirrhosis, pulmonary fibrosis, endomyocardial fibrosis, nephropathy, glomerulonephritis, interstitial renal fibrosis, fibrotic lesions as a consequence of diabetes, bone marrow fibrosis and similar fibrotic diseases, scleroderma, morphea, keloids, hypertrophic scars (including after surgery), naevi, diabetic retinopathy, proliferative vitreoretinopathy and connective tissue diseases (e.g. sarcoidosis).

Furthermore, the compounds according to the invention are suitable for controlling postoperative scarring, e.g. as a result of glaucoma operations.

The compounds according to the invention can also be used cosmetically for ageing and keratinizing skin.

Moreover, the compounds according to the invention are suitable for the treatment and/or prophylaxis of hepatitis, neoplasms, osteoporosis, glaucoma and gastroparesis.

The present invention further relates to the use of the compounds according to the invention for the treatment and/or prophylaxis of diseases, in particular the aforementioned diseases.

The present invention further relates to the use of the compounds according to the invention for the treatment and/or prophylaxis of heart failure, angina pectoris, hypertension, pulmonary hypertension, ischaemias, vascular diseases, renal insufficiency, thromboembolic diseases, fibrotic diseases and arteriosclerosis.

The present invention further relates to the compounds according to the invention for use in a method for the treatment and/or prophylaxis of heart failure, angina pectoris, hypertension, pulmonary hypertension, ischaemias, vascular diseases, renal insufficiency, thromboembolic diseases, fibrotic diseases and arteriosclerosis.

The present invention further relates to the use of the compounds according to the invention for producing a medicinal product for the treatment and/or prophylaxis of diseases, in particular the aforementioned diseases.

The present invention further relates to the use of the compounds according to the invention for producing a medicinal product for the treatment and/or prophylaxis of heart failure, angina pectoris, hypertension, pulmonary hypertension, ischaemias, vascular diseases, renal insufficiency, thromboembolic diseases, fibrotic diseases and arteriosclerosis.

The present invention further relates to a method for the treatment and/or prophylaxis of diseases, in particular the aforementioned diseases, using an effective amount of at least one of the compounds according to the invention.

The present invention further relates to a method for the treatment and/or prophylaxis of heart failure, angina pectoris, hypertension, pulmonary hypertension, ischaemias, vascular diseases, renal insufficiency, thromboembolic diseases, fibrotic diseases and arteriosclerosis, using an effective amount of at least one of the compounds according to the invention.

The compounds according to the invention can be used alone or in combination with other active substances if necessary. The present invention further relates to medicinal products containing at least one of the compounds according to the invention and one or more further active substances, in particular for the treatment and/or prophylaxis of the aforementioned diseases. As suitable combination active substances, we may mention for example and preferably:

- organic nitrates and NO-donors, for example sodium nitroprusside, nitroglycerin, isosorbide mononitrate, isosorbide dinitrate, molsidomine or SIN-1, and inhalational NO;

- compounds that inhibit the degradation of cyclic guanosine monophosphate (cGMP), for example inhibitors of phosphodiesterases (PDE) 1, 2 and/or 5, in particular PDE-5 inhibitors such as sildenafil, vardenafil and tadalafil;

- antithrombotic agents, for example and preferably from the group of platelet aggregation inhibitors, anticoagulants or profibrinolytic substances;

- active substances for lowering blood pressure, for example and preferably from the group of calcium antagonists, angiotensin AII antagonists, ACE inhibitors, endothelin antagonists, renin inhibitors, alpha-blockers, beta-blockers, mineralocorticoid receptor antagonists and diuretics; and/or

- active substances that alter fat metabolism, for example and preferably from the group of thyroid receptor agonists, cholesterol synthesis inhibitors such as for example and preferably HMG-CoA-reductase or squalene synthesis inhibitors, ACAT inhibitors, CETP inhibitors, MTP inhibitors, PPAR-alpha, PPAR-gamma and/or PPAR-delta agonists, cholesterol absorption inhibitors, lipase inhibitors, polymeric bile acid adsorbers, bile acid reabsorption inhibitors and lipoprotein(a) antagonists.

Antithrombotic agents are preferably to be understood as compounds from the group of platelet aggregation inhibitors, anticoagulants or profibrinolytic substances.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a platelet aggregation inhibitor, for example and preferably aspirin, clopidogrel, ticlopidine or dipyridamole.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a thrombin inhibitor, for example and preferably ximelagatran, dabigatran, melagatran, bivalirudin or Clexane.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a GPIIb/IIIa antagonist, for example and preferably tirofiban or abciximab.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a factor Xa inhibitor, for example and preferably rivaroxaban (BAY 59-7939), DU-176b, apixaban, otamixaban, fidexaban, razaxaban, fondaparinux, idraparinux, PMD-3112, YM-150, KFA-1982, EMD-503982, MCM-17, MLN-1021, DX 9065a, DPC 906, JTV 803, SSR-126512 or SSR-128428.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with heparin or a low molecular weight (LMW) heparin derivative.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a vitamin K antagonist, for example and preferably coumarin.

The agents for lowering blood pressure are preferably to be understood as compounds from the group of calcium antagonists, angiotensin AII antagonists, ACE inhibitors, endothelin antagonists, renin inhibitors, alpha-blockers, beta-blockers, mineralocorticoid-receptor antagonists and diuretics.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a calcium antagonist, for example and preferably nifedipine, amlodipine, verapamil or diltiazem.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an alpha-1-receptor blocker, for example and preferably prazosin.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a beta-blocker, for example and preferably propranolol, atenolol, timolol, pindolol, alprenolol, oxprenolol, penbutolol, bupranolol, metipranolol, nadolol, mepindolol, carazolol, sotalol, metoprolol, betaxolol, celiprolol, bisoprolol, carteolol, esmolol, labetalol, carvedilol, adaprolol, landiolol, nebivolol, epanolol or bucindolol.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an angiotensin AII antagonist, for example and preferably losartan, candesartan, valsartan, telmisartan or embursatan.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an ACE inhibitor, for example and preferably enalapril, captopril, lisinopril, ramipril, delapril, fosinopril, quinopril, perindopril or trandopril.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an endothelin antagonist, for example and preferably bosentan, darusentan, ambrisentan or sitaxsentan.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a renin inhibitor, for example and preferably aliskiren, SPP-600 or SPP-800.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a mineralocorticoid-receptor antagonist, for example and preferably spironolactone or eplerenone.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a loop diuretic, for example furosemide, torasemide, bumetanide

and piretanide, with potassium-sparing diuretics for example amiloride and triamterene, with aldosterone antagonists, for example spironolactone, potassium canrenoate and eplerenone and thiazide diuretics, for example hydrochlorothiazide, chlorthalidone, xipamide, and indapamide.

Agents altering fat metabolism are preferably to be understood as compounds from the group of CETP inhibitors, thyroid receptor agonists, cholesterol synthesis inhibitors such as HMG-CoA-reductase or squalene synthesis inhibitors, the ACAT inhibitors, MTP inhibitors, PPAR-alpha, PPAR-gamma and/or PPAR-delta agonists, cholesterol-absorption inhibitors, polymeric bile acid adsorbers, bile acid reabsorption inhibitors, lipase inhibitors and the lipoprotein(a) antagonists.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a CETP inhibitor, for example and preferably dalcetrapib, BAY 60-5521, anacetrapib or CETP-vaccine (CETi-1).

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a thyroid receptor agonist, for example and preferably D-thyroxin, 3,5,3'-triiodothyronin (T3), CGS 23425 or axitirome (CGS 26214).

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an HMG-CoA-reductase inhibitor from the class of statins, for example and preferably lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, rosuvastatin or pitavastatin.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a squalene synthesis inhibitor, for example and preferably BMS-188494 or TAK-475.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an ACAT inhibitor, for example and preferably avasimibe, melinamide, pactimibe, eflucimibe or SMP-797.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with an MTP inhibitor, for example and preferably implitapide, BMS-201038, R-103757 or JTT-130.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a PPAR-gamma agonist, for example and preferably pioglitazone or rosiglitazone.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a PPAR-delta agonist, for example and preferably GW 501516 or BAY 68-5042.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a cholesterol-absorption inhibitor, for example and preferably ezetimibe, tiqueside or pamaqueside.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a lipase inhibitor, for example and preferably orlistat.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a polymeric bile acid adsorber, for example and preferably cholestyramine, colestipol, colesolvam, CholestaGel or colestimide.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a bile acid reabsorption inhibitor, for example and preferably ASBT (= IBAT) inhibitors, e.g. AZD-7806, S-8921, AK-105, BARI-1741, SC-435 or SC-635.

In a preferred embodiment of the invention, the compounds according to the invention are administered in combination with a lipoprotein(a) antagonist, for example and preferably gemcabene calcium (CI-1027) or nicotinic acid.

The present invention further relates to medicinal products that contain at least one compound according to the invention, usually together with one or more inert, non-toxic, pharmaceutically suitable excipients, and use thereof for the aforementioned purposes.

The compounds according to the invention can have systemic and/or local action. For this purpose they can be applied in a suitable way, e.g. by oral, parenteral, pulmonary, nasal, sublingual, lingual, buccal, rectal, dermal, transdermal, conjunctival, or otic administration or as implant or stent.

For these routes of application, the compounds according to the invention can be administered in suitable dosage forms.

Dosage forms functioning according to the prior art, for rapid and/or modified release of the compounds according to the invention, which contain the compounds according to the invention in crystalline and/or amorphized and/or dissolved form, e.g. tablets (uncoated or coated tablets, for example with enteric coatings or coatings with delayed dissolution or insoluble coatings, which control the release of the compound according to the invention), tablets or films/wafers that disintegrate rapidly in the oral cavity, films/lyophilizates, capsules (for example hard or soft gelatin

capsules), sugar-coated pills, granules, pellets, powders, emulsions, suspensions, aerosols or solutions, are suitable for oral administration.

Parenteral administration can take place avoiding an absorption step (e.g. intravenous, intraarterial, intracardiac, intraspinal or intralumbar) or including absorption (e.g. intramuscular, subcutaneous, intracutaneous, percutaneous or intraperitoneal). Injection and infusion preparations in the form of solutions, suspensions, emulsions, lyophilizates or sterile powders are suitable, among others, as dosage forms for parenteral application.

Inhaled pharmaceutical forms (including powder inhalers, nebulizers), nasal drops, solutions or sprays, tablets, films/wafers or capsules for lingual, sublingual or buccal application, suppositories, ear or eye preparations, vaginal capsules, aqueous suspensions (lotions, shaking mixtures), lipophilic suspensions, ointments, creams, transdermal therapeutic systems (e.g. patches), milk, pastes, foams, dusting powders, implants or stents for example are suitable for other routes of administration.

Oral or parenteral administration is preferred, especially oral administration.

The compounds according to the invention can be transformed to the aforementioned dosage forms. This can take place in a manner known per se by mixing with inert, non-toxic, pharmaceutically suitable excipients. These excipients include *inter alia* carriers (for example microcrystalline cellulose, lactose, mannitol), solvents (e.g. liquid polyethylene glycols), emulsifiers and dispersants or wetting agents (for example sodium dodecyl sulphate, polyoxysorbitan oleate), binders (for example polyvinylpyrrolidone), synthetic and natural polymers (for example albumin), stabilizers (e.g. antioxidants such as ascorbic acid), colorants (e.g. inorganic pigments, for example iron oxides) and taste and/or odour correctants.

In general, it has proved advantageous, in the case of parenteral administration, to administer amounts of about 0.001 to 1 mg/kg, preferably about 0.01 to 0.5 mg/kg body weight to achieve effective results. For oral application, the dosage is about 0.001 to 2 mg/kg, preferably about 0.001 to 1 mg/kg body weight.

Nevertheless, it may optionally be necessary to deviate from the stated amounts, namely depending on body weight, route of administration, individual response to the active substance, type of preparation and time point or interval when application takes place. Thus, in some cases it may be sufficient to use less than the aforementioned minimum amount, whereas in other cases the stated upper limit must be exceeded. When applying larger amounts, it may be advisable to distribute these in several individual doses throughout the day.

The following practical examples explain the invention. The invention is not limited to the examples.

The percentages in the following tests and examples are percentages by weight, unless stated otherwise; parts are parts by weight. Proportions of solvents, dilution ratios and concentrations for liquid/liquid solutions refer in each case to the volume.

A. Examples

Abbreviations and acronyms:

abs.	absolute (= dried)
aq.	aqueous solution
br	broad signal (NMR coupling pattern)
conc.	concentrated
δ	shift in the NMR spectrum (stated in ppm)
d	doublet (NMR coupling pattern)
DCI	direct chemical ionization (in MS)
DMAP	4-*N,N*-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethyl sulphoxide
ent	enantiomerically pure
eq.	equivalent(s)
ESI	electrospray ionization (in MS)
Et	ethyl
h	hour(s)
HATU	(1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo-[4,5-b]pyridinium 3-oxide hexafluorophosphate)
HPLC	high pressure, high performance liquid chromatography
HRMS	high resolution mass spectrometry
LC/MS	liquid chromatography-coupled mass spectrometry
LiHMDS	lithium hexamethyldisilazide
m	multiplet
Me	methyl
min	minute(s)
MS	mass spectrometry
NMR	nuclear magnetic resonance spectrometry

Ph	phenyl
q	quartet (NMR coupling pattern)
quint.	quintet (NMR coupling pattern)
rac	racemic
RT	room temperature
R_t	retention time (in HPLC)
s	singlet (NMR coupling pattern)
t	triplet (NMR coupling pattern)
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TBTU	(benzotriazol-1-yloxy)bisdimethylaminomethylium fluoroborate
UV	ultraviolet spectrometry
v/v	ratio by volume (of a solution)
XPHOS	dicyclohexyl-(2',4',6'-triisopropylbiphenyl-2-yl)phosphine

LC/MS and HPLC methods:

Method 1 (LC-MS):

Instrument: Micromass Quattro Premier with Waters UPLC Acquity; column: Thermo Hypersil GOLD 1.9 µ 50 x 1 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 90% A → 0.1 min 90% A → 1.5 min 10% A → 2.2 min 10% A oven: 50°C; flow rate: 0.33 ml/min; UV detection: 210 nm.

Method 2 (LC-MS):

Instrument: Waters ACQUITY SQD UPLC System; column: Waters Acquity UPLC HSS T3 1.8 µ 50 x 1 mm; mobile phase A: 1 l of water + 0.25 ml of 99% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.25 ml of 99% strength formic acid; gradient: 0.0 min 90% A → 1.2 min 5% A → 2.0 min 5% A oven: 50°C; flow rate: 0.40 ml/min; UV detection: 210 – 400 nm.

Method 3 (LC-MS):

MS instrument type: Waters Micromass Quattro Micro; HPLC instrument type: Agilent 1100 Series; column: Thermo Hypersil GOLD 3 µ 20 mm x 4 mm; mobile phase A: 1 l of water + 0.5 ml

of 50%- strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 100% A → 3.0 min 10% A → 4.0 min 10% A → 4.01 min 100% A (flow rate 2.5 ml/min) → 5.00 min 100% A; oven: 50°C; flow rate: 2 ml/min; UV detection: 210 nm.

Method 4 (DCI-MS):

Instrument: Thermo Fisher-Scientific DSQ; chemical ionization; reactant gas NH3; source temperature: 200°C; ionization energy 70eV.

Method 5 (LC-MS):

MS instrument type: Waters (Micromass) Quattro Micro; HPLC instrument type: Agilent 1100 Series; column: Thermo Hypersil GOLD 3 µ 20 x 4 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 100% A → 3.0 min 10% A → 4.0 min 10% A; oven: 50°C; flow rate: 2 ml/min; UV detection: 210 nm

Method 6 (GC-MS):

Instrument: Micromass GCT, GC6890; column: Restek RTX-35, 15 m x 200 µm x 0.33 µm; constant helium flow rate: 0.88 ml/min; oven: 70°C; inlet: 250°C; gradient: 70°C, 30°C/min → 310°C (maintained for 3 min).

Method 7 (LC-MS):

Instrument: Waters ACQUITY SQD UPLC System; column: Waters Acquity UPLC HSS T3 1.8 µ 30 x 2 mm; mobile phase A: 1 l of water + 0.25 ml of 99% strength formic acid , mobile phase B: 1 l of acetonitrile + 0.25 ml of 99% strength formic acid; gradient: 0.0 min 90% A → 1.2 min 5% A → 2.0 min 5% A oven: 50°C; flow rate: 0.60 ml/min; UV detection: 208 – 400 nm.

Method 8 (LC-MS):

MS instrument: Waters SQD; HPLC instrument: Waters UPLC; column: Zorbax SB-Aq (Agilent), 50 mm x 2.1 mm, 1.8 µm; mobile phase A: water + 0.025% formic acid, mobile phase B: acetonitrile (ULC) + 0.025% formic acid; gradient: 0.0 min 98%A - 0.9 min 25%A – 1.0 min 5%A - 1.4 min 5%A – 1.41 min 98%A – 1.5 min 98%A; oven: 40°C; flow rate: 0.600 ml/min; UV detection: DAD; 210 nm.

Method 9 (preparative HPLC):

Column: Macherey-Nagel VP 50/21 Nucleosil 100-5 C18 Nautilus. Flow rate: 25 ml/min. gradient: A = water + 0.1 % conc. aqueous ammonia, B = methanol, 0 min = 30 % B, 2 min = 30% B, 6 min = 100% B, 7 min = 100% B, 7.1 min = 30% B, 8 min = 30% B, flow rate 25 ml/min, UV detection 220 nm.

Method 10 (FIA/MS, ES):

Instrument: Waters ZQ 2000; electrospray ionization; mobile phase A: 1 l of water + 0.25 ml of 99% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.25 ml of 99% strength formic acid; 25% A, 75% B; flow rate: 0.25 ml/min

Method 11:

MS instrument: Waters (Micromass) Quattro Micro; HPLC instrument: Agilent 1100 Series; column: YMC-Triart C18 3 µ 50 x 3 mm; mobile phase A: 1 l of water + 0.01 mol of ammonium carbonate, mobile phase B: 1 l of acetonitrile; gradient: 0.0 min 100% A → 2.75 min 5% A → 4.5 min 5% A; oven: 40°C; flow rate: 1.25 ml/min; UV detection: 210 nm

Method 12 (preparative LC-MS):

MS instrument: Waters, HPLC instrument: Waters (column Waters X-Bridge C18, 18 mm x 50 mm, 5 µm, mobile phase A: water + 0.05% triethylamine, mobile phase B: acetonitrile (ULC) + 0.05% triethylamine, gradient: 0.0 min 95%A – 0.15 min 95%A – 8.0 min 5%A – 9.0 min 5%A; flow rate: 40 ml/min; UV detection: DAD; 210 – 400 nm).

or

MS instrument: Waters, HPLC instrument: Waters (column Phenomenex Luna 5µ C18(2) 100A, AXIA Tech. 50 x 21.2 mm, mobile phase A: water + 0.05% formic acid, mobile phase B: acetonitrile (ULC) + 0.05% formic acid, gradient: 0.0 min 95%A – 0.15 min 95%A – 8.0 min 5%A – 9.0 min 5%A; flow rate: 40 ml/min; UV detection: DAD; 210 – 400 nm).

Method 13

Instrument: Micromass Quattro Premier with Waters UPLC Acquity; column: Thermo Hypersil GOLD 1.9 µ 50 x 1 mm; mobile phase A: 1 l of water + 0.5 ml of 50% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.5 ml of 50% strength formic acid; gradient: 0.0 min 97% A → 0.5 min 97% A → 3.2 min 5% A → 4.0 min 5% A oven: 50°C; flow rate: 0.3 ml/min; UV-detection: 210 nm.

Method 14:

Instrument: Thermo Scientific DSQII, Thermo Scientific Trace GC Ultra; column: Restek RTX-35MS, 15 m x 200 µm x 0.33 µm; constant helium flow rate: 1.20 ml/min; oven: 60°C; inlet: 220°C; gradient: 60°C, 30°C/min → 300°C (maintained for 3.33 min).

Method 15:

MS instrument: Waters (Micromass) QM; HPLC instrument: Agilent 1100 Series; column: Agilent ZORBAX Extend-C18 3.0 x 50 mm 3.5-micron; mobile phase A: 1 l of water + 0.01 mol of

ammonium carbonate, mobile phase B: 1 l of acetonitrile; gradient: 0.0 min 98% A → 0.2 min 98% A → 3.0 min 5% A→ 4.5 min 5% A; oven: 40°C; flow rate: 1.75 ml/min; UV detection: 210 nm.

Method 16 (LC-MS):

Instrument: Agilent MS Quad 6150; HPLC: Agilent 1290; column: Waters Acquity UPLC HSS T3 1.8 µ 50 x 2.1 mm; mobile phase A: 1 l of water + 0.25 ml of 99% strength formic acid, mobile phase B: 1 l of acetonitrile + 0.25 ml of 99% strength formic acid; gradient: 0.0 min 90% A → 0.3 min 90% A → 1.7 min 5% A → 3.0 min 5% A oven: 50°C; flow rate: 1.20 ml/min; UV detection: 205 – 305 nm.

If compounds according to the invention are purified by preparative HPLC according to the methods described above where the mobile phases contain additives such as trifluoroacetic acid, formic acid or ammonia, the compounds according to the invention may be obtained in salt form, for example as trifluoroacetate, formate or ammonium salt, if the compounds according to the invention contain a functionality which is sufficiently basic or acidic. Such a salt may be converted by various methods known to the person skilled in the art into the corresponding free base or acid, respectively.

Salts may be present in substoichiometric or superstoichiometric amounts, in particular if an amine or a carboxylic acid is present. In addition, in the case of the present imidazopyridines, under acidic conditions there may always be salts present, even in substoichiometric amounts, without this being obvious from the ^{1}H NMR, and without particular indication and labelling of these in the respective IUPAC names and structural formulae.

All ^{1}H NMR spectra data indicate the chemical shifts δ in ppm.

The multiplicities of proton signals in the ^{1}H NMR spectra given in the paragraphs below indicate the signal form observed in each case and do not take into account any higher order signal phenomena.

The methyl group of the chemical system "2-methylimidazo[1,2-a]pyridine" appears in ^{1}H NMR spectra as a singlet (often in DMSO-d_6 and in the range of 2.40 – 2.60 ppm) and is either clearly recognizable as such, is superimposed by the solvent signals or is completely under the signals of the solvent. In the ^{1}H NMR spectra, this signal can be indicated by way of anticipation.

X-ray structure analysis:

Transmission diffractometer:	Bruker diffractometer with Apex-II-CCD detector
Radiation:	copper, K alpha

Primary monochromator:	focussing X-ray mirror
Messuring range:	4.73-67.08°
Room conditions:	20°C

General Working Procedures

Representative Working Procedure 1

Reduction of amino acids using lithium borohydride and chlorotrimethylsilane.

1.7-2.5 equivalents of lithium borohydride were initially charged in THF (about 0.1-0.5 M based on the amino acid), 3.4-5.0 equivalents of chlorotrimethylsilane were added (at 0°C or RT) and the mixture was stirred at RT for five to 30 min. 1 equivalent of the amino acid was then carefully added a little at a time at 0°C or RT and the reaction mixture was stirred at RT overnight.

Exemplary work-up of the reaction mixture: Methanol was added and the mixture was concentrated. A 20% potassium hydroxide solution was added to the residue and the mixture was extracted three times with dichloromethane. The combined organic phases were dried over sodium sulphate, filtered and concentrated.

Representative Working Procedure 2

Amide formation using TBTU as coupling agent.

1 equivalent of the carboxylic acid to be coupled (for example Example 3A), 1.1 – 1.5 equivalents of (benzotriazol-1-yloxy)bisdimethylaminomethylium fluoroborate (TBTU) and 3-6 equivalents of 4-methylmorpholine were initially charged in DMF or dichloromethane (about 0.1-0.2 M based on the carboxylic acid to be coupled). 1.1 to 1.5 equivalents of the amine to be coupled were then added, and the mixture was stirred at RT overnight.

Exemplary work-up of the reaction mixture: Water was added to the reaction solution and the precipitate formed stirred for 0.5-1.0 h, filtered off, washed thoroughly with water and dried under high vacuum overnight. Alternatively, the reaction mixture was concentrated directly, purified further by preparative HPLC and dried under high vacuum overnight.

If appropriate, the reaction mixture was filtered off and the precipitate was washed with diethyl ether and dried under high vacuum.

If appropriate, the reaction mixture was diluted with diethyl ether, the precipitate was filtered off and the filtrate was partitioned between ethyl acetate or dichloromethane and saturated aqueous sodium bicarbonate solution. The organic phase was washed with saturated aqueous sodium chloride solution, dried over sodium sulphate and filtered, and the filtrate was concentrated and dried under high vacuum.

Representative Working Procedure 3

Amide formation using HATU as coupling agent.

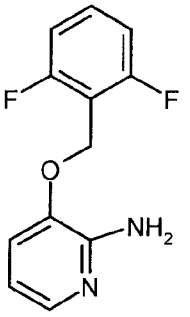
1 equivalent of the carboxylic acid to be coupled (for example Example 3A, 6A, 11A, 16A, 19A, 21A, 25A, 28A or 30A), 1.1 to 2.5 equivalents of *O*-(7-azabenzotriazol-1-yl)-*N,N,N'N'*-tetramethyluronium hexafluorophosphate (HATU) and 3 to 4 equivalents of *N,N*-diisopropylethylamine were initially charged in DMF (about 0.2 M based on the carboxylic acid to be coupled), 1.2 to 2.0 equivalents of the amine to be coupled were added and the mixture was stirred at RT overnight.

Exemplary work-up of the reaction mixture: Water was added to the reaction solution and the precipitate formed stirred for 30 min, filtered off, washed thoroughly with water and dried under high vacuum overnight. Alternatively, either directly after concentration under reduced pressure or after extractive work-up, the reaction mixture was purified further by preparative HPLC.

Starting materials and intermediates:

Example 1A

3-[(2,6-Difluorobenzyl)oxy]pyridine-2-amine

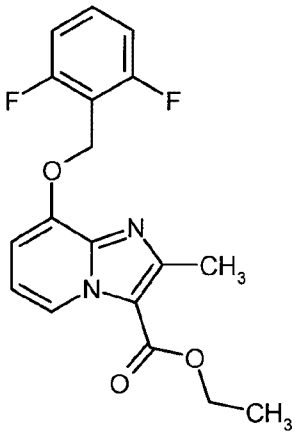


At RT, 51 g of sodium methoxide (953 mmol, 1.05 equivalents) were initially charged in 1000 ml of methanol, 100 g of 2-amino-3-hydroxypyridine (908 mmol, 1 equivalent) were added and the mixture was stirred at RT for another 15 min. The reaction mixture was concentrated under reduced pressure, the residue was taken up in 2500 ml of DMSO and 197 g of 2,6-difluorobenzyl bromide (953 mmol, 1.05 equivalents) were added. After 4 h at RT, the reaction mixture was poured into 20 l of water and stirred for 15 min, and the solid was filtered off. The solid was washed with 1 l of water, 100 ml of isopropanol and 500 ml of petroleum ether and dried under high vacuum. This gave 171 g of the title compound (78% of theory).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.10 (s, 2 H); 5.52 (br. s, 2 H), 6.52 (dd, 1 H); 7.16 – 7.21 (m, 3 H); 7.49 – 7.56 (m, 2 H).

Example 2A

Ethyl 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylate



170 g of 3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine (Example 1A; 719 mmol, 1 equivalent) were initially charged in 3800 ml of ethanol, and 151 g of powdered molecular sieve 3Å and 623 g of ethyl 2-chloroacetoacetate (3.6 mol, 5 equivalents) were added. The reaction mixture was heated at reflux for 24 h and then filtered off through silica gel and concentrated under reduced pressure. The mixture was kept at RT for 48 h, and the solid formed was filtered off. The solid was then stirred three times with a little isopropanol and then filtered off and washed with diethyl ether. This gave 60.8 g (23% of theory) of the title compound. The combined filtrates of the filtration steps were concentrated and the residue was chromatographed on silica gel using cyclohexane/diethyl ether as mobile phase. This gave a further 46.5 g (18% of theory; total yield: 41% of theory) of the title compound.

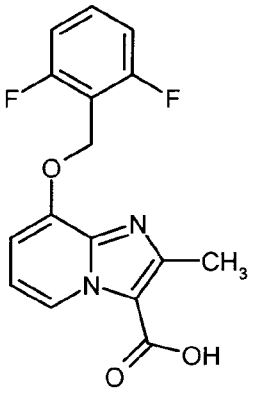
LC-MS (Method 2): R_t = 1.01 min

MS (ESpos): m/z = 347 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.36 (t, 3 H); 2.54 (s, 3 H; obscured by DMSO signal); 4.36 (q, 2 H); 5.33 (s, 2 H); 7.11 (t, 1 H); 7.18 – 7.27 (m, 3 H); 7.59 (quint, 1 H); 8.88 (d, 1 H).

Example 3A

8-[(2,6-Difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid



107 g of ethyl 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylate (Example 2A; 300 mmol, 1 equivalent) were dissolved in 2.8 l of THF/methanol (1:1), 1.5 l of 1 N aqueous lithium hydroxide solution (1.5 mol, 5 equivalents) were added and the mixture was stirred at RT for 16 h. The organic solvents were removed under reduced pressure and the resulting aqueous solution was adjusted in an ice bath to pH 3-4 using 1 N aqueous hydrochloric acid. The resulting solid was filtered off, washed with water and isopropanol and dried under reduced pressure. This gave 92 g (95% of theory) of the title compound.

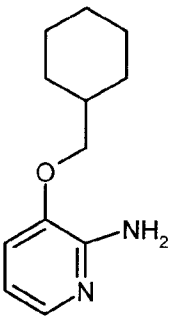
LC-MS (Method 2): R_t = 0.62 min

MS (ESpos): m/z = 319.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.55 (s, 3 H; superimposed by DMSO signal); 5.32 (s, 2 H); 7.01 (t, 1 H); 7.09 (d, 1 H); 7.23 (t, 2 H); 7.59 (quint, 1 H); 9.01 (d, 1 H).

Example 4A

3-(Cyclohexylmethoxy)pyridine-2-amine



At RT, 96 g of sodium hydroxide 45% strength in water (1081 mmol, 1 equivalent) were initially charged in 1170 ml of methanol, 119 g of 2-amino-3-hydroxypyridine (1080 mmol, 1 equivalent)

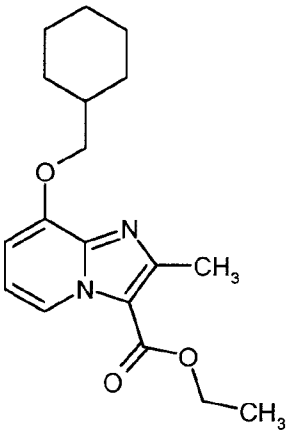
were added and the mixture was stirred at RT for 10 min. The reaction mixture was concentrated under reduced pressure, the residue was taken up in 2900 ml of DMSO and 101 g of cyclohexylmethyl bromide (1135 mmol, 1.05 equivalents) were added. After 16 h at RT, the reaction mixture was added slowly to 6 l of water and the aqueous solution was extracted twice with in each case 2 l of ethyl acetate. The combined organic phases were washed with in each case 1 l of saturated aqueous sodium bicarbonate solution and water, dried, filtered and concentrated. The residue was triturated with 500 ml of n-pentane, filtered and dried under reduced pressure. This gave 130 g (58% of theory) of the title compound.

LC-MS (Method 3): R_t = 1.41 min

MS (ESpos): m/z = 207.1 $(M+H)^+$

Example 5A

Ethyl 8-(cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylate



130 g of 3-(cyclohexylmethoxy)pyridine-2-amine (Example 4A; 630 mmol, 1 equivalent) were initially charged in 3950 ml of ethanol, and 436 ml of ethyl 2-chloroacetoacetate (3.2 mol, 5 equivalents) were added. The mixture was heated under reflux for 24 h and then concentrated under reduced pressure. The crude product obtained in this manner was chromatographed on silica gel using cyclohexane/diethyl ether as mobile phase, giving 66.2 g (33% of theory) of the title compound.

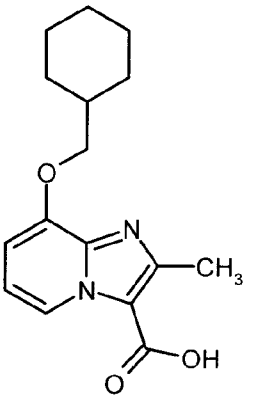
LC-MS (Method 2): R_t = 1.17 min

MS (ESpos): m/z = 317.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.02-1.31 (m, 5 H); 1.36 (t, 3 H); 1.64 – 1.77 (m, 3 H); 1.79 – 1.90 (m, 3 H); 2.60 (s, 3 H); 3.97 (d, 2 H); 4.35 (q, 2 H); 6.95 (d, 1 H); 7.03 (t, 1 H); 8.81 (d, 1 H).

Example 6A

8-(Cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid



50 g of ethyl 8-(cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylate (Example 5A; 158 mmol, 1 equivalent) were dissolved in 600 ml of 1,4-dioxane, 790 ml of 2 N aqueous sodium hydroxide solution (1.58 mol, 10 equivalents) were added and the mixture was stirred at RT for 16 h. 316 ml of 6 N hydrochloric acid were added, and the mixture was reduced to about 1/5 of the total volume. The resulting solid was filtered off, washed with water and tert-butyl methyl ether and dried under reduced pressure. This gave 35 g (74% of theory) of the title compound.

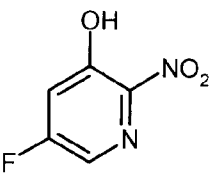
LC-MS (Method 2): R_t = 0.81 min

MS (ESpos): m/z = 289.0 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.03-1.44 (m, 5 H); 1.64 – 1.78 (m, 3 H); 1.81 – 1.92 (m, 3 H); 2.69 (s, 3 H); 4.07 (d, 2 H); 7.30 – 7.36 (m, 2 H); 9.01 (d, 1 H).

Example 7A

5-Fluoro-2-nitropyridin-3-ol



With ice cooling, 5 g of 5-fluoropyridin-3-ol (44 mmol, 1 equivalent) were dissolved in 43 ml of concentrated sulphuric acid, and, at 0°C, 2.8 ml of concentrated nitric acid were added over a period of 5 min. The reaction was warmed to RT, and stirring was continued overnight. The mixture was added to 100 g of ice and stirred for 30 min. The solid obtained was filtered off and dried under reduced pressure. This gave 5.6 g (81% of theory) of the title compound, which were used without further purification for the next reaction.

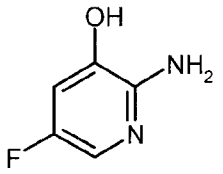
LC-MS (Method 2): R_t = 0.45 min

MS (ESneg): m/z = 156.9 $(M-H)^-$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.5 (dd, 1 H); 8.08 (d, 1 H); 12.2 (br. s, 1 H).

Example 8A

2-Amino-5-fluoropyridin-3-ol



5.6 g of 5-fluoro-2-nitropyridin-3-ol (Example 7A; 36 mmol) were dissolved in 2 l of ethanol, a catalytic amount of palladium on activated carbon (10%) was added and the mixture was hydrogenated under standard hydrogen pressure for 16 h. The mixture was filtered off through silica gel and the filtrate was concentrated (product batch 1). The filter cake was rinsed with methanol until the colour of the filtrate was no longer yellowish. The filtrate was concentrated, giving a second product batch. This gave 4.26 g (85% of theory) of the title compound.

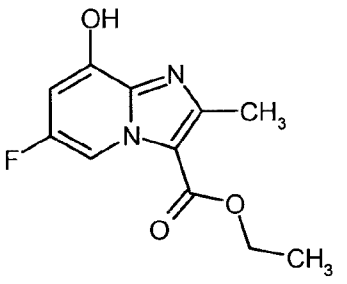
LC-MS (Method 2): R_t = 0.17 min

MS (ESpos): m/z = 128.9 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.4 (br. s, 2 H); 6.8 (dd, 1 H); 7.4 (d, 1 H).

Example 9A

Ethyl 6-fluoro-8-hydroxy-2-methylimidazo[1,2-a]pyridine-3-carboxylate



3.2 g of 2-amino-5-fluoropyridin-3-ol (Example 8A; 25 mmol, 1 equivalent) were initially charged in 155 ml of ethanol, 1.5 g of powdered molecular sieve 3Å and 20.6 g of ethyl 2-chloroacetoacetate (125 mmol, 5 equivalents) were added and the mixture was boiled at reflux overnight. The reaction solution was concentrated and chromatographed (Biotage Isolera Four; SNAP Cartridge KP-Sil 50 g; cyclohexane/ethyl acetate gradient; then dichloromethane/methanol gradient). The crude product was partly dissolved in a little methanol, and tert-butyl methyl ether was added. The solid was filtered off and washed with tert-butyl methyl ether. This gave 570 mg (10% of theory) of the title compound.

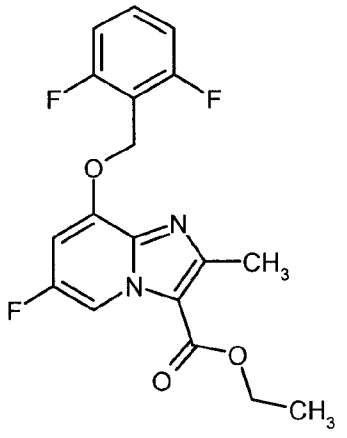
LC-MS (Method 2): R_t = 0.77 min

MS (ESpos): m/z = 239.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.39 (t, 3 H); 2.64 (s, 3 H); 4.40 (q, 2 H); 7.20 (br. d, 1 H); 8.9 (dd, 1 H); 12.5 (br. s, 1 H).

Example 10A

Ethyl 8-[(2,6-difluorobenzyl)oxy]-6-fluoro-2-methylimidazo[1,2-a]pyridine-3-carboxylate



560 mg of ethyl 6-fluoro-8-hydroxy-2-methylimidazo[1,2-a]pyridine-3-carboxylate (Example 9A; 2.4 mmol, 1.0 equivalent), 1.7 g of caesium carbonate (5.17 mmol, 2.2 equivalents) and 535 mg of 2,6-difluorobenzyl bromide (2.6 mmol, 1.1 equivalents) were initially charged in 34 ml of dry DMF, and the mixture was heated at 50°C for 15 min. Water was added, the mixture was stirred for 30 min and the solid was filtered off and washed with water. This gave 560 mg of the title compound (65% of theory).

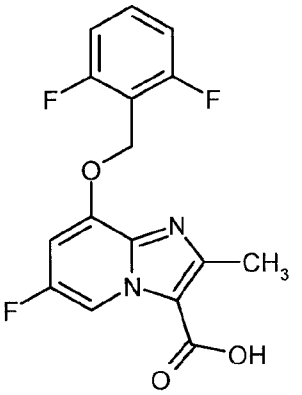
LC-MS (Method 2): R_t = 1.18 min

MS (ESpos): m/z = 365.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.37 (t, 3 H); 2.55 (s, 3 H; superimposed by DMSO signal); 4.38 (q, 2 H); 5.89 (s, 2 H); 7.23 (t, 2 H); 7.44 (dd, 1 H); 7.60 (q, 1 H); 8.90 (dd, 1 H).

Example 11A

8-[(2,6-Difluorobenzyl)oxy]-6-fluoro-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid



550 mg of ethyl 8-[(2,6-difluorobenzyl)oxy]-6-fluoro-2-methylimidazo[1,2-a]pyridine-3-carboxylate (Example 10A; 1.5 mmol, 1 equivalent) were dissolved in 64 ml of THF and 12 ml of methanol, 7.5 ml of 1 N aqueous lithium hydroxide solution were added and the mixture was stirred at RT overnight. 8 ml of 1 N aqueous hydrochloric acid were then added, and the mixture was concentrated under reduced pressure. The solid formed was filtered off and washed with water. This gave 429 mg of the title compound (80% of theory).

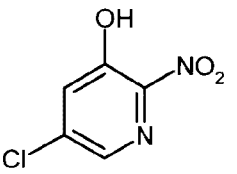
LC-MS (Method 1): R_t = 0.90 min

MS (ESpos): m/z = 337.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.54 (s, 3 H; superimposed by DMSO signal); 5.84 (s, 2 H); 7.23 (t, 2 H); 7.40 (dd, 1 H); 7.51 (q, 1 H); 8.92 (dd, 1 H); 13.28 (br. s, 1 H).

Example 12A

5-Chloro-2-nitropyridin-3-ol



With ice cooling, 30 g of 5-chloropyridin-3-ol (232 mmol, 1 equivalent) were dissolved in 228 ml of concentrated sulphuric acid, and, at 0°C, 24 ml of concentrated nitric acid were added slowly. The reaction was warmed to RT, stirred overnight and then stirred into an ice/water mixture and stirred for another 30 min. The solid was filtered off, washed with cold water and air-dried. This gave 33 g (82% of theory) of the title compound, which were used without further purification for the next reaction.

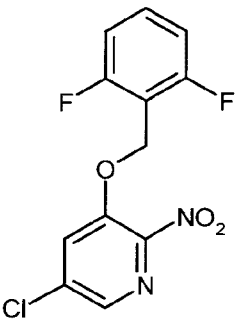
LC-MS (Method 2): R_t = 0.60 min

MS (ESneg): m/z = 172.9/174.9 $(M-H)^-$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.71 (d, 1 H); 8.10 (d, 1 H); 12.14 (br. 1 H).

Example 13A

5-Chloro-3-[(2,6-difluorobenzyl)oxy]-2-nitropyridine

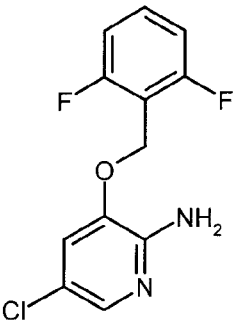


33 g of 5-chloro-2-nitropyridin-3-ol (Example 12A; 189 mmol, 1 equivalent) and 61.6 g of caesium carbonate (189 mmol, 1 equivalent) were initially charged in 528 ml of DMF, 40.4 g of 2,6-difluorobenzyl bromide (189 mmol, 1 equivalent) were added and the mixture was stirred at RT overnight. The reaction mixture was stirred into water/1N aqueous hydrochloric acid. The solid was filtered off, washed with water and air-dried. This gave 54.9 g (97% of theory) of the title compound.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.46 (s, 2 H); 7.22 (t, 2 H); 7.58 (q, 1 H); 8.28 (d, 1 H); 8.47 (d, 1 H).

Example 14A

5-Chloro-3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine



59.7 g of 5-chloro-3-[(2,6-difluorobenzyl)oxy]-2-nitropyridine (Example 13A; 199 mmol, 1 equivalent) were initially charged in 600 ml of ethanol, 34.4 g of iron powder (616 mmol, 3.1 equivalents) were added and the mixture was heated to reflux. 152 ml of concentrated hydrochloric acid were slowly added dropwise and the mixture was boiled at reflux for a further 30 min. The reaction mixture was cooled and stirred into an ice/water mixture. The resulting mixture was adjusted to pH 5 using sodium acetate. The solid was filtered off, washed with water and air-dried and then dried under reduced pressure at 50°C. This gave 52.7 g (98% of theory) of the title compound.

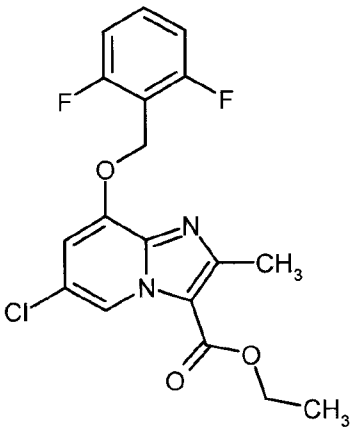
LC-MS (Method 2): R_t = 0.93 min

MS (ESpos): m/z = 271.1/273.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.14 (s, 2 H); 5.82 (br. s, 2 H); 7.20 (t, 2 H); 7.35 (d, 1 H); 7.55 (q, 1 H); 7.56 (d, 1 H).

Example 15A

Ethyl 6-chloro-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylate



40 g of 5-chloro-3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine (Example 14A; 147.8 mmol; 1 equivalent) were initially charged in 800 ml of ethanol, 30 g of powdered molecular sieve 3Å and 128 g of ethyl 2-chloroacetoacetate (739 mmol, 5 equivalents) were added and the mixture was heated at reflux overnight. The reaction mixture was concentrated and the residue was taken up in ethyl acetate and filtered. The ethyl acetate phase was washed with water, dried, filtered and concentrated. This gave 44 g (78% of theory) of the title compound.

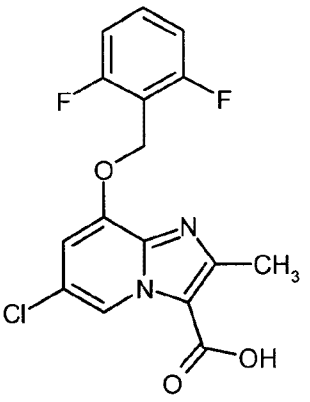
LC-MS (Method 2): R_t = 1.27 min

MS (ESpos): m/z = 381.2/383.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.36 (t, 3 H); 2.54 (s, 3 H; obscured by DMSO signal); 4.37 (q, 2 H); 5.36 (s, 2 H); 7.26 (t, 2 H); 7.38 (d, 1 H); 7.62 (q, 1 H); 8.92 (d, 1 H).

Example 16A

6-Chloro-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid



44 g of ethyl 6-chloro-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylate (Example 15A; 115 mmol, 1 equivalent) were dissolved in 550 ml of THF and 700 ml of methanol, 13.8 g of lithium hydroxide (dissolved in 150 ml of water; 577 mmol, 5 equivalents) were added and the mixture was stirred at RT overnight. 1 N aqueous hydrochloric acid was added and the mixture was concentrated under reduced pressure. The solid obtained was filtered off and washed with water. This gave 34 g of the title compound (84% of theory).

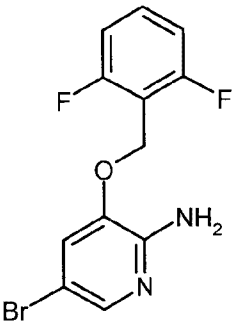
LC-MS (Method 1): R_t = 1.03 min

MS (ESpos): m/z = 353.0/355.0 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.54 (s, 3 H; superimposed by DMSO signal); 5.36 (s, 2 H); 7.26 (t, 2 H); 7.34 (d, 1 H); 7.61 (q, 1 H); 8.99 (d, 1 H); 13.36 (br. s, 1 H).

Example 17A

5-Bromo-3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine



32.6 g of 3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine (Example 1A; 138 mmol, 1 equivalent) were suspended in 552 ml of 10% strength sulphuric acid, and the mixture was cooled to 0°C. 8.5 ml of bromine (165 mmol, 1.2 equivalents) were dissolved in 85 ml of acetic acid and then, over a period of 90 min, added dropwise to the ice-cooled reaction solution. After the dropwise addition had ended, the mixture was stirred at 0°C for 90 min and then diluted with 600 ml of ethyl acetate, and the aqueous phase was separated off. The aqueous phase was extracted with ethyl acetate. The organic phases were combined, washed with saturated aqueous sodium bicarbonate solution, dried and concentrated. The residue was dissolved in dichloromethane and chromatographed on silica gel (petroleum ether/ethyl acetate gradient as mobile phase). This gave 24 g (55% of theory) of the title compound.

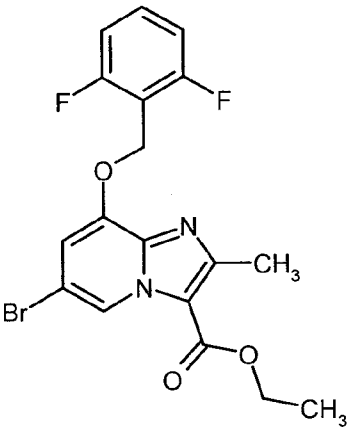
LC-MS (Method 2): R_t = 0.96 min

MS (ESpos): m/z = 315.1/317.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 5.14 (s, 2 H); 5.83 (br. s, 2 H); 7.20 (t, 2 H); 7.42 (d, 1 H); 7.54 (q, 1 H); 7.62 (d, 1 H).

Example 18A

Ethyl 6-bromo-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylate



16 g of powdered molecular sieve 3Å and 52.7 ml of ethyl 2-chloroacetoacetate (380.8 mmol; 5 equivalents) were added to 24 g of 5-bromo-3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine (Example 17A; 76.2 mmol; 1 equivalent) in 400 ml of ethanol, and the mixture was heated at reflux overnight. A further 8 g of molecular sieve were added, and the mixture was heated at reflux for a further 24 h. The reaction mixture was concentrated under reduced pressure and the residue was taken up in dichloromethane and chromatographed on silica gel (dichloromethane/methanol 20:1 as mobile phase). The product-containing fractions were concentrated and the residue was stirred with 100 ml of diethyl ether for 30 min. The product was then filtered off, washed with a little diethyl ether and dried. This gave 15 g (45% of theory) of the title compound.

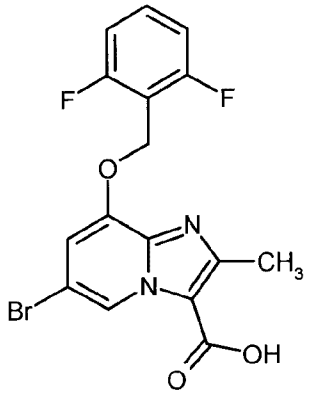
LC-MS (Method 1): R_t = 1.43 min

MS (ESpos): m/z = 414.9/416.8 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.36 (t, 3 H); 2.54 (s, 3 H; obscured by DMSO signal); 4.37 (q, 2 H); 5.36 (s, 2 H); 7.25 (t, 2 H); 7.42 (d, 1 H); 7.61 (q, 1 H); 9.00 (d, 1 H).

Example 19A

6-Bromo-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid



1.5 g of ethyl 6-bromo-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylate (Example 18A; 3.5 mmol, 1 equivalent) were dissolved in 72 ml of THF/methanol 5:1, 17.6 ml of 1N aqueous lithium hydroxide solution (17.6 mmol, 5 equivalents) were added and the mixture was warmed to 40°C and stirred at this temperature for 6 h. Using 6 N aqueous hydrochloric acid, the mixture was then adjusted to pH 4 and concentrated under reduced pressure. Water was added to the solid formed and the solid was triturated, filtered off, washed with water and dried under reduced pressure. This gave 1.24 g of the title compound (88% of theory).

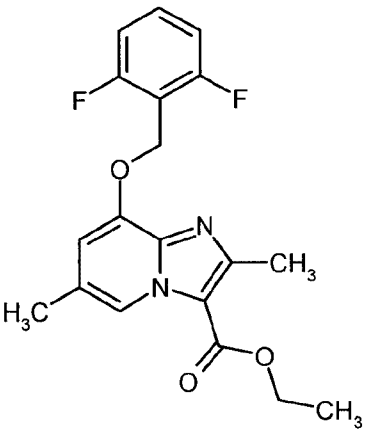
LC-MS (Method 2): R_t = 0.93 min

MS (ESpos): m/z = 397.0/399.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.54 (s, 3 H; superimposed by DMSO signal); 5.36 (s, 2 H); 7.25 (t, 2 H); 7.40 (d, 1 H); 7.61 (q, 1 H); 9.06 (d, 1 H); 13.35 (br. s, 1 H).

Example 20A

Ethyl 8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxylate



20.00 g (85.38 mmol) of ethyl 8-hydroxy-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxylate from Example 239A, 19.44 g (93.91 mmol) of 2,6-difluorobenzyl bromide and 61.20 g (187.83 mmol) of caesium carbonate in 1.18 l of DMF were stirred at 60°C for 5 h. The reaction mixture was then poured into 6.4 l of 10% strength aqueous sodium chloride solution and then extracted twice with ethyl acetate. The combined organic phases were washed with 854 ml of 10% strength aqueous sodium chloride solution, dried, concentrated and dried under high vacuum at RT overnight. This gave 28.2 g (92% of theory; purity about 90%) of the title compound.

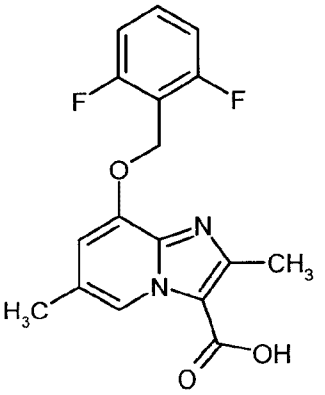
LC-MS (Method 2): R_t = 1.05 min

MS (ESpos): m/z = 361.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.38 (t, 3 H); 2.36 (s, 3 H); 4.35 (q, 2 H); 5.30 (s, 2 H); 7.10 (s, 1 H); 7.23 (t, 2 H); 7.59 (q, 1 H); 8.70 (s, 1 H).

Example 21A

8-[(2,6-Difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxylic acid



220 mg of ethyl 8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxylate (Example 20A; 0.524 mmol, 1 equivalent) were dissolved in 7 ml of THF/methanol 1:1, 2.6 ml of 1 N aqueous lithium hydroxide solution (2.6 mmol, 5 equivalents) were added and the mixture was stirred at RT for 16 h. The mixture was concentrated under reduced pressure and the residue was acidified with 1N aqueous hydrochloric acid and stirred for 15 min. The solid was filtered off, washed with water and dried under reduced pressure. This gave 120 mg of the title compound (60% of theory).

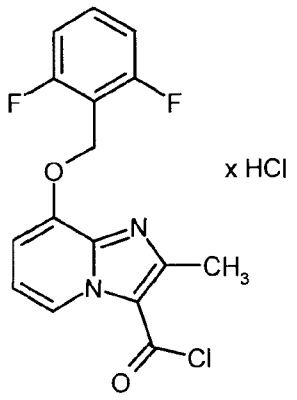
LC-MS (Method 2): R_t = 0.68 min

MS (ESpos): m/z = 333.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.34 (s, 3 H); 5.28 (s, 2 H); 7.09 (s, 1 H); 7.23 (t, 2 H); 7.58 (q, 1 H); 8.76 (s, 1 H); 13.1 (br. s, 1 H), [further signal hidden under DMSO signal].

Example 22A

8-[(2,6-Difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carbonyl chloride hydrochloride

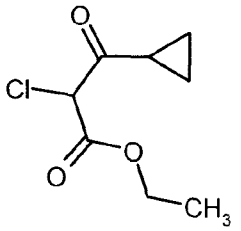


4 drops of DMF were added to 2.0 g of 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxylic acid (6.28 mmol, 1 equivalent) in 25 ml of dry THF, followed by the dropwise addition of 3.19 g of oxalyl chloride (25.14 mmol, 4 equivalents). The reaction mixture was stirred at RT for 3 h. Another 0.80 g of oxalyl chloride (6.28 mmol, 1 equivalent) were added, and the reaction was stirred at RT for a further 4 h. The reaction mixture was concentrated and co-evaporated with toluene three times, and the residue was dried under high vacuum. This gave 2.43 g of the title compound (103% of theory).

DCI-MS (Method 4): MS (ESpos): m/z = 437 $(M-HCl+H)^+$

Example 23A

Ethyl 2-chloro-3-cyclopropyl-3-oxopropanoate

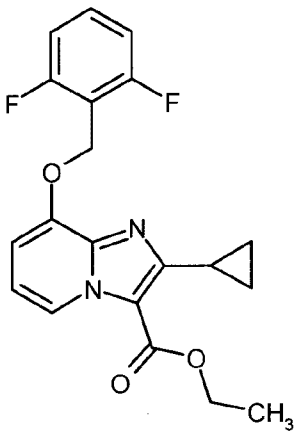


3.1 ml of sulphuryl chloride (38.2 mmol, 1.05 equivalents) were initially charged in 21 ml of dichloromethane, and 5.68 g of ethyl 3-cyclopropyl-3-oxopropanoate (36.4 mmol) were added

dropwise on a water bath. The reaction mixture was stirred at RT for 2 h. The mixture was then washed with water, 5% strength aqueous sodium bicarbonate solution and saturated aqueous sodium chloride solution, dried over magnesium sulphate and concentrated. The crude product (6.8 g) was used without further purification for the next reaction.

Example 24A

Ethyl 2-cyclopropyl-8-[(2,6-difluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxylate



1.69 g of 3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine (Example 1A; 7.13 mmol, 1 equivalent) were initially charged in 44.4 ml of ethanol, and 425 mg of powdered molecular sieve 3Å and 6.8 g of ethyl 2-chloro-3-cyclopropyl-3-oxopropanoate (crude product from Example 23A) were added. The reaction mixture was heated at reflux for 48 h and then concentrated under reduced pressure, and the residue was chromatographed (cyclohexane/ethyl acetate as mobile phase). The product-containing fractions were combined and concentrated under reduced pressure. The residue obtained in this manner was taken up in methanol, DMSO and water. The solid obtained was filtered off and dried under high vacuum. This gave 410 mg (15.4% of theory) of the title compound.

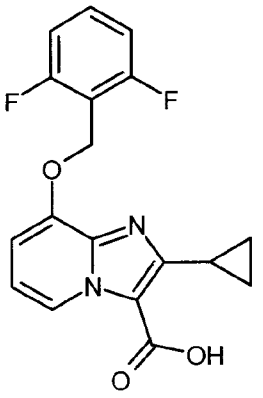
LC-MS (Method 2): R_t = 1.22 min

MS (ESpos): m/z = 373.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.95 – 1.05 (m, 4 H); 1.39 (t, 3 H); 2.36 (s, 3 H); 2.70 – 2.80 (m, 1 H); 4.39 (q, 2 H); 5.30 (s, 2 H); 7.08 (t, 1 H); 7.15 (d, 1 H); 7.20 (t, 2 H); 7.59 (q, 1 H); 8.88 (d, 1 H).

Example 25A

2-Cyclopropyl-8-[(2,6-difluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxylic acid



410 mg of ethyl 2-cyclopropyl-8-[(2,6-difluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxylate (Example 24A, 1.1 mmol, 1 equivalent) were initially charged in 15 ml of methanol/THF (1:1), and 5.5 ml of a 1 N aqueous lithium hydroxide solution (5.5 mmol, 5 equivalents) were added. The reaction mixture was stirred at RT overnight. Another 5.5 ml of 1 N aqueous lithium hydroxide solution were added, and the mixture was stirred at RT for another night. The mixture was then concentrated under reduced pressure and the residue was taken up in water and acidified with 1 N aqueous hydrochloric acid. The precipitated product was filtered off and dried under high vacuum. This gave 293 mg (77% of theory) of the title compound.

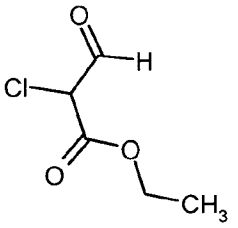
LC-MS (Method 2): R_t = 0.83 min

MS (ESpos): m/z = 345.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.95 – 1.02 (m, 4 H); 2.80 (q, 1 H); 5.30 (s, 2 H); 7.02 (t, 1 H); 7.15 (d, 1 H); 7.22 (t, 2 H); 7.59 (q, 1 H); 8.92 (s, 1 H); 13.3 (br. s, 1 H).

Example 26A

Ethyl 2-chloro-3-oxopropanoate

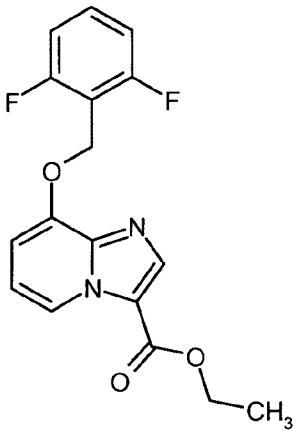


139 ml of a 21% strength solution of sodium ethoxide in ethanol (371 mmol, 0.91 equivalent) were initially charged in 200 ml of diethyl ether, and a solution of 43.7 ml of ethyl chloroacetate (408 mmol, 1 equivalent) and 32.9 ml of ethyl formate (408 mmol, 1 equivalent) in 150 ml of diethyl

ether was added dropwise at RT. The reaction mixture was stirred overnight and the solid was filtered off and washed with diethyl ether. The solid was dissolved in water and the aqueous phase was, with ice bath cooling, adjusted to pH4 using concentrated hydrochloric acid. The mixture was extracted repeatedly with diethyl ether and the combined organic phases were washed with saturated aqueous sodium chloride solution, dried with magnesium sulphate, filtered and concentrated. The crude product obtained (8.2 g) was freed from residual solvent under high vacuum and used without further purification for the next reaction.

Example 27A

Ethyl 8-[(2,6-difluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxylate



1.93 g of 3-[(2,6-difluorobenzyl)oxy]pyridine-2-amine (Example 1A; 8.2 mmol, 1 equivalent) were initially charged in 50 ml of ethanol, and 8.2 g of ethyl 2-chloro-3-oxopropanoate (75% pure, crude product from Example 26A, 40.8 mmol, 5 equivalents) were added. The reaction mixture was heated at reflux overnight. The mixture was then concentrated under reduced pressure and the crude product obtained was chromatographed on 340 g of silica gel (Biotage Isolera) (mobile phase: cyclohexane:ethyl acetate gradient; R_f value of the product in cyclohexane:ethyl acetate 2:1 = 0.36). The product fractions were combined and concentrated and the residue obtained was triturated with diisopropyl ether. The solid was filtered off and dried under high vacuum. This gave 2.02 g of the title compound (71% of theory).

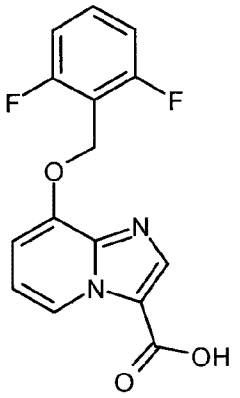
LC-MS (Method 2): R_t = 1.08 min

MS (ESpos): m/z = 333.1 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.35 (t, 3 H); 4.39 (q, 2 H); 5.35 (s, 2 H); 7.15 – 7.28 (m, 4 H); 7.58 (q, 1 H); 8.18 (s, 1 H); 8.90 (d, 1 H).

Example 28A

8-[(2,6-Difluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxylic acid



1 g of ethyl 8-[(2,6-difluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxylate (Example 27A, 3 mmol, 1 equivalent) were initially charged in 60 ml of methanol/THF (5:1), 15 ml of a 1 N aqueous lithium hydroxide solution (15 mmol, 5 equivalents) were added and the mixture was warmed to 40°C and stirred at this temperature for 4 h. The mixture was then cooled and, with ice cooling, adjusted to pH 4 using 6 N aqueous hydrochloric acid. The organic solvents were removed on a rotary evaporator, water was added to the precipitated product and the product was filtered, washed with water and dried under high vacuum. This gave 797 mg (87% of theory) of the title compound.

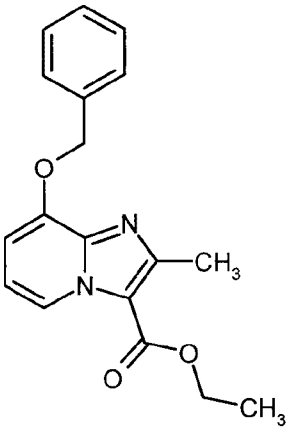
LC-MS (Method 2): R_t = 0.66 min

MS (ESpos): m/z = 305.1 $(M+H)^+$

1H NMR (400 MHz, DMSO-d6): δ = 5.38 (s, 2 H); 7.10 – 7.28 (m, 4 H); 7.59 (q, 1 H); 8.12 (s, 1 H); 8.92 (s, 1 H); 13.1 (br. s, 1 H).

Example 29A

Ethyl 8-(benzyloxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylate



25 g of 2-amino-3-benzyloxypyridine (124.8 mmol, 1 equivalent) were dissolved in 781 ml of ethanol, and 102.7 g of ethyl 2-chloroacetoacetate (624.2 mmol, 5 equivalents) and 15 g of 4Å molecular sieve were added. The mixture was heated at reflux for 2 d (bath temperature 100°C). The mixture was then concentrated and excess ethyl 2-chloroacetoacetate was distilled off on a rotary evaporator with dry ice-cooling. The residue was purified by silica gel chromatography (mobile phase cyclohexane:ethyl acetate 9:1, 4:1). This gave 20.81 g of the title compound (54% of theory).

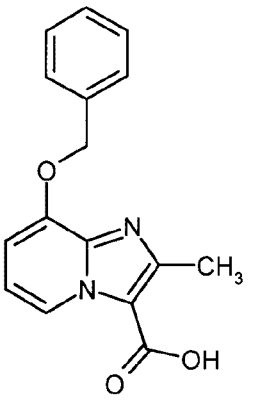
LC-MS (Method 1): R_t = 1.12 min

MS (ESpos): m/z = 311 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.35 (t, 3H), 2.59 (s, 3H), 4.34 (q, 2H), 5.32 (s, 2H), 7.01-7.09 (m, 2H), 7.33-7.48 (m, 3H), 7.52 (d, 2H), 8.81-8.86 (m, 1H).

Example 30A

8-(Benzyloxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid



253 ml of 2 N aqueous sodium hydroxide solution were added to a solution of 15.7 g of ethyl 8-(benzyloxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylate (50.59 mmol) in 253 ml of 1,4-dioxane, and the mixture was stirred at RT for 14 h. 101 ml of 6 N aqueous hydrochloric acid were then added. The solid formed was filtered off, washed with water and methyl tert-butyl ether and then dried under reduced pressure at 40°C overnight. This gave 15.49 g (108% of theory) of 8-(benzyloxy)-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid.

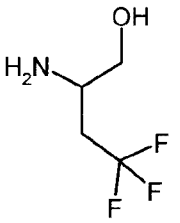
LC-MS (Method 1): R_t = 0.66 min

MS (ESpos): m/z = 283.0 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.67 (s, 3H), 3.2 – 3.8 (very broad water peak), 5.41 (s, 2H), 7.30 (m, 1H), 7.35 – 7.48 (m, 4H), 7.57 (d, 2H), 9.02 (d, 1H).

Example 31A

rac-2-Amino-4,4,4-trifluorobutan-1-ol



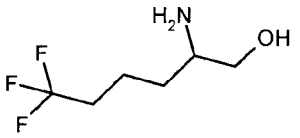
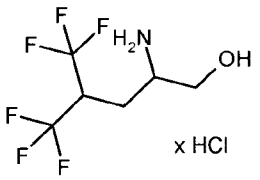
0.32 ml of lithium borohydride (2 M in THF, 0.65 mmol, 2.5 equivalents) were initially charged in 0.5 ml of abs. THF, 0.16 ml of chlorotrimethylsilane (1.28 mmol, 5 equivalents) were added at RT and the mixture was stirred at RT for 5 min. 50 mg of 2-amino-4,4,4-trifluorobutanoic acid hydrochloride (0.26 mmol, 1 equivalent) were then added a little at a time, and the reaction mixture was stirred at RT overnight. 0.5 ml of methanol was added, and the mixture was then concentrated. 0.6 ml of a 20% strength solution of potassium hydroxide was then added, and the mixture was extracted three times with dichloromethane. The combined organic phases were dried over sodium sulphate, filtered and concentrated. This gave 33 mg of the title compound (88% of theory).

DCI-MS (Method 4): MS (ESpos): m/z = 144 (M+H)+

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.08-2.20 (m, 1H), 2.22-2.38 (m, 1H), 3.25-3.32 (m, 1H), 3.39-3.44 (m, 1H), 3.59-3.65 (m, 1H).

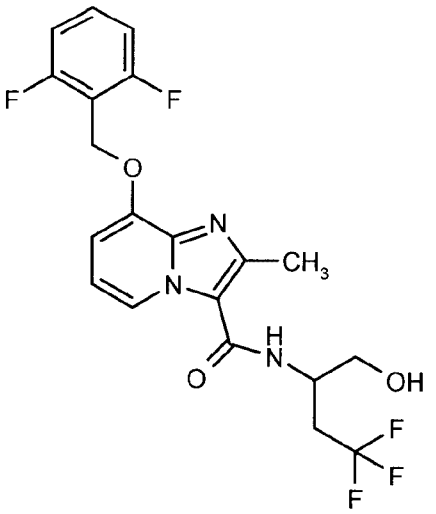
The examples shown in Table 1A were prepared analogously to Example 31A by reacting lithium borohydride (1.7-2.5 equivalents) and chlorotrimethylsilane (3.4-5 equivalents) with the appropriate commercially available amino acids according to General Working Procedure 1:

Table 1A:

Example	IUPAC name / structure (yield)	Analytical data
32A	*rac*-2-amino-6,6,6-trifluorohexan-1-ol  (75% of theory)	DCI-MS (Method 4): MS (ESpos): m/z = 172 $(M+H)^+$
33A	*rac*-2-amino-5,5,5-trifluoro-4-(trifluoromethyl)pentan-1-ol hydrochloride  (55% of theory)	DCI-MS (Method 4): MS (ESpos): m/z = 226 $(M+H)^+$

Example 34A

rac-8-[(2,6-Difluorobenzyl)oxy]-2-methyl-N-(4,4,4-trifluoro-1-hydroxybutan-2-yl)imidazo[1,2-a]-pyridine-3-carboxamide



330 mg of 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid (1.04 mmol), 399 mg of (benzotriazol-1-yloxy)bisdimethylaminomethylium fluoroborate (TBTU, 1.24 mmol) and 524 mg of 4-methylmorpholine (5.18 mmol) were initially charged in 6.6 ml of DMF. After 10 min at RT, 371 mg (1.56 mmol, purity about 60%) of 2-amino-4,4,4-trifluorobutan-1-ol (Example 31A) were added and the mixture was stirred at RT overnight. About 200 ml of water were added, the reaction solution was stirred for another 30 min and the precipitate formed was filtered off, washed with water and dried under high vacuum overnight. This gave 439 mg of the title compound (96% of theory).

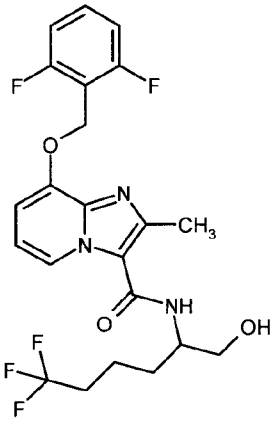
LC-MS (Method 5): R_t = 1.62 min

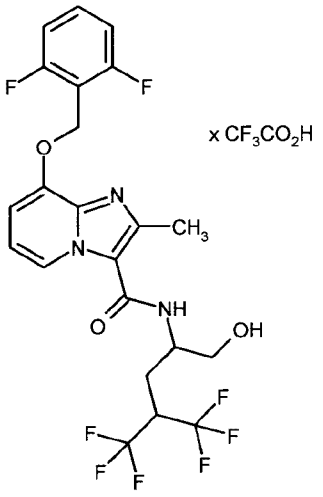
MS (ESpos): m/z = 444 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.50 (s, 3H), 2.55-2.72 (m, 2H), 3.38-3.47 (m, 1H), 3.51-3.62 (m, 1H), 4.29-4.40 (m, 1H), 5.12 (t, 1H), 5.30 (s, 2H), 6.92 (t, 1H), 7.02 (d, 1H), 7.23 (t, 2H), 7.59 (quint, 1H), 7.80 (d, 1H), 8.56 (d, 1H).

The examples shown in Table 2A were prepared analogously to Example 34A by reacting 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid with the appropriate commercially available amines under the reaction conditions described in the General Working Procedure 2:

Table 2A:

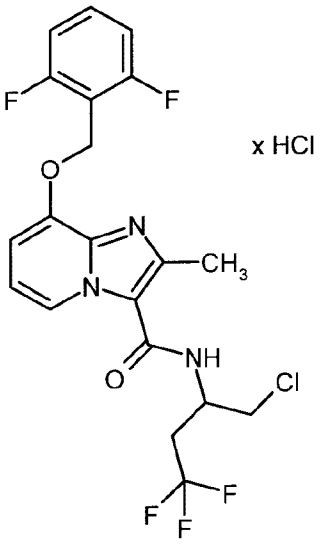
Example	IUPAC name / structure (yield)	Analytical data
35A	*rac*-8-[(2,6-difluorobenzyl)oxy]-2-methyl-*N*-(6,6,6-trifluoro-1-hydroxyhexan-2-yl)imidazo[1,2-a]pyridine-3-carboxamide  (76% of theory)	LC-MS (Method 2): R_t = 0.88 min MS (ESpos): m/z = 472 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.51-1.79 (m, 4H), 2.19-2.40 (m, 2H), 2.50 (s, 3H), 3.41-3.57 (m, 2H), 3.96-4.08 (m, 1H), 4.82 (t, 1H), 5.30 (s, 2H), 6.91 (t, 1H), 6.99 (d, 1H), 7.22 (t, 2H), 7.56-7.62 (m, 2H), 8.52 (d, 1H).

Example	IUPAC name / structure (yield)	Analytical data
36A	*rac*-8-[(2,6-difluorobenzyl)oxy]-2-methyl-*N*-[5,5,5-trifluoro-1-hydroxy-4-(trifluoromethyl)pentan-2-yl]imidazo[1,2-a]-pyridine-3-carboxamide trifluoroacetate [a)]  x CF_3CO_2H (52% of theory)	LC-MS (Method 2): R_t = 0.90 min MS (ESpos): m/z = 526 $(M\text{-}TFA+H)^+$

a) Alternative work-up: The crude reaction mixture was purified directly by preparative HPLC (RP18 column, mobile phase: acetonitrile/water gradient with addition of 0.1% TFA).

Example 37A

rac-*N*-(1-Chloro-4,4,4-trifluorobutan-2-yl)-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxamide hydrochloride



2.48 g of *rac*-8-[(2,6-difluorobenzyl)oxy]-2-methyl-N-(4,4,4-trifluoro-1-hydroxybutan-2-yl)-imidazo-[1,2-a]pyridine-3-carboxamide (Example 34A, 5.59 mmol) were initially charged in dichloromethane. At 0°C, 1.22 ml of thionyl chloride (16.77 mmol) were added dropwise, and the mixture was stirred at RT overnight. The reaction solution was concentrated and dried under high vacuum. This gave 2.78 g of the title compound (99.8% of theory).

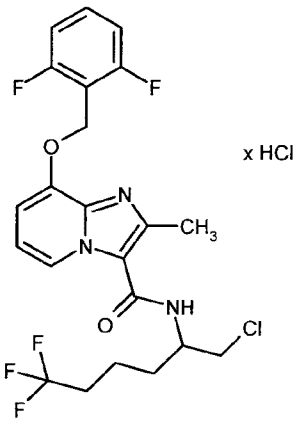
LC-MS (Method 2): R_t = 0.94 min

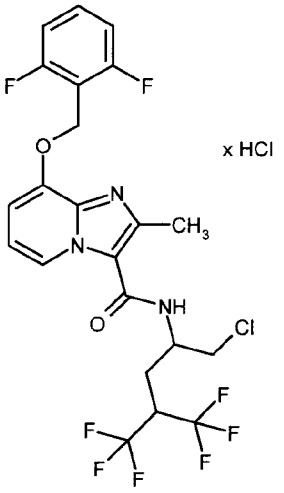
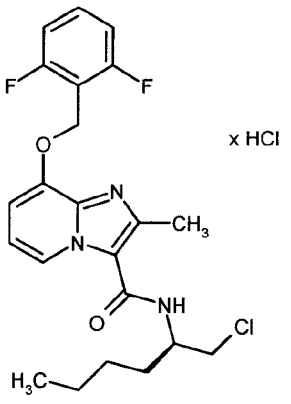
MS (ESpos): m/z = 462 $(M-HCl+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.60 (s, 3H), 2.70-2.84 (m, 2H), 3.82-3.92 (m, 2H), 4.55-4.67 (m, 1H), 5.43 (s, 2H), 7.23 (t, 2H), 7.31-7.43 (m, 1H), 7.51-7.66 (m, 2H), 8.63 (d, 1H), 8.82 (br s, 1H).

The examples shown in Table 3A were prepared analogously to Example 37A.

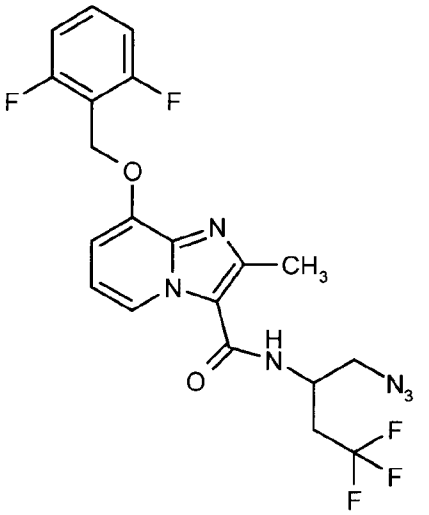
Table 3A:

Example	IUPAC name / structure (yield)	Analytical data
38A	*rac-N*-(1-chloro-6,6,6-trifluorohexan-2-yl)-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxamide hydrochloride  x HCl (99% of theory)	LC-MS (Method 2): R_t = 1.05 min MS (ESpos): m/z = 490 $(M-HCl+H)^+$ ^1H NMR (400 MHz, DMSO-d_6): δ = 1.52-1.81 (m, 4H), 2.20-2.42 (m, 2H), 2.60 (s, 3H), 3.72-3.87 (m, 2H), 4.21-4.33 (m, 1H), 5.45 (s, 2H), 7.23 (t, 2H), 7.40 (br s, 1H), 7.52-7.68 (m, 2H), 8.54 (br s, 1H), 8.61 (d, 1H).

Example	IUPAC name / structure (yield)	Analytical data
39A	*rac*-*N*-[1-chloro-5,5,5-trifluoro-4-(trifluoromethyl)pentan-2-yl]-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxamide hydrochloride  (98% of theory)	LC-MS (Method 2): R_t = 1.15 min MS (ESpos): m/z = 544 $(M-HCl+H)^+$
40A	*N*-[(2*R*)-1-chlorohexan-2-yl]-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxamide hydrochloride  (98% of theory)	LC-MS (Method 2): R_t = 1.06 min MS (ESpos): m/z = 436 $(M-HCl+H)^+$

Example 41A

rac-*N*-(1-Azido-4,4,4-trifluorobutan-2-yl)-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxamide



195 mg of *rac*-N-(1-chloro-4,4,4-trifluorobutan-2-yl)-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxamide hydrochloride (Example 37A, 0.39 mmol) were initially charged in 3.4 ml of DMF, 254 mg of sodium azide (3.91 mmol) were added and the mixture was stirred at 40°C for 4 h. The mixture was then stirred at 60°C for 5 h. Water was added, and the reaction mixture was extracted three times with ethyl acetate. The combined organic phases were dried over sodium sulphate and filtered, the filtrate was concentrated and the residue was purified by silica gel chromatography (mobile phase: cyclohexane:ethyl acetate 7:3, isocratic). This gave 50 mg of the title compound (27% of theory).

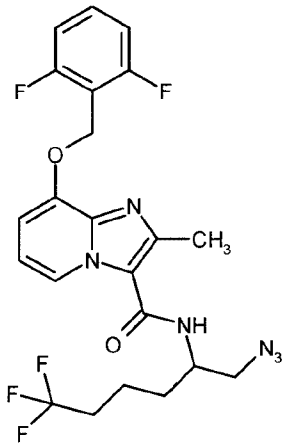
LC-MS (Method 2): R_t = 0.97 min

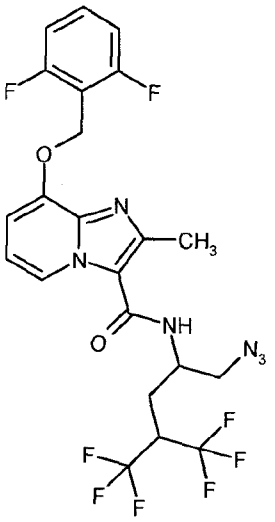
MS (ESpos): m/z = 469 $(M+H)^+$

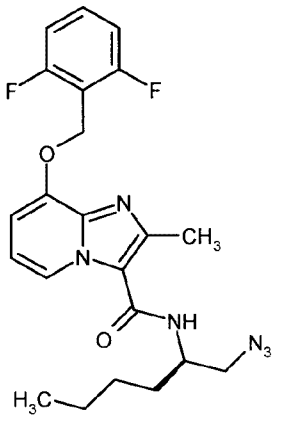
^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.50 (s, 3H), 2.58-2.78 (m, 2H), 3.52-3.63 (m, 2H), 4.47-4.58 (m, 1H), 5.30 (s, 2H), 6.93 (t, 1H), 7.02 (d, 1H), 7.22 (t, 2H), 7.59 (quint, 1H), 8.09 (d, 1H), 8.55 (d, 1H).

The examples shown in Table 4A were prepared analogously to Example 41A by reacting sodium azide (5-20 equivalents) with the appropriate chlorides. The crude products were purified by silica gel chromatography (mobile phase: cyclohexane:ethyl acetate gradient or isocratic).

Table 4A:

Example	IUPAC name / structure (yield)	Analytical data
42A	*rac*-*N*-(1-azido-6,6,6-trifluorohexan-2-yl)-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxamide [a)]  (25% of theory)	LC-MS (Method 2): R_t = 1.03 min MS (ESpos): m/z = 497 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.52-1.70 (m, 4H), 2.20-2.41 (m, 2H), 2.50 (s, 3H), 3.52 (d, 2H), 4.18-4.26 (m, 1H), 5.30 (s, 2H), 6.93 (t, 1H), 7.01 (d, 1H), 7.23 (t, 2H), 7.59 (quint, 1H), 7.91 (d, 1H), 8.50 (d, 1H).

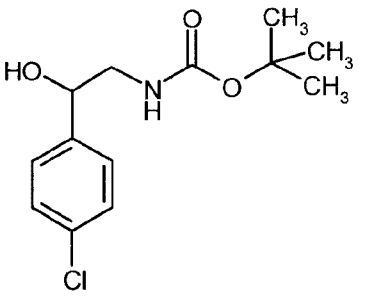
Example	IUPAC name / structure (yield)	Analytical data
43A	*rac-N*-[1-azido-5,5,5-trifluoro-4-(trifluoromethyl)pentan-2-yl]-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxamide  (45% of theory)	LC-MS (Method 2): R_t = 1.08 min MS (ESpos): m/z = 551 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.06-2.19 (m, 2H), 2.52 (s, 3H), 3.61 (d, 2H), 3.98-4.13 (m, 1H), 4.26-4.38 (m, 1H), 5.30 (s, 2H), 6.94 (t, 1H), 7.03 (d, 1H), 7.23 (t, 2H), 7.59 (quint, 1H), 7.89 (d, 1H), 8.59 (d, 1H).

Example	IUPAC name / structure (yield)	Analytical data
44A	*ent-N*-[(2*R*)-1-azidohexan-2-yl]-8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridine-3-carboxamide  (37% of theory)	LC-MS (Method 2): R_t = 1.04 min MS (ESpos): m/z = 443 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.88 (t, 3H), 1.22-1.42 (m, 4H), 1.49-1.61 (m, 2H), 2.50 (s, 3H), 3.48 (d, 2H), 4.10-4.21 (m, 1H), 5.30 (s, 2H), 6.93 (t, 1H), 6.99 (d, 1H), 7.23 (t, 2H), 7.59 (quint, 1H), 7.88 (d, 1H), 8.50 (d, 1H).

a) 20 equivalents of sodium azide were used.

Example 45A

rac-tert-Butyl [2-(4-chlorophenyl)-2-hydroxyethyl]carbamate



First, 2.43 g of triethylamine (24.03 mmol) and then 2.35 g of di-tert-butyl dicarbonate (10.76 mmol) were added to 2.0 g of *rac*-2-amino-1-(4-chlorophenyl)ethanol hydrochloride (9.61 mmol) in 14 ml of dichloromethane. The reaction mixture was stirred at RT for 2 h. The mixture was diluted with dichloromethane, washed with saturated aqueous sodium bicarbonate solution and with saturated aqueous sodium chloride solution, dried over sodium sulphate, filtered, concentrated

under reduced pressure and dried under high vacuum. This gave 2.72 g of the title compound (104% of theory).

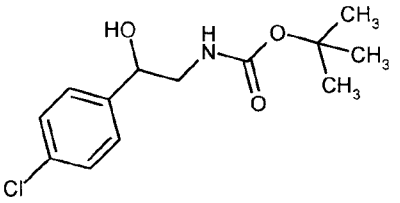
LC-MS (Method 2): R_t = 0.97 min

MS (ESneg): m/z = 272 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.33 (s, 9H), 2.97-3.13 (m, 2H), 4.54-4.62 (m, 1H), 5.44 (d, 1H), 6.73 (t, 1H), 7.31 (d, 2H), 7.38 (d, 2H).

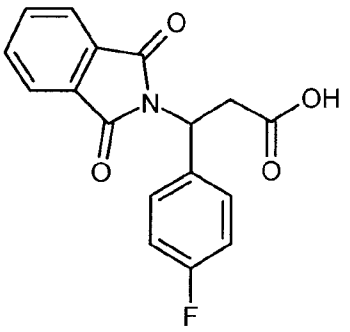
The example shown in Table 5A was prepared analogously to Example 45A by reacting di-tert-butyl dicarbonate in dichloromethane with the appropriate commercially available amine.

Table 5A:

Example	IUPAC name / structure (yield)	Analytical data
46A	*rac*-tert-butyl (2-hydroxy-2-phenylethyl)carbamate  (104% of theory)	LC-MS (Method 4): MS (ESpos): m/z = 272 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.33 (s, 9H), 2.97-3.13 (m, 2H), 4.54-4.62 (m, 1H), 5.44 (d, 1H), 6.73 (t, 1H), 7.19-7.38 (d, 2H).

Example 47A

rac-3-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-(4-fluorophenyl)propanoic acid



2.0 g of *rac*-3-amino-3-(4-fluorophenyl)propanoic acid (10.92 mmol) and 1.62 g of phthalic anhydride (10.92 mmol) were dissolved in 9 ml of DMF and heated at reflux at 135°C overnight. The reaction solution was added to about 200 ml of water. The solid formed was stirred at RT for about 30 min and then filtered off, washed with water and dried under high vacuum. This gave 3.43 g of the title compound (86% of theory, purity about 86%).

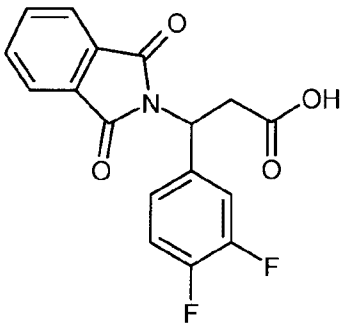
LC-MS (Method 1): R_t = 1.09 min

MS (ESpos): m/z = 314 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.24-3.3.34 (m, 1H), 3.44-3.53 (m, 1H), 5.63-5.70 (m, 1H), 7.18 (t, 2H), 7.48 (dd, 1H), 7.82-7.90 (m, 4H), 12.48 (br s, 1H).

Example 48A

rac-3-(3,4-Difluorophenyl)-3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanoic acid



Step 1:

Under argon, 697 g of 3,4-difluorobenzaldehyde (4.76 mol, 1 equivalent), 495 g of malonic acid (4.76 mol, 1 equivalent) and 733 g of ammonium acetate (9.52 mol, 2 equivalents) were stirred at reflux in 2788 ml of ethanol for 20 h. The mixture was then cooled to RT and stirred at RT overnight. The precipitated crystals were filtered off with suction, washed with ethanol and diethyl ether and dried under reduced pressure. This gave 590 g (62% of theory) of *rac*-3-amino-3-(3,4-difluorophenyl)propanoic acid.

rac-3-Amino-3-(3,4-difluorophenyl)propanoic acid:
LC-MS (Method 1): R_t = 0.27 min

MS (ESpos): m/z = 202.0 $(M+H)^+$

Step 2:

0.20 g (0.99 mmol) of *rac*-3-amino-3-(3,4-difluorophenyl)propanoic acid and 0.15 g (0.99 mmol) of phthalic anhydride were dissolved in 0.8 ml of DMF and heated at reflux at 135°C overnight. The reaction solution was added to about 9 ml of water. The resulting suspension was extracted twice with ethyl acetate. The combined organic phases were washed with water, dried over sodium sulphate, filtered and concentrated. The crude product was purified by preparative HPLC (RP18 column, mobile phase: acetonitrile/water gradient with addition of 0.1% TFA). This gave 0.2 g of the title compound (61% of theory).

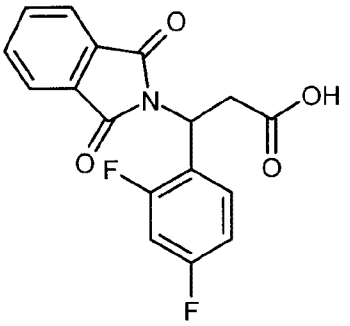
LC-MS (Method 2): R_t = 0.97 min

MS (ESpos): m/z = 332 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.24-3.3.33 (m, 1H), 3.44-3.52 (m, 1H), 5.63-5.70 (m, 1H), 7.23-7.28 (m, 1H), 7.36-7.47 (m, 1H), 7.49-7.57 (m, 1H), 7.82-7.90 (m, 4H), 12.51 (br s, 1H).

Example 49A

rac-3-(2,4-Difluorophenyl)-3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanoic acid



5.0 g of *rac*-3-amino-3-(2,4-difluorophenyl)propanoic acid (24.85 mmol) and 3.68 g of phthalic anhydride (24.85 mmol) were dissolved in 20 ml of DMF and the mixture was heated at reflux at 135°C overnight. The reaction solution was added to about 160 ml of water and extracted twice with ethyl acetate. The combined organic phases were washed with water, dried over sodium sulphate, filtered and concentrated. The crude product was purified by silica gel chromatography (mobile phase: dichloromethane/methanol 80:1, isocratic) and then by preparative HPLC (RP18 column, mobile phase: acetonitrile/water gradient with addition of 0.1% TFA). This gave 3.43 g of the title compound (27% of theory).

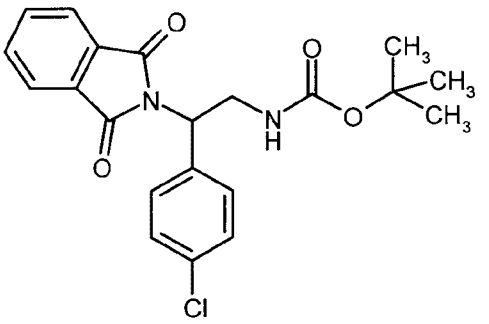
LC-MS (Method 1): R_t = 1.11 min

MS (ESpos): m/z = 332 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.24-3.3.34 (m, 1H), 3.40-3.49 (m, 1H), 5.89 (t, 1H), 7.09-7.15 (m, 1H), 7.19-7.28 (m, 1H), 7.70 (q, 1H), 7.82-7.89 (m, 4H), 12.55 (br s, 1H).

Example 50A

rac-tert-Butyl [2-(4-chlorophenyl)-2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]carbamate



At RT, 2.61 g of *rac*-tert-butyl [2-(4-chlorophenyl)-2-hydroxyethyl]carbamate (Example 45A, 9.62 mmol), 1.42 g of phthalimide (9.62 mmol) and 3.78 g of triphenylphosphine (14.43 mmol) were initially charged in abs. THF. 4.03 g (14.43 mmol) of diisopropyl azodicarboxylate were then added dropwise, and the mixture was stirred at RT for 30 min. The reaction mixture was concentrated and purified by silica gel chromatography (mobile phase: cyclohexane:ethyl acetate 10:1). This gave 2.92 g of the title compound (55% of theory, purity about 73%).

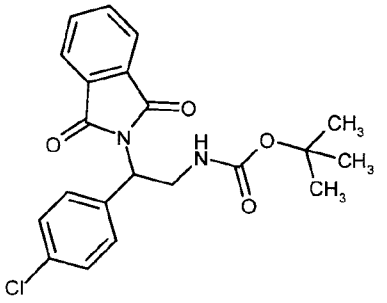
LC-MS (Method 2): R_t = 1.22 min

MS (ESpos): m/z = 401 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.26 (s, 9H), 3.70-3.79 (m, 1H), 3.82-3.93 (m, 1H), 5.32-5.38 (m, 1H), 7.22 (t, 1H), 7.38-7.44 (m, 4H), 7.80-7.85 (m, 4H).

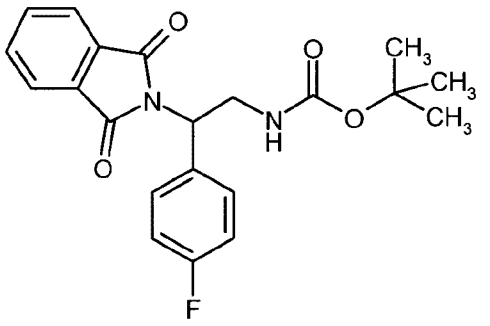
The example shown in Table 6A was prepared analogously to Example 50A by reacting phthalimide, triphenylphosphine and diisopropyl azodicarboxylate in THF with the appropriate alcohol.

Table 6A:

Example	IUPAC name / structure (yield)	Analytical data
51A	*rac*-tert-butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]carbamate  (55% of theory, purity about 73%)	LC-MS (Method 2): R_t = 1.22 min MS (ESpos): m/z = 401 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.26 (s, 9H), 3.70-3.79 (m, 1H), 3.82-3.93 (m, 1H), 5.32-5.38 (m, 1H), 7.22 (t, 1H), 7.38-7.44 (m, 4H), 7.80-7.85 (m, 4H).

Example 52A

rac-tert-Butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-2-(4-fluorophenyl)ethyl]carbamate



Under argon, a solution of 3.2 g of *rac*-3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-(4-fluorophenyl)propanoic acid (Example 47A, 8.78 mmol) in 32 ml of toluene was initially charged, and 1.33 g of triethylamine (13.18 mmol), 98 mg of 1,4-diazabicyclo[2.2.2]octane (0.88 mmol), 3.14 g of diphenylphosphoryl azide (11.42 mmol) and 6.51 g of tert-butanol (87.84 mmol) were added. The reaction mixture was heated at reflux overnight and then diluted with ethyl acetate and washed with water. The organic phase was dried over sodium sulphate, filtered and concentrated. The crude product was purified by silica gel chromatography (mobile phase: cyclohexane/ethyl acetate 8:1; 6:1). This gave 959 mg of the title compound (28% of theory).

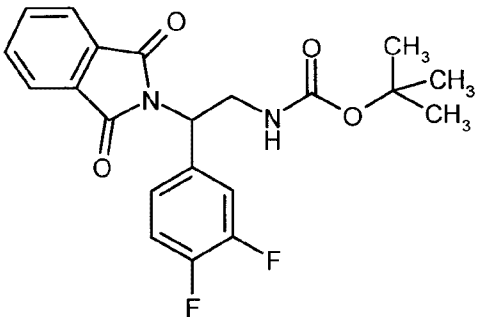
LC-MS (Method 2): R_t = 1.11 min

MS (ESpos): m/z = 385 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.26 (s, 9H), 3.69-3.78 (m, 1H), 3.84-3.95 (m, 1H), 5.32-5.39 (m, 1H), 7.15-7.26 (m, 3H), 7.41-7.48 (m, 2H), 7.80-7.89 (m, 4H).

Example 53A

rac-tert-Butyl [2-(3,4-difluorophenyl)-2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]carbamate



Under argon, a solution of 5.0 g of *rac*-3-(3,4-difluorophenyl)-3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanoic acid (Example 48A, 15.09 mmol) and 3.06 g of triethylamine (30.19 mmol) in 65 ml of toluene was initially charged, 4.36 g of diphenylphosphoryl azide (15.85 mmol) were added and the mixture was stirred at RT for 3.5 h. 65 ml of tert-butanol were then added, and the mixture was stirred under reflux overnight. After cooling, the reaction solution was concentrated and purified by flash chromatography (mobile phase: petroleum ether/ethyl acetate 2:1, isocratic). This gave 3.1 g of the title compound (45% of theory).

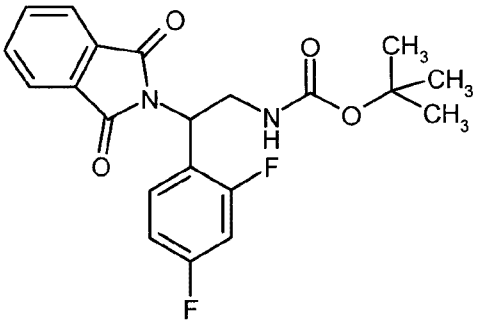
LC-MS (Method 2): R_t = 1.19 min

MS (ESpos): m/z = 403 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.26 (s, 9H), 3.73-3.90 (m, 2H), 5.32-5.39 (m, 1H), 7.20-7.27 (m, 2H), 7.36-7.46 (m, 1H), 7.48-7.56 (m, 1H), 7.81-7.91 (m, 4H).

Example 54A

rac-tert-Butyl [2-(2,4-difluorophenyl)-2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]carbamate



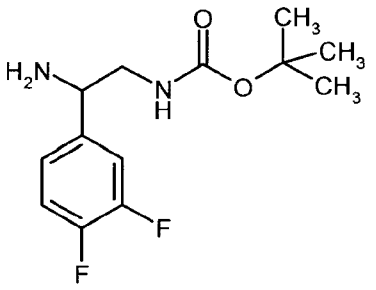
Under argon, 2.17 g of *rac*-3-(2,4-difluorophenyl)-3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-propanoic acid (Example 49A, 6.54 mmol) and 1.32 g of triethylamine (13.07 mmol) were initially charged in 23.8 ml of abs. toluene. 1.89 g of diphenylphosphoryl azide (6.86 mmol) were added at RT, and the mixture was stirred at RT with water cooling for 3.5 h, 23.8 ml of tert-butanol were then added and the mixture was stirred under reflux overnight. After cooling, the reaction solution was concentrated and purified by flash chromatography (mobile phase: cyclohexane/ethyl acetate 2:1). This gave 650 mg of the title compound (24% of theory).

LC-MS (Method 2): R_t = 1.11 min

MS (ESpos): m/z = 403 $(M+H)^+$

Example 55A

rac-tert-Butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate



6.13 g of *rac*-tert-butyl [2-(3,4-difluorophenyl)-2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-carbamate (Example 53A, purity about 60%, about 9.14 mmol) were initially charged in 13.1 ml of 40% strength aqueous methylamine solution and stirred in a closed vessel at 60°C overnight. The reaction mixture was concentrated and the residue was purified by silica gel chromatography (mobile phase: dichloromethane:methanol:diethylamine 30:1:0.1; 20:1:0.1). This gave 1.83 g of the title compound (74% of theory).

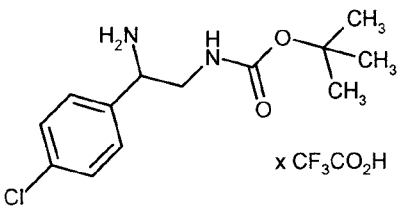
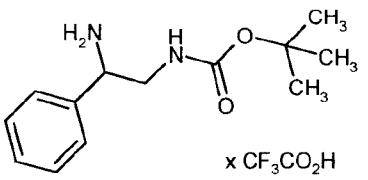
LC-MS (Method 1): R_t = 0.65 min

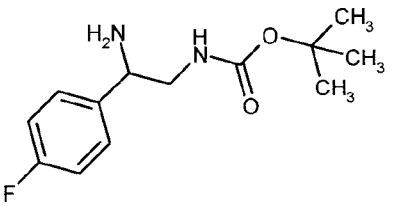
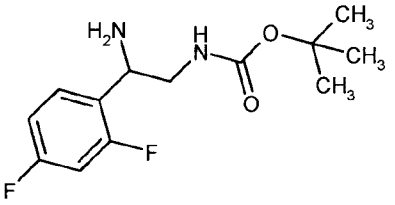
MS (ESpos): m/z = 273 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.33 (s, 9H), 1.96 (br s, 2H), 2.92-3.10 (m, 2H), 3.81-3.88 (m, 1H), 6.76-6.82 (m, 1H), 7.11-7.17 (m, 1H), 7.27-7.40 (m, 2H).

The examples shown in Table 7A were prepared analogously to Example 55A by reacting a solution of methylamine with the appropriate phthalimides.

Table 7A:

Example	**IUPAC name / structure (yield)**	**Analytical data**
56A	*rac*-tert-butyl [2-amino-2-(4-chlorophenyl)ethyl]carbamate trifluoroacetate [1)]  (41% of theory)	LC-MS (Method 2): R_t = 0.68 min MS (ESpos): m/z = 271 $(M+H-TFA)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.31 (s, 9H), 3.28-3.44 (m, 2H), 4.31 (br s, 1H), 7.00 (t, 1H), 7.43 (d, 2H), 7.52 (d, 2H), 8.42 (br s, 3H).
57A	*rac*-tert-butyl (2-amino-2-phenylethyl)carbamate trifluoroacetate [1)]  (45% of theory)	LC-MS (Method 2): R_t = 0.59 min MS (ESpos): m/z = 237 $(M+H-TFA)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.34 (s, 9H), 3.28-3.46 (m, 2H), 4.29 (br s, 1H), 7.01 (t, 1H), 7.35-7.48 (m, 5H), 8.43 (br s, 3H).

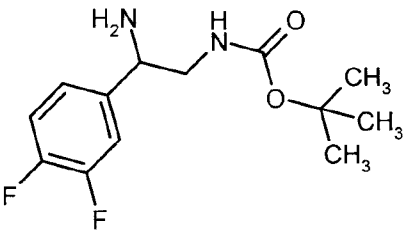
Example	IUPAC name / structure (yield)	Analytical data
58A	*rac*-tert-butyl [2-amino-2-(4-fluorophenyl)ethyl]carbamate [2)]  (85% of theory)	LC-MS (Method 2): R_t = 0.60 min MS (ESpos): m/z = 255 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.33 (s, 9H), 1.89 (br s, 2H), 2.88-2.97 (m, 1H), 3.04-3.11 (m, 1H), 3.84-3.90 (m, 1H), 6.80 (t, 1H), 7.11 (t, 2H), 7.36 (dd, 2H).
59A	*rac*-tert-butyl [2-amino-2-(2,4-difluorophenyl)ethyl]carbamate  (about 86% of theory)	LC-MS (Method 2): R_t = 0.65 min MS (ESpos): m/z = 273 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.31 (s, 9H), 1.91 (br s, 2H), 2.97-3.14 (m, 2H), 4.12 (t, 1H), 6.81 (t, 1H), 6.99-7.17 (m, 2H), 7.54 (q, 1H).

[1)] The crude product obtained was concentrated and re-purified by preparative HPLC (RP18 column, mobile phase: acetonitrile/water gradient with addition of 0.1% TFA).

[2)] Reaction conditions: 20 eq. of methylamine [40% strength solution in water]; 7 h at 60°C.

Example 60A

ent-tert-Butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate (enantiomer A)



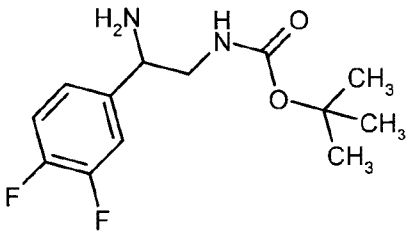
100 mg of *rac*-tert-butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate (Example 55A) were separated into the enantiomers on a chiral phase [column: Daicel Chiralpak AY-H, 5 µm, 250 x 20 mm, mobile phase: 80% isohexane, 20% ethanol + 0.2% diethylamine, flow rate 15 ml/min; 30°C, detection: 220 nm].

Yield: 43 mg of enantiomer A (99% pure, >99% ee)

R_t = 4.58 min [Daicel Chiralpak AY-H, 5µm, 250 x 4.6 mm; mobile phase: 80% isohexane, 20% ethanol + 0.2% diethylamine; flow rate 1.0 ml/min; 30°C; detection: 220 nm].

Example 61A

ent-tert-Butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate (enantiomer B):

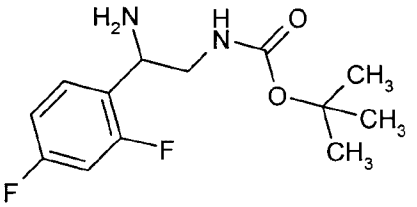


100 mg of *rac*-tert-butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate (Example 55A) were separated into the enantiomers on a chiral phase [column: Daicel Chiralpak AY-H, 5 µm, 250 x 20 mm, mobile phase: 80% isohexane, 20% ethanol + 0.2% diethylamine, flow rate 15 ml/min; 30°C, detection: 220 nm].

Yield: 44 mg of enantiomer B (99% pure, >99% ee) R_t = 5.61 min [Daicel Chiralpak AY-H, 5µm, 250 x 4.6 mm; mobile phase: 80% isohexane, 20% ethanol + 0.2% diethylamine; flow rate 1.0 ml/min; 30°C; detection: 220 nm].

Example 62A

ent-tert-Butyl [2-amino-2-(2,4-difluorophenyl)ethyl]carbamate (enantiomer A)



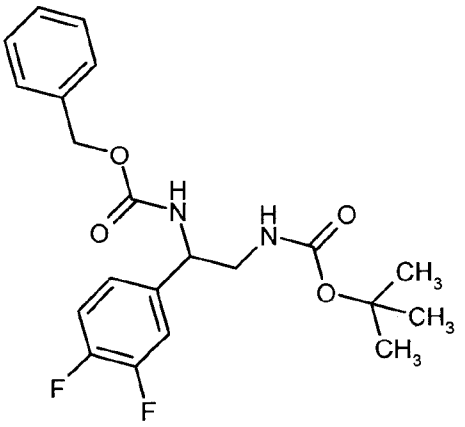
435 mg of Example 59A were separated into the enantiomers on a chiral phase [column: Daicel Chiralpak AY-H, 5 µm, 250 x 20 mm, mobile phase: 80% isohexane, 20% ethanol + 0.2% diethylamine, flow rate 15 ml/min; 30°C, detection: 220 nm]. To remove residual solvent, the product was dissolved in acetonitrile/water and lyophilized.

Yield: 182 mg (97% pure, >99% ee)

Enantiomer B: R_t = 5.25 min [Daicel Chiralpak AY-H, 5µm, 250 x 4.6 mm; mobile phase: 80% isohexane, 20% ethanol + 0.2% diethylamine; flow rate 1.0 ml/min; 30°C; detection: 220 nm].

Example 63A

ent-Benzyl tert-butyl [1-(3,4-difluorophenyl)ethane-1,2-diyl]biscarbamate



300 mg of *ent*-tert-butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate (enantiomer A) (Example 60A; 1.10 mmol) were initially charged in 5 ml of dry THF, and 1.15 ml of diisopropylethylamine (6.6 mmol, 6 equivalents), 26 mg of *N,N*-dimethylaminopyridine (0.22 mmol, 0.2 equivalents) and then, dropwise, 0.31 ml of of benzyl chloroformate (2.2 mmol, 2 equivalents) were added. The reaction mixture was stirred at RT for 48 h, then concentrated, taken up in ethyl acetate and washed with water. The combined organic phases were washed with saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered and concentrated. The residue was chromatographed on silica gel (mobile phase: cyclohexane/ethyl acetate 1:1). This gave 336 mg (75% of theory) of the title compound.

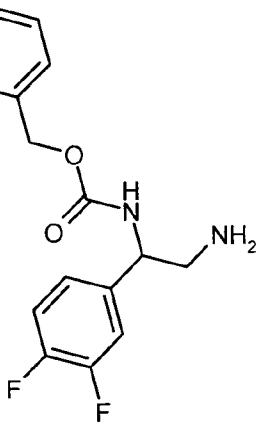
LC-MS (Method 2): R_t = 1.14 min

MS (ESpos): m/z = 407.3 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.3 (s, 9 H); 3.13 (t, 2 H); 4.65 (q, 1 H); 5.00 (q, 2 H); 6.88 (t, 1 H); 7.1 (br. s., 1 H); 7.21 – 7.40 (m, 7 H); 7.80 (d, 1 H).

Example 64A

ent-Benzyl [2-amino-1-(3,4-difluorophenyl)ethyl]carbamate



16.5 ml of a 2 N solution of hydrochloric acid in diethyl ether were added to 335 mg of *ent*-benzyl tert-butyl [1-(3,4-difluorophenyl)ethane-1,2-diyl]biscarbamate (Example 63A; 0.824 mmol), and the mixture was stirred at RT overnight. Another 16.5 ml of a 4 N solution of hydrochloric acid in 1,4-dioxane were added, and the mixture was stirred at RT for a further 3 h. The reaction mixture was concentrated, saturated aqueous sodium bicarbonate solution was added and the mixture was extracted three times with ethyl acetate. The combined organic phases were washed with saturated aqueous sodium chloride solution, dried over magnesium sulphate, filtered and concentrated. This gave 252.4 mg (84% of theory) of the title compound.

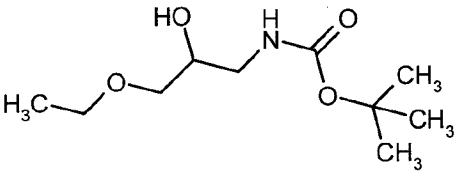
LC-MS (Method 2): R_t = 0.74 min

MS (ESpos): m/z = 307.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.82 – 1.95 (br. s, 2 H); 2.70 (d, 2 H); 4.49 (q, 1 H); 5.00 (m, 2 H); 7.1 (br. s., 1 H); 7.21 – 7.40 (m, 7 H); 7.80 (d, 1 H).

Example 65A

rac-tert-Butyl (3-ethoxy-2-hydroxypropyl)carbamate

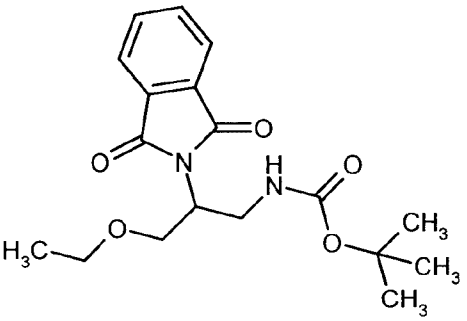


3 g of *rac*-1-amino-3-ethoxy-2-propanol hydrochloride (19.28 mmol, 1 equivalent) were initially charged in 40 ml of dichloromethane, and 5.7 ml of triethylamine (40.9 mmol, 2.1 equivalents) and then 4.96 ml of di-tert-butyl dicarbonate (21.6 mmol, 1.12 equivalents) were added. The reaction mixture was stirred at RT for 2 h, diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate solution and with saturated aqueous sodium chloride solution. The organic phase was dried with magnesium sulphate, filtered and concentrated. The residue was dried under high vacuum. This gave 3.73 g of crude product (88% of theory) which were reacted further without any work-up.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.10 (t, 3H); 1.39 (s, 9 H); 2.85 (dt, 1 H); 3.02 (dt, 1 H); 3.20 – 3.30 (m, 2 H); 3.40 (q, 2 H); 3.55 – 3.60 (m, 1 H); 4.75 (d, 1 H); 6.61 (t, 1 H).

Example 66A

rac-tert-Butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-ethoxypropyl]carbamate



At RT, 3.73 g of *rac*-tert-butyl (3-ethoxy-2-hydroxypropyl)carbamate (17 mmol, 1 equivalent), 2.50 g of phthalimide (17 mmol, 1 equivalent) and 6.69 g of triphenylphosphine (25.52 mmol, 1.5 equivalents) were initially charged in 70 ml of dry THF. 5.06 ml of diisopropyl azodicarboxylate (25.5 mmol, 1.5 equivalents) were added dropwise, and the mixture was stirred at RT for 2 h. The reaction mixture was concentrated under reduced pressure. The crude product was diluted with methanol, acetonitrile and water to 90 ml and purified by preparative HPLC (column material: Sunfire C18 5 µm 75x30 mm; flow rate 56 ml/min; mobile phase: 45% Milli-Q-water/50% acetonitrile/5% 1% aqueous formic acid; injection volume: 0.5 ml; detection wavelength: 210 nm). This gave 4.88 g of the title compound (82% of theory).

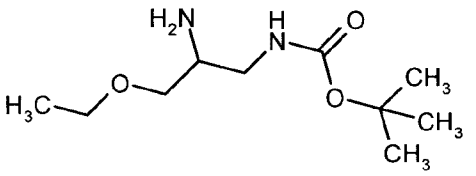
LC-MS (Method 2): R_t = 1.04 min

MS (ESpos): m/z = 349.3 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.02 (t, 3H); 1.25 (s, 9 H); 3.34 – 3.48 (m, 4 H); 3.65 (dd, 1 H); 3.81 (dd, 1 H); 4.32 – 4.38 (m, 1 H); 7.10 (t, 1 H); 7.80 – 7.90 (m, 4 H).

Example 67A

rac-tert-Butyl (2-amino-3-ethoxypropyl)carbamate

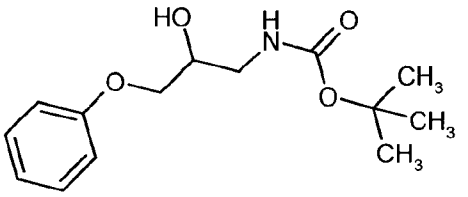


4.88 g of *rac*-tert-butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-ethoxypropyl]carbamate (14.0 mmol, 1 equivalent) were initially charged in 12 ml of 40% strength aqueous methylamine solution and reated in a microwave at 100°C for 1.5 h. The reaction mixture was concentrated, the residue was taken up in 10 ml of toluene and concentrated again. This step was repeated several times. The residue was then chromatographed on silica gel (mobile phase: dichloromethane/methanol 10:1). This gave 470 mg (15% of theory) of the title compound.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.10 (t, 3H); 1.38 (s, 9 H); 3.03 – 3.20 (m, 3 H); 3.34 – 3.48 (m, 4 H); 6.95 (t, 1 H).

Example 68A

rac-tert-Butyl (2-hydroxy-3-phenoxypropyl)carbamate



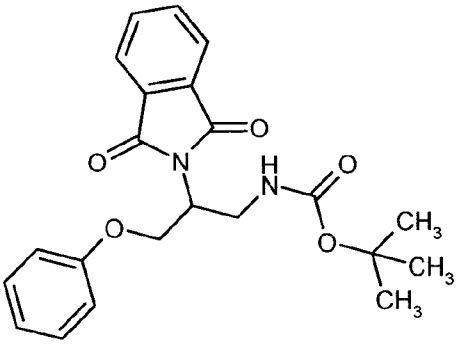
1.13 g of *rac*-1-amino-3-phenoxypropan-2-ol hydrochloride (5.5 mmol, 1 equivalent) were initially charged in 11.5 ml of dichloromethane, and 1.64 ml of triethylamine (11.7 mmol, 2.1 equivalents) and then 1.43 ml of di-tert-butyl dicarbonate (6.21 mmol, 1.12 equivalents) were added. The reaction mixture was stirred at RT for 2 h, diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate solution and with saturated aqueous sodium chloride solution. The organic phase was dried with magnesium sulphate, filtered and concentrated. The residue was dried under high vacuum. This gave 1.5 g of crude product (quantitative yield) which was reacted further without further purification.

LC-MS (Method 2): R_t = 0.88 min

MS (ESpos): m/z = 268.2 $(M+H)^+$

Example 69A

rac-tert-Butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-phenoxypropyl]carbamate



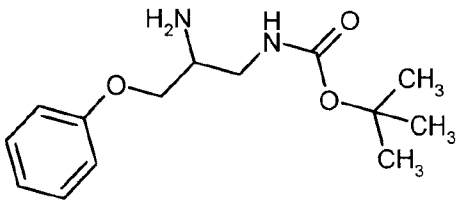
At RT, 1.5 g of *rac*-tert-butyl (2-hydroxy-3-phenoxypropyl)carbamate (5.6 mmol, 1 equivalent), 0.99 g of phthalimide (6.73 mmol, 1.2 equivalents) and 2.21 g of triphenylphosphine (8.4 mmol, 1.5 equivalents) were initially charged in 23 ml of dry tetrahydrofuran. 1.70 ml of diisopropyl azodicarboxylate (8.4 mmol, 1.5 equivalents) were added dropwise, and the mixture was stirred at RT for 2 h. LC/MS showed complete conversion of the reaction. The reaction mixture was concentrated and purified by chromatography on silica gel (Biotage Isolera; cyclohexane/ethyl acetate gradient as mobile phase). This gave 1.08 g of the title compound (48% of theory).

LC-MS (Method 2): R_t = 1.13 min

MS (ESpos): m/z = 397.3 $(M+H)^+$

Example 70A

rac-tert-Butyl (2-amino-3-phenoxypropyl)carbamate



1.08 g of *rac*-tert-butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-phenoxypropyl]carbamate (2.72 mmol, 1 equivalent) were initially charged in 5 ml of 40% strength aqueous methylamine solution and reacted in a microwave at 100°C for 2 h. The reaction mixture was concentrated and

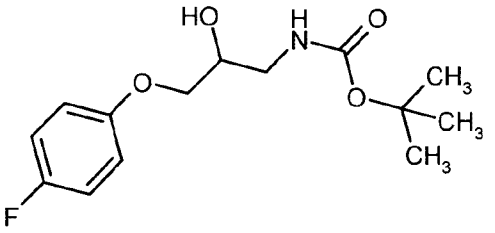
the residue was then chromatographed on silica gel (Biotage Isolera; mobile phase: dichloromethane/methanol gradient). This gave 200 mg (27% of theory) of the title compound.

LC-MS (Method 2): R_t = 0.57 min

MS (ESpos): m/z = 267.1 $(M+H)^+$

Example 71A

rac-tert-Butyl [3-(4-fluorophenoxy)-2-hydroxypropyl]carbamate



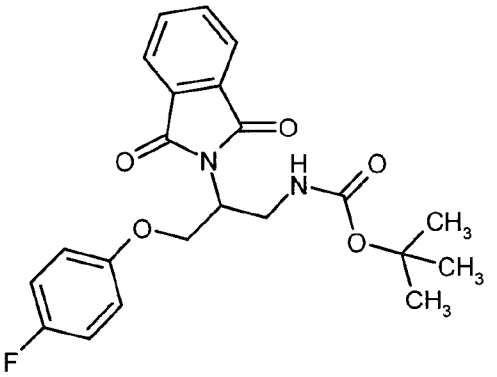
0.93 g of *rac*-1-amino-3-(4-fluorophenoxy)propan-2-ol (5.07 mmol, 1 equivalent) were initially charged in 10.5 ml of dichloromethane, and first 1.5 ml of triethylamine (10.7 mmol, 2.1 equivalents) and then 1.31 ml of di-tert-butyl dicarbonate (5.68 mmol, 1.12 equivalents) were added. The reaction mixture was stirred at RT for 2 h. The mixture was then diluted with dichloromethane and washed with saturated aqueous sodium bicarbonate solution and with saturated aqueous sodium chloride solution. The organic phase was dried over magnesium sulphate, filtered and concentrated. The residue was used without further purification for the next reaction.

LC-MS (Method 2): R_t = 0.89 min

MS (ESpos): m/z = 286.2 $(M+H)^+$

Example 72A

rac-tert-Butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-(4-fluorophenoxy)propyl]carbamate



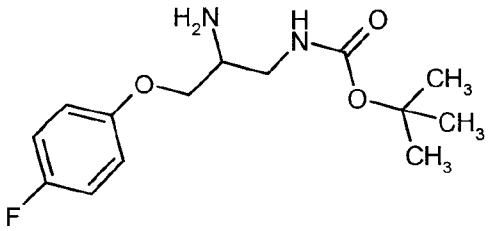
At RT, 1.5 g of *rac*-tert-butyl [3-(4-fluorophenoxy)-2-hydroxypropyl]carbamate (5.26 mmol, 1 equivalent), 0.93 g of phthalimide (6.31 mmol, 1.2 equivalents) and 2.07 g of triphenylphosphine (7.9 mmol, 1.5 equivalents) were initially charged in 22 ml of dry THF. 1.56 ml of diisopropyl azodicarboxylate (7.9 mmol, 1.5 equivalents) were added dropwise, and the mixture was stirred at RT for 2 h. The reaction mixture was concentrated under reduced pressure and purified by chromatography on silica gel (Biotage Isolera; cyclohexane/ethyl acetate gradient as mobile phase). This gave 1.97 g of the title compound (90% of theory).

LC-MS (Method 2): R_t = 1.14 min

MS (ESpos): m/z = 415.3 $(M+H)^+$

Example 73A

rac-tert-Butyl [2-amino-3-(4-fluorophenoxy)propyl]carbamate



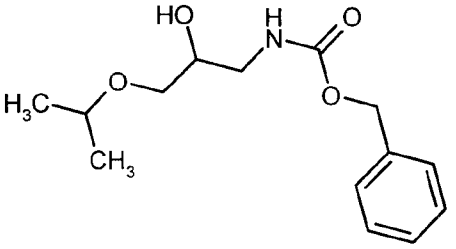
1.97 g of *rac*-tert-butyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-(4-fluorophenoxy)propyl]-carbamate (4.75 mmol, 1 equivalent) were initially charged in 5 ml of 40% strength aqueous methylamine solution, and the mixture was reacted in a microwave at 100°C for 2 h. The reaction mixture was concentrated and the residue was then chromatographed on silica gel (Biotage Isolera; mobile phase: dichloromethane/methanol gradient). This gave 900 mg (67% of theory) of the title compound.

LC-MS (Method 2): R_t = 0.58 min

MS (ESpos): m/z = 285.1 $(M+H)^+$

Example 74A

rac-Benzyl (2-hydroxy-3-isopropoxypropyl)carbamate



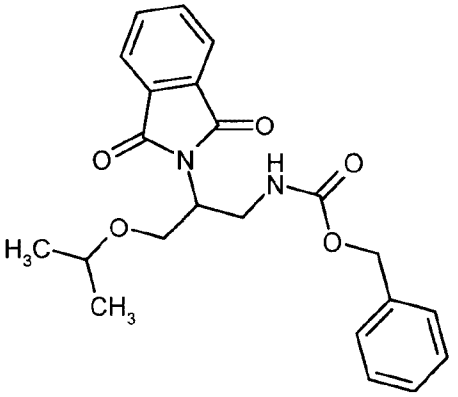
1 g of *rac*-1-amino-3-isopropoxypropan-2-ol (7.5 mmol, 1 equivalent) were initially charged in 25 ml of THF, and 1.16 ml of benzyl chloroformate (8.3 mmol, 1.1 equivalents), 3.9 ml of diisopropylethylamine (22.5 mmol, 3 equivalents) and 183 mg of *N,N*-dimethylaminopyridine (1.5 mmol, 0.2 equivalents) were added. The reaction mixture was stirred at RT, and after about 30 min 5 ml of DMF were added. After a further 2.5 h at RT, the mixture was concentrated to dryness. The residue was taken up in ethyl acetate and washed with saturated aqueous sodium bicarbonate solution and then with saturated aqueous sodium chloride solution. The organic phase was dried over magnesium sulphate, filtered and concentrated. The residue was used without further purification for the next reaction.

LC-MS (Method 2): R_t = 0.80 min

MS (ESpos): m/z = 268.2 $(M+H)^+$

Example 75A

rac-Benzyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-isopropoxypropyl]carbamate



At RT, 1.28 g of racemic benzyl (2-hydroxy-3-isopropoxypropyl)carbamate (4.79 mmol, 1 equivalent), 0.85 g of phthalimide (5.75 mmol, 1.2 equivalents) and 1.88 g of triphenylphosphine (7.2 mmol, 1.5 equivalent) were initially charged in 20 ml of dry tetrahydrofuran. 1.42 ml of diisopropyl azodicarboxylate (7.2 mmol, 1.5 equivalent) were added dropwise, and the mixture was stirred at RT for 2 h. The reaction mixture was concentrated under reduced pressure and purified by chromatography on silica gel (Biotage Isolera; cyclohexane/ethyl acetate gradient as mobile phase). This gave 2.3 g (66% pure; 78% of theory) of the title compound (contaminated with diisopropyl hydrazine-1,2-dicarboxylate).

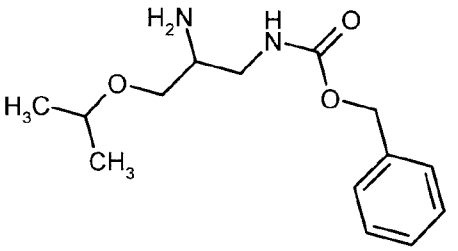
LC-MS (Method 2): R_t = 1.12 min

MS (ESpos): m/z = 397.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.91 (d, 3 H), 1.00 (d, 3 H), 3.42 – 3.48 (m, 2 H), 3.50 (hept, 1 H), 3.69 (dd, 1 H), 3.79 (t, 1 H), 4.31 (q, 1 H), 4.91 (s, 2 H), 7.20 – 7.30 (m, 5 H), 7.52 (t, 1 H), 7.80 – 7.86 (m, 4 H).

Example 76A

rac-Benzyl (2-amino-3-isopropoxypropyl)carbamate



2.3 g of *rac*-benzyl [2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-3-isopropoxypropyl]carbamate (5.6 mmol, 1 equivalent) were dissolved in 30 ml of ethanol, 7.3 ml of 40% strength aqueous methylamine solution (84.4 mmol, 15 equivalent) were added and the mixture was stirred at 60°C overnight. The reaction mixture was concentrated and the residue was then chromatographed on silica gel (Biotage Isolera; mobile phase: dichloromethane/methanol gradient). This gave 730 mg (49% of theory) of the title compound.

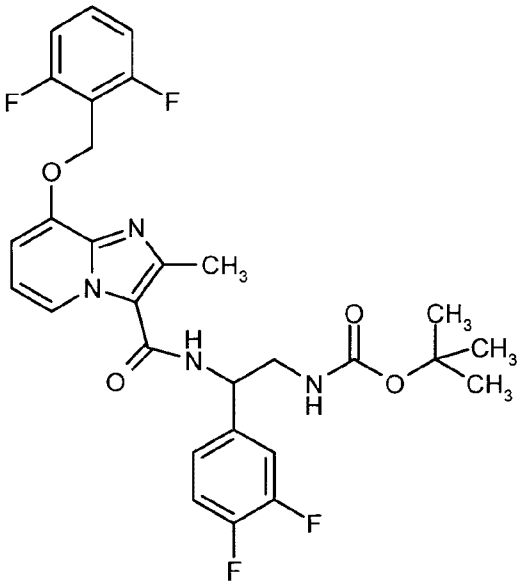
LC-MS (Method 2): R_t = 0.59 min

MS (ESpos): m/z = 267.2 $(M+H)^+$

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.05 (d, 6 H), 1.74 (br. s, 2 H), 2.79 – 2.90 (m, 2 H), 3.02 - 3.12 (m, 1 H), 3.18 (dd, 1 H), 3.21 (dd, 1 H), 3.50 (q, 1 H), 5.00 (s, 2 H), 7.18 (t, 1 H), 7.28 – 7.39 (m, 5 H).

Example 77A

rac-tert-Butyl {2-[({8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridin-3-yl}carbonyl)-amino]-2-(3,4-difluorophenyl)ethyl}carbamate



200 mg of 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid (0.63 mmol), 242 mg of *rac*-(benzotriazol-1-yloxy)bisdimethylaminomethylium fluoroborate (TBTU, 0.75 mmol) and 318 mg of 4-methylmorpholine (3.14 mmol) were initially charged in 4.3 ml of DMF. At RT, 242 mg of *rac*-tert-butyl [2-amino-2-(3,4-difluorophenyl)ethyl]carbamate (Example 55A, 0.75 mmol) were added, and the mixture was stirred at RT overnight. About 16 ml of water were added to the reaction solution, the mixture was stirred for another 30 min and the precipitate formed was filtered off and washed with water. The solid was treated in an ultrasonic bath with about 4 ml of acetonitrile for 10 min, filtered off and dried under high vacuum overnight. This gave 355 mg of the title compound (96% of theory).

LC-MS (Method 2): R_t = 1.10 min

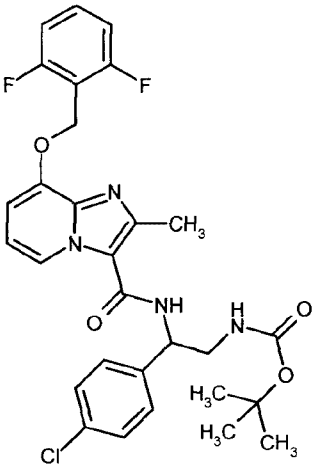
MS (ESpos): m/z = 573 $(M+H)^+$

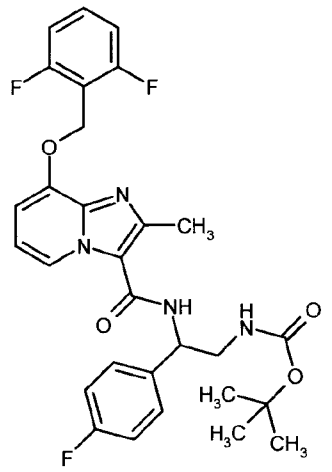
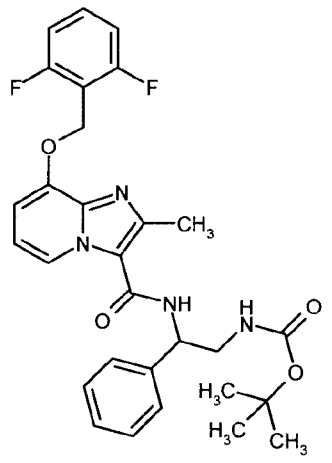
^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.32 (s, 9H), 2.59 (s, 3H), 3.29-3.46 (m, 2H), 5.15 (q, 1H), 5.31 (s, 2H), 6.91 (t, 1H), 7.01 (d, 1H), 7.08 (t, 1H), 7.19-7.27 (m, 3H), 7.36-7.51 (m, 2H), 7.59 (q, 1H), 8.21 (d, 1H), 8.56 (d, 1H).

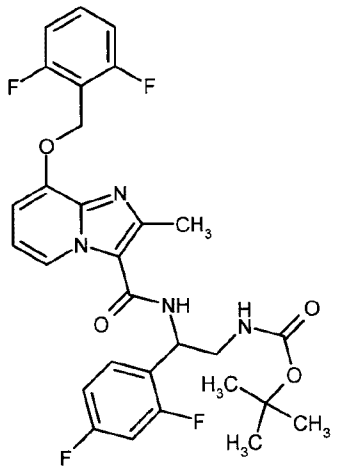
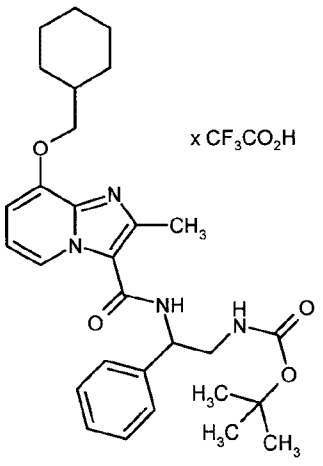
The examples shown in Table 8A were prepared by reacting 8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridine-3-carboxylic acid with the amines, prepared as described above or

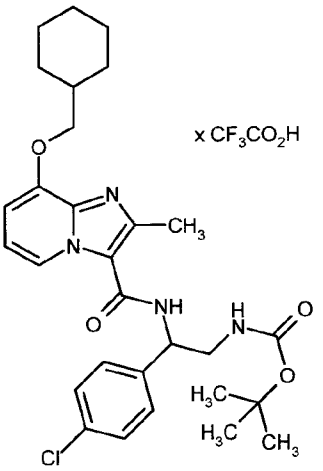
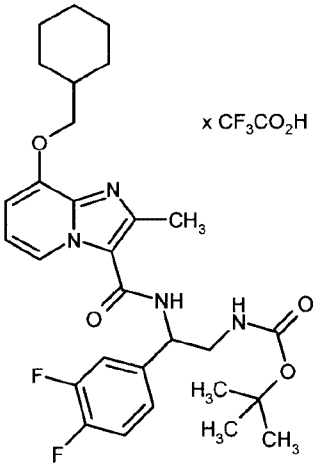
commercially available, (1.1-1.5 equivalents) and 4-methylmorpholine (4-6 equivalents) under the reaction conditions described in the General Working Procedure 3.

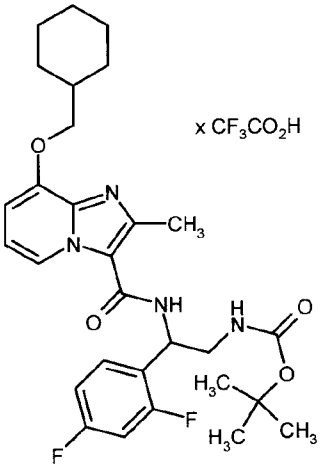
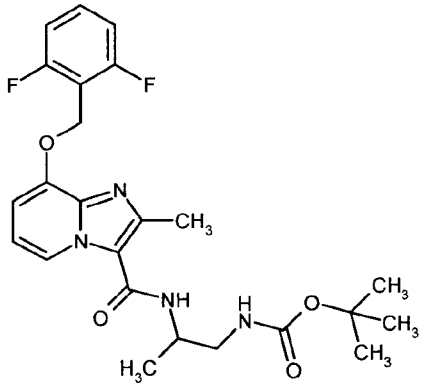
Table 8A:

Example	IUPAC name / structure (yield)	Analytical data
78A	*rac*-tert-butyl {2-(4-chlorophenyl)-2-[({8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]-pyridin-3-yl}carbonyl)amino]ethyl}carbamate  (88% of theory)	LC-MS (Method 2): R_t = 1.13 min MS (ESpos): m/z = 571 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.32 (s, 9H), 2.58 (s, 3H), 3.29-3.46 (m, 2H), 5.16 (q, 1H), 5.31 (s, 2H), 6.91 (t, 1H), 7.02 (d, 1H), 7.09 (t, 1H), 7.23 (t, 2H), 7.38-7.45 (m, 4H), 7.59 (quint, 1H), 8.21 (d, 1H), 8.56 (d, 1H).

Example	IUPAC name / structure (yield)	Analytical data
79A	*rac*-tert-butyl {2-[({8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridin-3-yl}carbonyl)-amino]-2-(4-fluorophenyl)ethyl}carbamate  (99% of theory)	LC-MS (Method 2): R_t = 1.03 min MS (ESpos): m/z = 555 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.32 (s, 9H), 2.58 (s, 3H), 3.29-3.46 (m, 2H), 5.18 (q, 1H), 5.31 (s, 2H), 6.91 (t, 1H), 7.02 (d, 1H), 7.08 (t, 1H), 7.13-7.26 (m, 4H), 7.43 (dd, 2H), 7.59 (quint, 1H), 8.19 (d, 1H), 8.56 (d, 1H).
80A	*rac*-tert-butyl {2-[({8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridin-3-yl}carbonyl)-amino]-2-phenylethyl}carbamate  (63% of theory)	LC-MS (Method 2): R_t = 1.06 min MS (ESpos): m/z = 537 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.32 (s, 9H), 2.59 (s, 3H), 3.28-3.46 (m, 2H), 5.19 (q, 1H), 5.31 (s, 2H), 6.91 (t, 1H), 7.01 (d, 1H), 7.08 (t, 1H), 7.20-7.28 (m, 3H), 7.38 (t, 2H), 7.40 (d, 2H), 7.59 (quint, 1H), 8.19 (d, 1H), 8.57 (d, 1H).

Example	IUPAC name / structure (yield)	Analytical data
81A	*ent*-tert-butyl {2-[({8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridin-3-yl}carbonyl)-amino]-2-(2,4-difluorophenyl)ethyl}carbamate  (64% of theory)	LC-MS (Method 2): R_t = 1.07 min MS (ESpos): m/z = 573 $(M+H)^+$
82A	*rac*-tert-butyl [2-({[8-(cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridin-3-yl]carbonyl}-amino)-2-phenylethyl]carbamate trifluoroacetate  (41% of theory)	LC-MS (Method 2): R_t = 1.09 min MS (ESpos): m/z = 507 $(M-TFA+H)^+$

Example	IUPAC name / structure (yield)	Analytical data
83A	*rac*-tert-butyl [2-(4-chlorophenyl)-2-({[8-(cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridin-3-yl]carbonyl}amino)ethyl]carbamate trifluoroacetate  (67% of theory)	LC-MS (Method 2): R_t = 1.17 min MS (ESpos): m/z = 541 $(M\text{-}TFA+H)^+$
84A	*rac*-tert-butyl [2-({[8-(cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridin-3-yl]carbonyl}-amino)-2-(3,4-difluorophenyl)ethyl]carbamate trifluoroacetate  (58% of theory)	LC-MS (Method 2): R_t = 1.17 min MS (ESpos): m/z = 543 $(M\text{-}TFA+H)^+$

Example	IUPAC name / structure (yield)	Analytical data
85A	*ent*-tert-butyl [2-({[8-(cyclohexylmethoxy)-2-methylimidazo[1,2-a]pyridin-3-yl]carbonyl}-amino)-2-(2,4-difluorophenyl)ethyl]carbamate trifluoroacetate  (42% of theory)	LC-MS (Method 2): R_t = 1.17 min MS (ESpos): m/z = 543 $(M\text{-}TFA+H)^+$
86A	*rac*-tert-butyl {2-[({8-[(2,6-difluorobenzyl)oxy]-2-methylimidazo[1,2-a]pyridin-3-yl}carbonyl)-amino]propyl}carbamate  (57% of theory)	LC-MS (Method 1): R_t = 1.04 min MS (ESpos): m/z = 475 $(M+H)^+$ ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.14 (d, 3H), 1.36 (s, 9H), 2.50 (s, 3H), 3.04-3.20 (m, 2H), 4.06-4.16 (m, 1H), 5.30 (s, 2H), 6.89-7.03 (m, 3H), 7.22 (t, 2H), 7.56-7.64 (m, 2H), 8.61 (d, 1H).

DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME __1___ DE __3___

NOTE: Pour les tomes additionels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

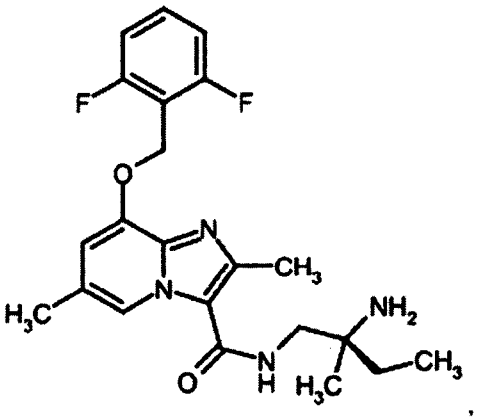
THIS IS VOLUME __1___ OF __3___

NOTE: For additional volumes please contact the Canadian Patent Office.

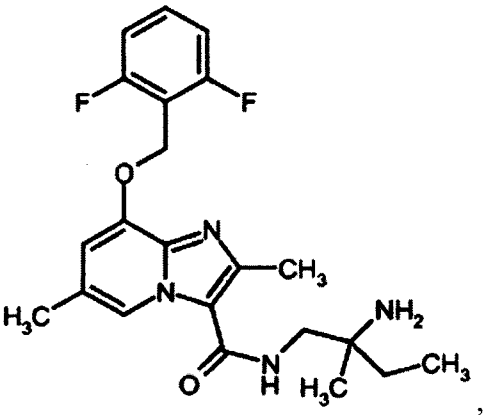
CLAIMS:

1. The compound:

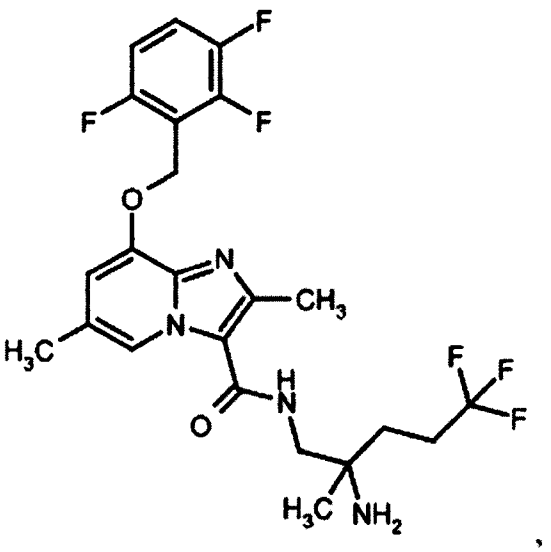
ent-N-[(2S)-amino-2-methylbutyl]-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



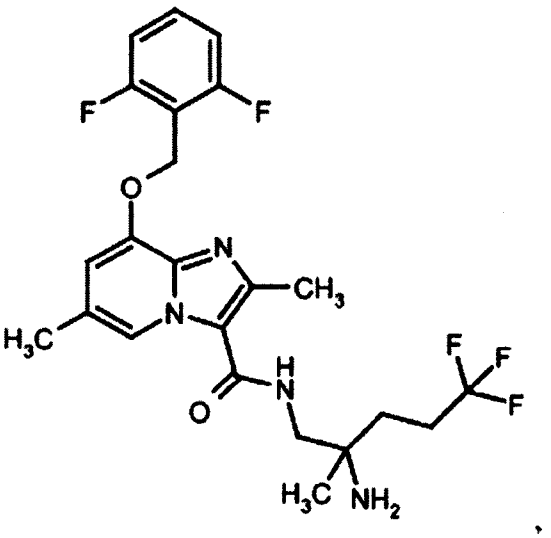
ent-N-(2-amino-2-methylbutyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



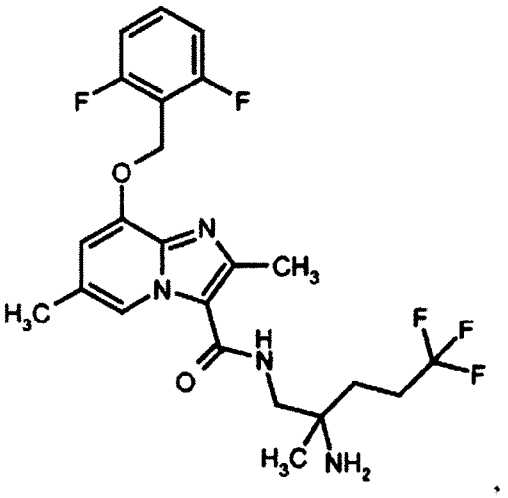
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



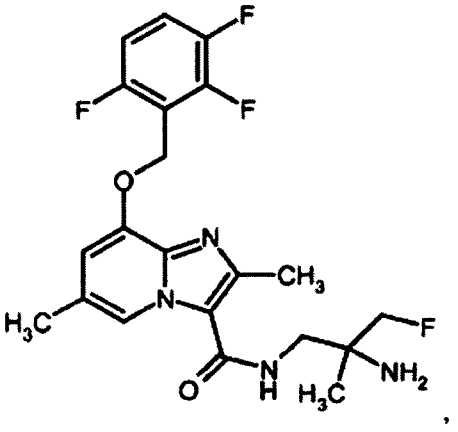
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



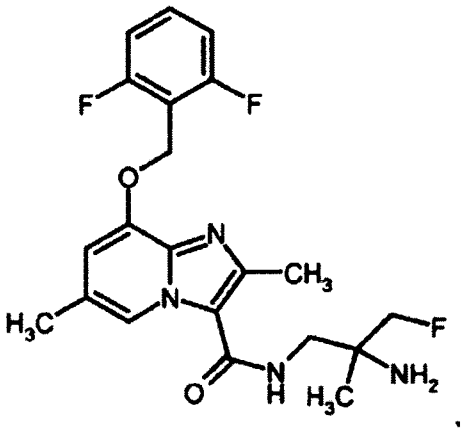
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



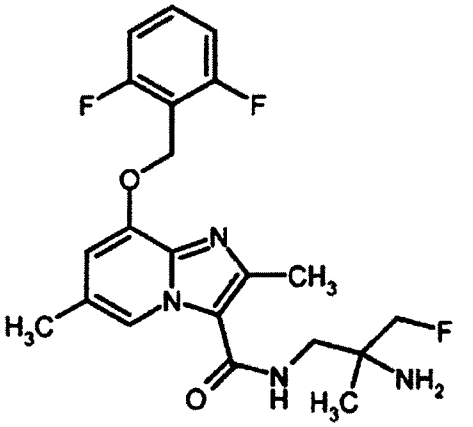
ent-N-(2-amino-3-fluoro-2-methylpropyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



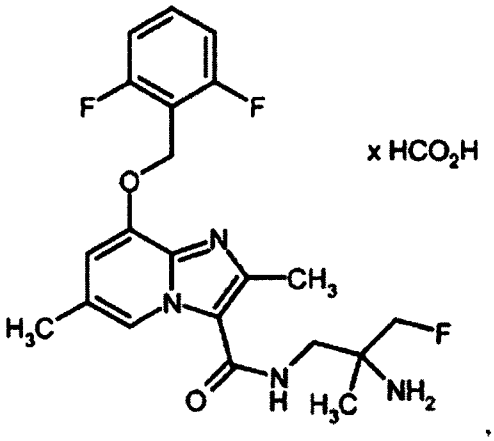
ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamixe (enantiomer B)



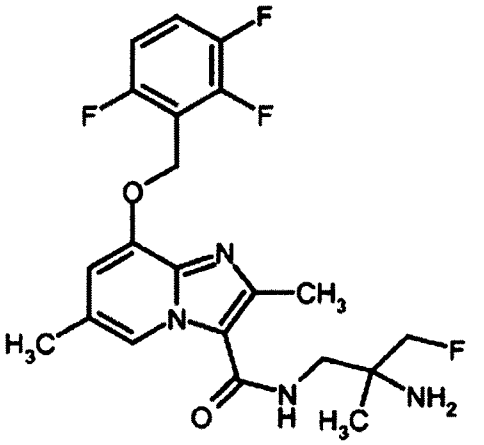
ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-diflurobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-carboxamide (enantiomer A)



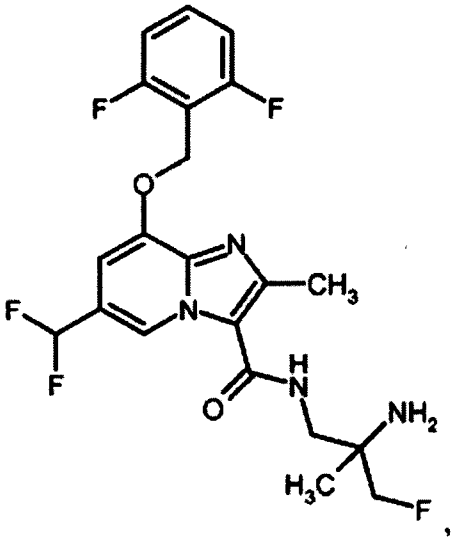
rac-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide formate



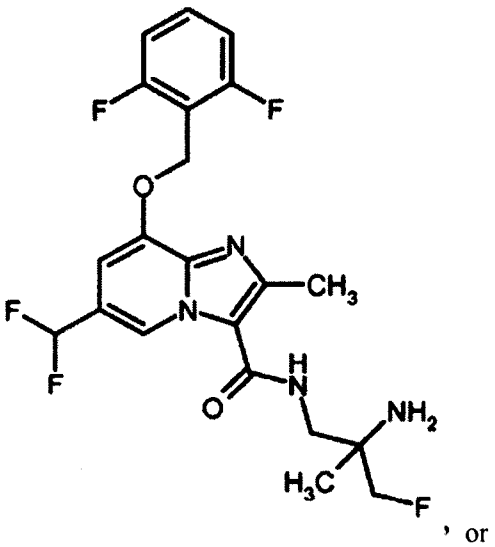
ent-N-(2-amino-3-fluoro-2-methylpropyl)-2,6-dimethyl-8-[(2,3,6-triflurobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(difluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)

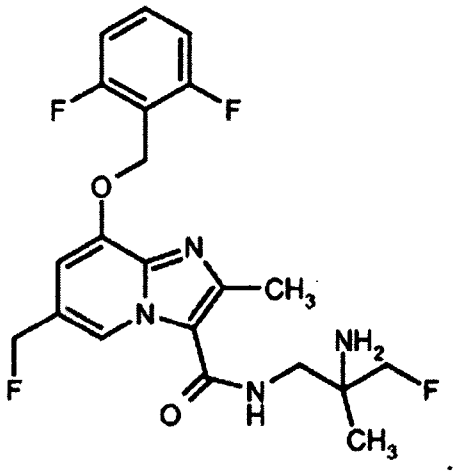


ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(difluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



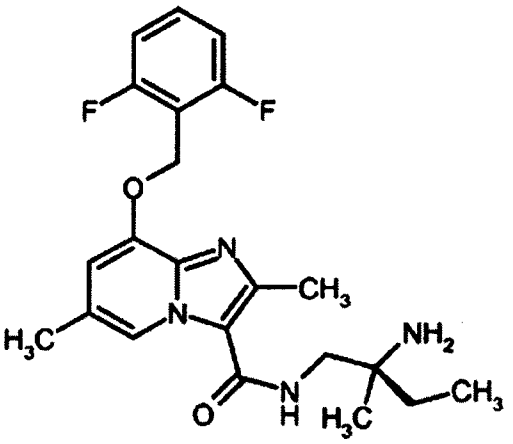
, or

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(fluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide



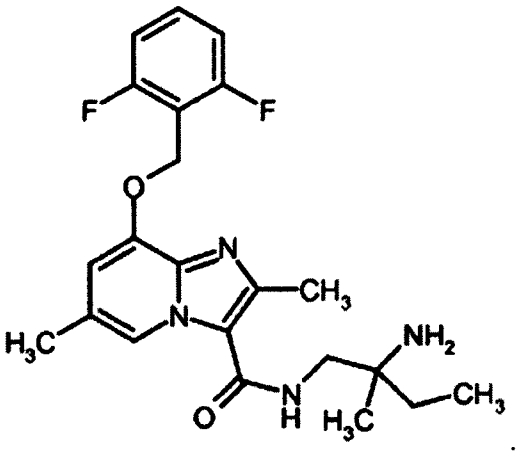
2. Compound according to claim 1

ent-N-[(2S)-amino-2-methylbutyl]-8-[2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



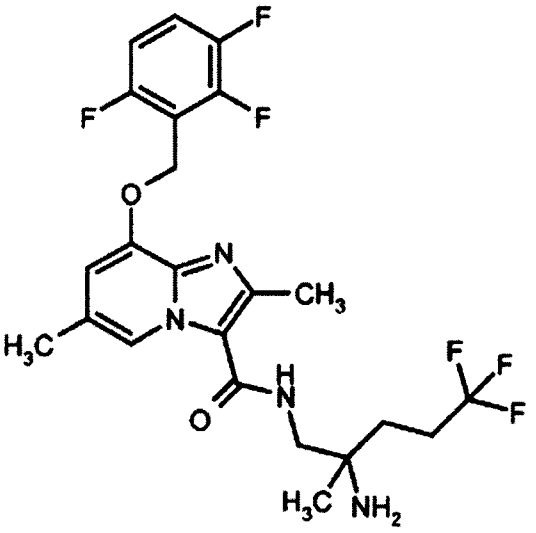
3. Compound according to claim 1

ent-N-(2-amino-2-methylbutyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



4. Compound according to claim 1

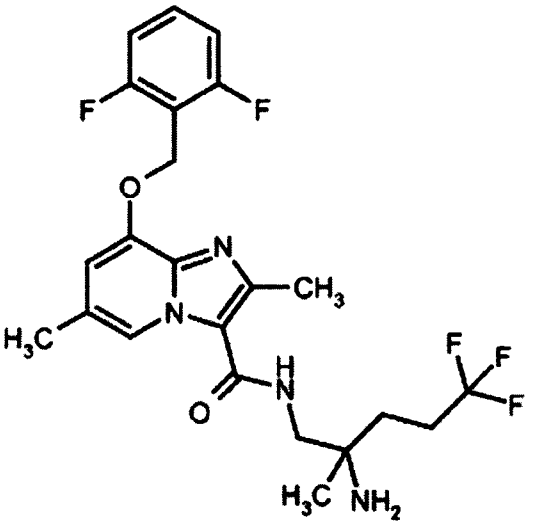
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]-imidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



5

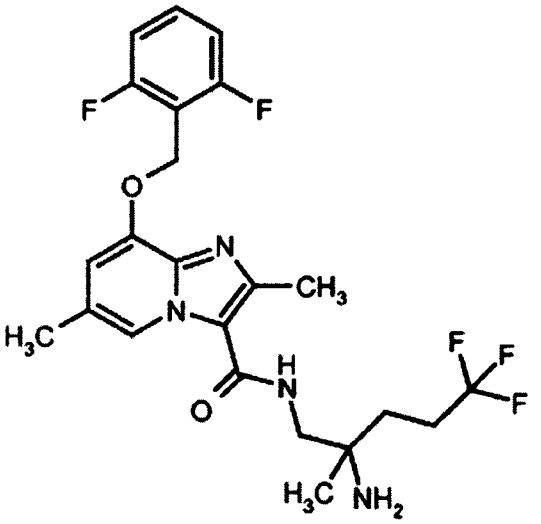
5. Compound according to claim 1

ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



6. Compound according to claim 1

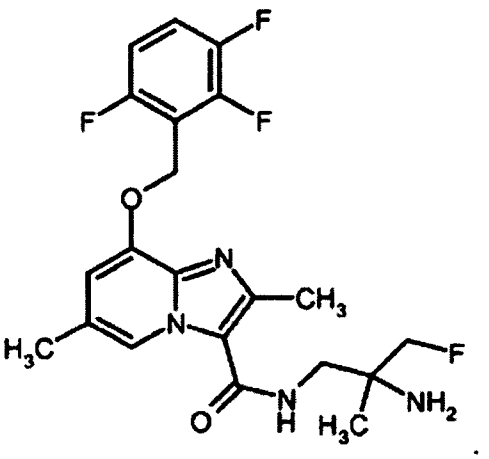
ent-N-(2-amino-5,5,5-trifluoro-2-methylpentyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



5

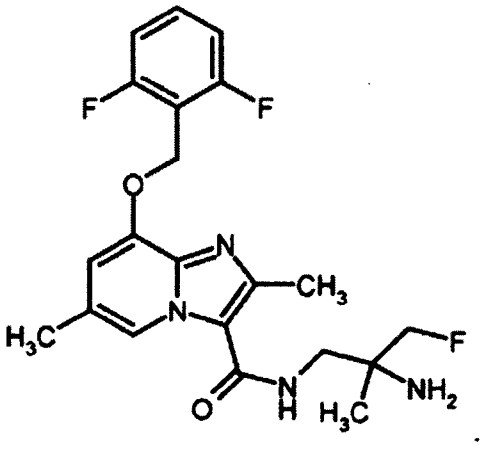
7. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



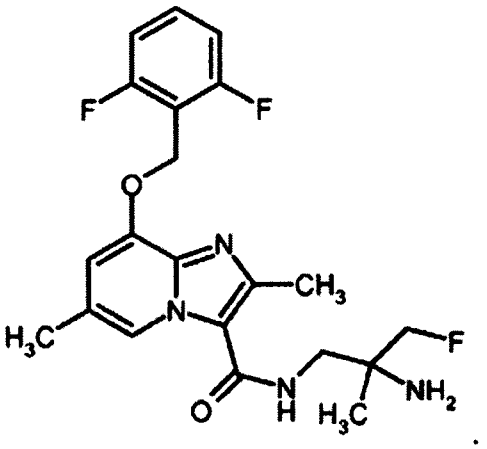
8. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



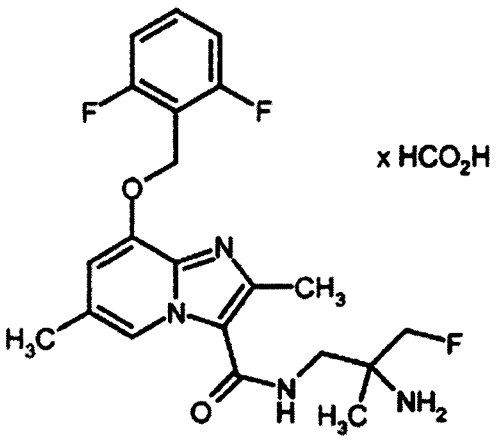
9. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



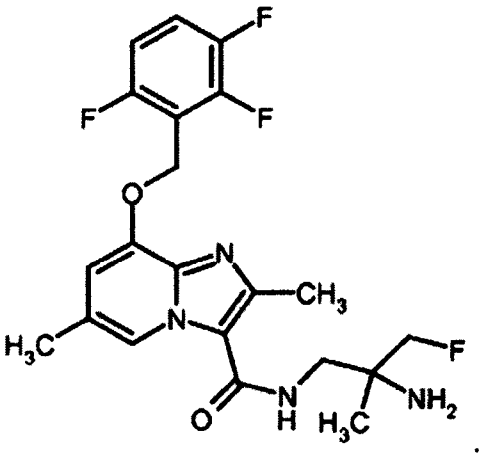
10. Compound according to claim 1

rac-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-2,6-dimethylimidazo[1,2-a]pyridine-3-carboxamide formate



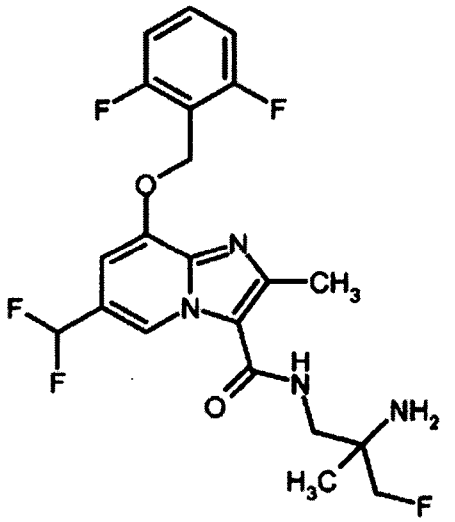
11. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-2,6-dimethyl-8-[(2,3,6-trifluorobenzyl)oxy]imidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)



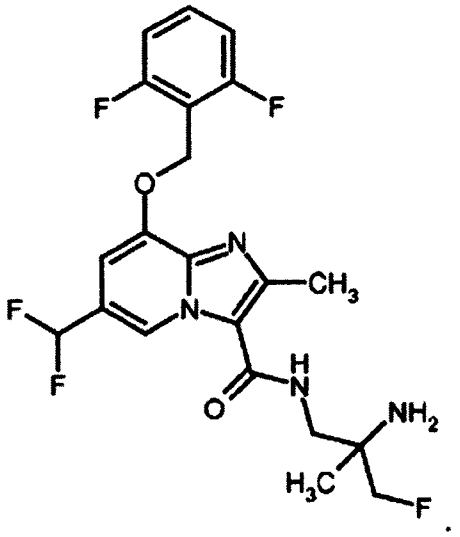
12. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(difluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer B)



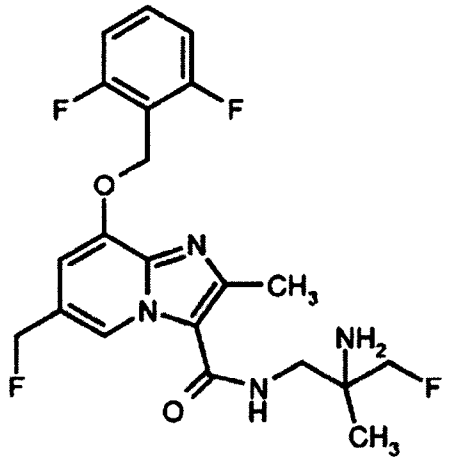
13. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(difluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide (enantiomer A)

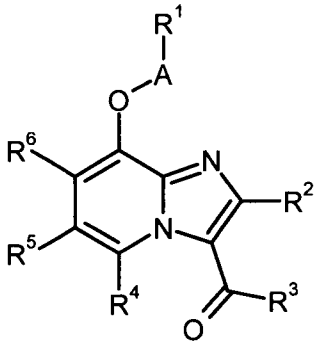


14. Compound according to claim 1

ent-N-(2-amino-3-fluoro-2-methylpropyl)-8-[(2,6-difluorobenzyl)oxy]-6-(fluoromethyl)-2-methylimidazo[1,2-a]pyridine-3-carboxamide



15. Process for preparing the compounds of the formula (I)



(I),

in which

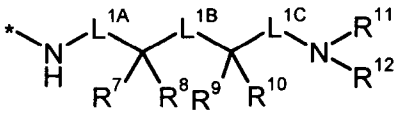
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

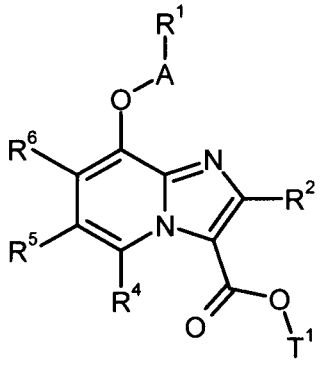
R^4 represents hydrogen,

R^5 represents methyl, fluoromethyl or difluoromethyl,

R^6 represents hydrogen,

characterized in that

[A] a compound of the formula (II)

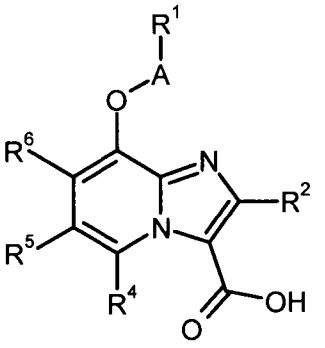


(II),

in which A, R^1, R^2, R^4, R^5 and R^6 each have the meanings given above and

T^1 represents (C_1-C_4)-alkyl or benzyl,

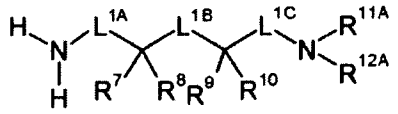
is reacted in an inert solvent in the presence of a suitable base or acid to give a carboxylic acid of the formula (III)



(III),

in which A, R^1, R^2, R^4, R^5 and R^6 each have the meanings given above,

and this is subsequently reacted in an inert solvent under amide coupling conditions with an amine of the formula (IV-A)



(IV-A)

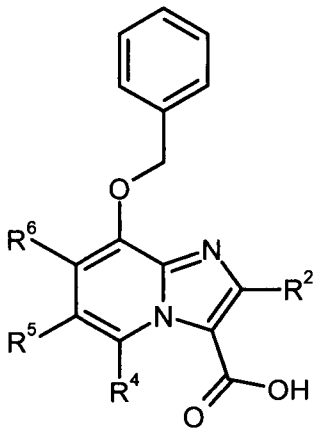
in which L^{1A}, L^{1B}, L^{1C}, R^7, R^8, R^9, and R^{10} each have the meanings given above

and

R^{11A} and R^{12A} have the meanings given above for R^{11} and R^{12}, respectively, or represent an amino protective group,

or

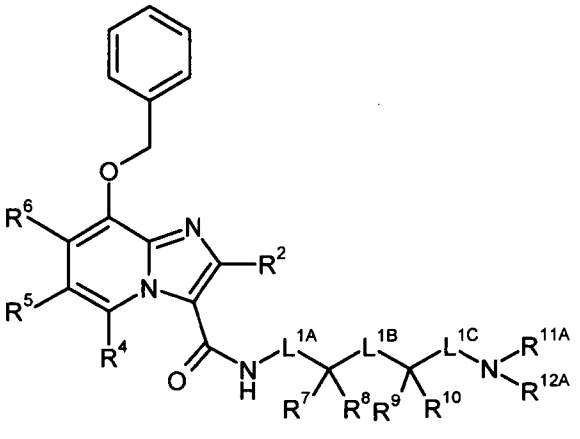
[B] a compound of the formula (III-B)



(III-B),

in which R^2, R^4, R^5 and R^6 each have the meanings given above,

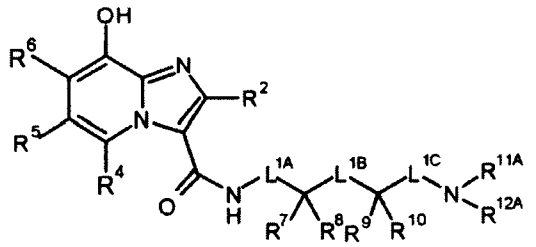
is reacted in an inert solvent under amide coupling conditions with an amine of the formula (IV) to give a compound of the formula (I-A),



(I-A)

in which R^2, R^4, R^5, R^6, L^{1A}, L^{1B}, L^{1C}, R^7, R^8, R^9, R^{10}, R^{11A} and R^{12A} each have the meanings given above,

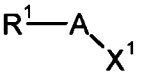
from this compound, the benzyl group is subsequently removed and the resulting compound of the formula (V-A)



(V-A)

in which R^2, R^4, R^5, R^6, L^{1A}, L^{1B}, L^{1C}, R^7, R^8, R^9, R^{10}, R^{11A} and R^{12A} each have the meanings given above,

is reacted in an inert solvent in the presence of a suitable base with a compound of the formula (VI)



(VI),

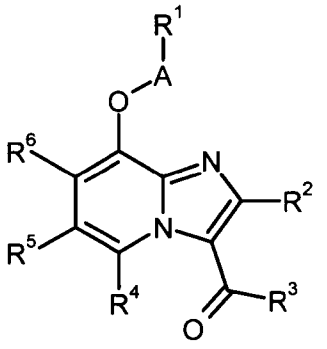
in which A and R^1 have the meanings given above and

X^1 represents a suitable leaving group,

any protective groups present are subsequently removed, and the resulting compounds of the formula (I) are optionally converted with the appropriate (i) solvents and/or (ii) acids or bases into their solvates, salts and/or solvates of the salts.

16. The process according to claim 15, wherein the amino protective group is tert-butoxycarbonyl, benzyloxycarbonyl or benzyl, and the leaving group is chlorine, bromine, iodine, mesylate, triflate or tosylate.

17. Compound of the formula (I):



(I),

in which

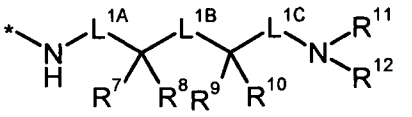
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

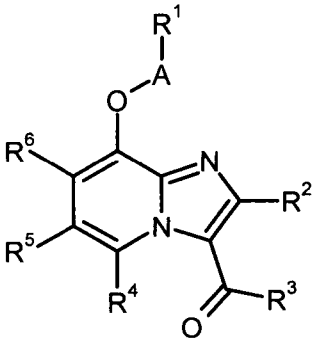
R^4 represents hydrogen,

R^5 represents methyl, fluoromethyl or difluoromethyl, and

R^6 represents hydrogen,

for the treatment and/or prophylaxis of diseases.

18. Use of a compound of the formula (I)



(I),

in which

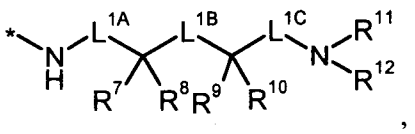
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents $(C_1$-$C_4)$-alkyl,

where $(C_1$-$C_4)$-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

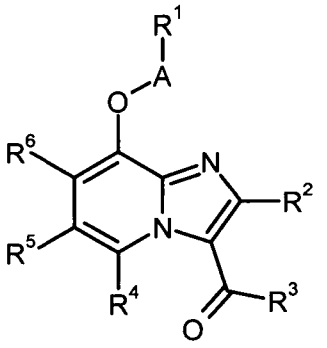
R^4 represents hydrogen,

R^5 represents methyl, fluoromethyl or difluoromethyl, and

R^6 represents hydrogen

for producing a medicament for the treatment and/or prophylaxis of heart failure, angina pectoris, hypertension, pulmonary hypertension, ischaemias, vascular disorders, kidney failure, thromboembolic disorders or arteriosclerosis.

19. A pharmaceutical composition comprising a compound of the formula (I)



(I),

in which

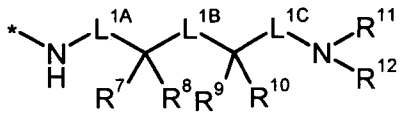
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



,

where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

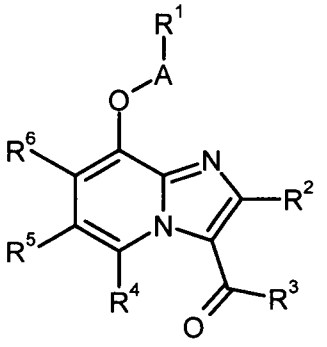
R^4 represents hydrogen,

R^5 represents methyl, fluoromethyl or difluoromethyl, and

R^6 represents hydrogen,

in combination with an inert, non-toxic, pharmaceutically suitable auxiliary.

20. Pharmaceutical composition comprising a compound of the formula (I)



(I),

in which

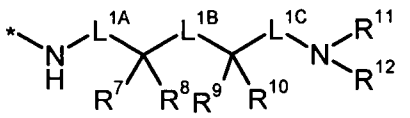
A represents CH_2,

R^1 represents phenyl,

where phenyl is substituted by 2 to 3 fluorine,

R^2 represents methyl,

R^3 represents a group of the formula



where

* represents the point of attachment to the carbonyl group,

L^{1A} represents a bond,

L^{1B} represents a bond,

L^{1C} represents a bond,

R^7 represents hydrogen,

R^8 represents hydrogen,

R^9 represents (C_1-C_4)-alkyl,

where (C_1-C_4)-alkyl is substituted up to five times by fluorine,

R^{10} represents methyl or ethyl,

R^{11} represents hydrogen,

R^{12} represents hydrogen,

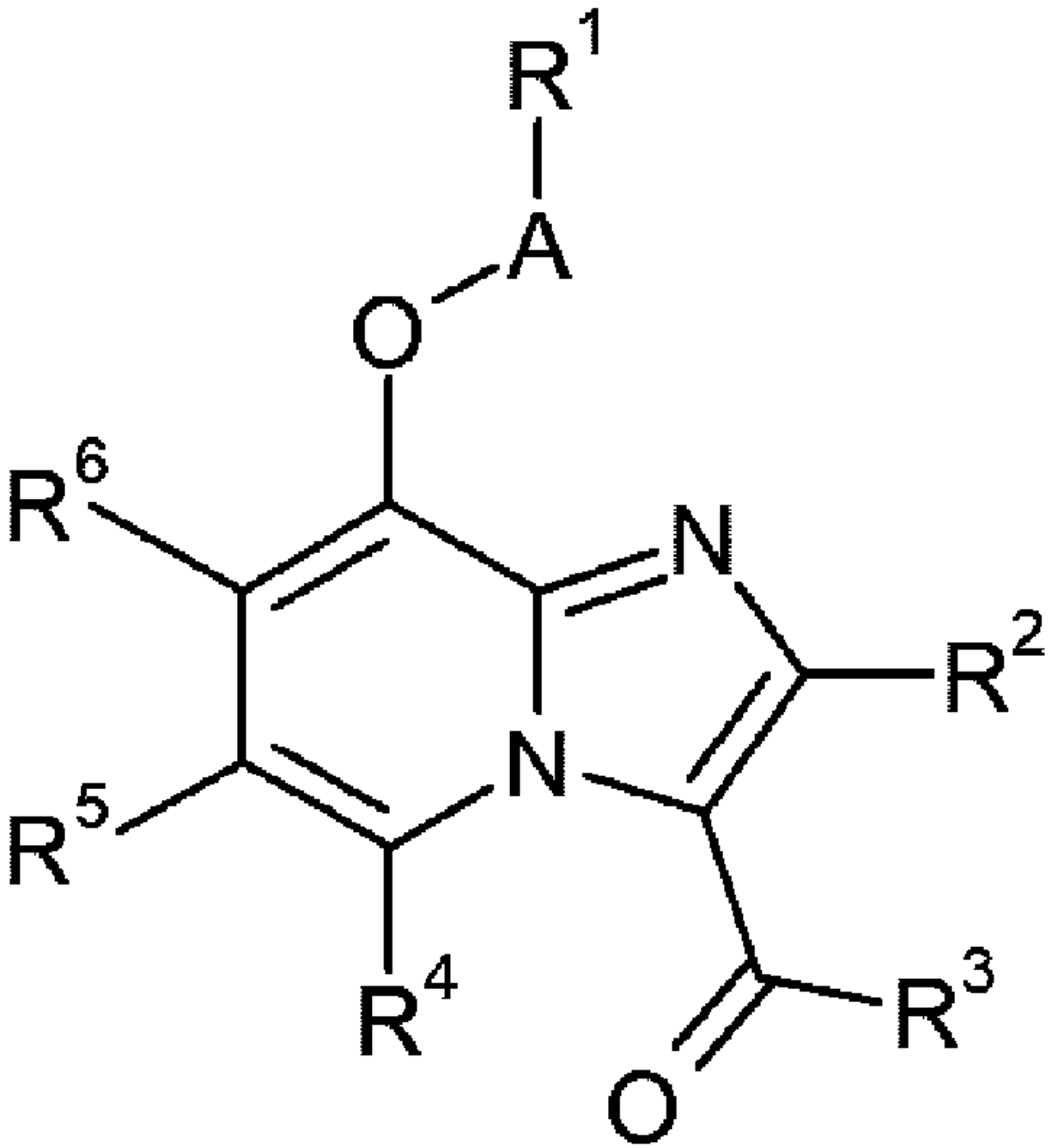
R^4 represents hydrogen,

R^5 represents methyl, fluoromethyl or difluoromethyl, and

R^6 represents hydrogen,

in combination with a further active compound selected from the group consisting of organic nitrates, NO donors, cGMP-PDE inhibitors, agents having antithrombotic activity, agents lowering blood pressure, and agents altering lipid metabolism.

21. Pharmaceutical composition according to claim 18 or 19 for the treatment and/or prophylaxis of heart failure, angina pectoris, hypertension, pulmonary hypertension, ischaemias, vascular disorders, kidney failure, thromboembolic disorders or arteriosclerosis.



(I)