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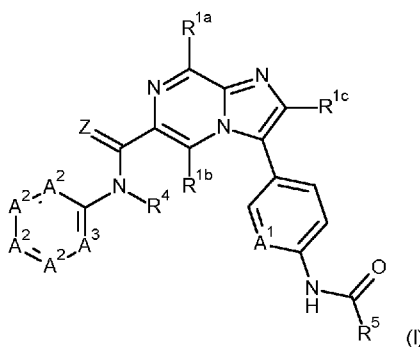
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- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- of inventorship (Rule 4.17(iv))

(54) Title: IMIDAZO[1,2-A]PYRAZINE DERIVATIVES



(57) Abstract: The current invention relates to compounds of the formula (I) wherein the substituents are as defined in claim 1, to processes and methods for preparing compounds of formula (I), to agrochemical compositions comprising compounds of formula (I) as defined in claim 1, to preparation of these compositions and to the use of the compounds or compositions in agriculture or horticulture for combating, preventing or controlling infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms, in particular fungi.



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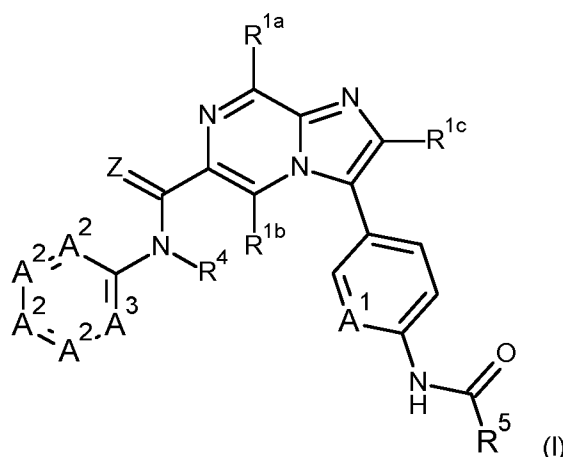
Imidazo[1,2-a]pyrazine derivatives

The present invention relates to microbiocidal imidazo[1,2-a]pyrazine derivatives, e.g. as active ingredients, which have microbiocidal activity, in particular fungicidal activity, more particularly activity
 5 against oomycetes. The invention also relates to preparation of these imidazo[1,2-a]pyrazine derivatives, to intermediates useful in the preparation of these imidazo[1,2-a]pyrazine derivatives, to the preparation of these intermediates, to agrochemical compositions which comprise at least one of the imidazo[1,2-a]pyrazine derivatives, to preparation of these compositions and to the use of the imidazo[1,2-a]pyrazine derivatives or compositions in agriculture or horticulture for combating,
 10 controlling or preventing infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms, in particular fungi, more particularly oomycetes.

It has now surprisingly been found that certain novel imidazo[1,2-a]pyrazine derivatives have favourable fungicidal properties, in particular against oomycetes.

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Therefore, in a first aspect, the present invention provides compounds of formula (I)



wherein Z is O or S, and preferably Z is O;

20 A¹ is CH or N, and preferably N;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;

25 R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;

A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more
 30 than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

R^2 are independently selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, di- C_{1-6} alkylaminocarbonyl, and C_{1-6} alkylcarbonyl, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, di- C_{1-6} alkylaminocarbonyl, and C_{1-6} alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

10 A^3 is independently CR^3 or N;

R^3 is selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, amino, C_{1-6} alkylamino, di- C_{1-6} alkylamino, and C_{3-6} cycloalkylamino, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, amino, C_{1-6} alkylamino, di- C_{1-6} alkylamino, and C_{3-6} cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

20 R^4 is selected from C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkylsulfanyl- C_{1-6} alkyl, C_{1-6} alkylsulfinyl- C_{1-6} alkyl, C_{1-6} alkylsulfonyl- C_{1-6} alkyl, C_{1-6} alkoxycarbonyl- C_{1-6} alkyl, C_{1-6} alkylaminocarbonyl- C_{1-6} alkyl, di- C_{1-6} alkylaminocarbonyl- C_{1-6} alkyl, and CN, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, C_{1-6} alkylsulfanyl- C_{1-6} alkyl, C_{1-6} alkylsulfinyl- C_{1-6} alkyl, C_{1-6} alkylsulfonyl- C_{1-6} alkyl, C_{1-6} alkoxycarbonyl- C_{1-6} alkyl, C_{1-6} alkylaminocarbonyl- C_{1-6} alkyl and di- C_{1-6} alkylaminocarbonyl- C_{1-6} alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN;

wherein A^3 and R^4 taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and

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R^5 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkylamino, di- C_{1-6} alkylamino, and C_{1-6} alkyl- C_{1-6} alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN;

35 or a salt or N-oxide thereof.

In a second aspect the present invention provides an agrochemical composition comprising a compound of formula (I), and more particularly an agrochemical composition comprising a fungicidally effective amount of a compound of formula (I). Said composition can further comprise at least one compound selected among an additional active ingredient, an appropriate formulation inert, a carrier, an adjuvant, and any mixtures thereof.

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Compounds of formula (I) may be used to control phytopathogenic microorganisms. Thus, in order to control a phytopathogen a compound of formula (I), or a composition comprising a compound of formula (I) according to the invention, may be applied directly to the phytopathogen, to the locus of a phytopathogen, in particular to a plant susceptible to attack by phytopathogens, or to a propagation material of a plant.

Thus, in a third aspect the present invention provides the use of a compound of formula (I), or a composition comprising a compound of formula (I), as described herein to combat, prevent or control a phytopathogen.

In a fourth aspect the present invention provides a method of combating, preventing or controlling phytopathogens, comprising applying a compound of formula (I), or a composition comprising a compound of formula (I), as described herein to said phytopathogen, to the locus of said phytopathogen, in particular to a plant susceptible to attack by a phytopathogen, or to a propagation material of a plant.

Compounds of formula (I) are particularly effective in combating, preventing or controlling phytopathogenic fungi, in particular oomycetes. Thus, in a fifth aspect the present invention provides the use of a compound of formula (I), or a composition comprising a compound of formula (I), as described herein to control phytopathogenic fungi, in particular oomycetes.

In a sixth aspect the present invention provides a method of combating, preventing or controlling phytopathogenic disease, such as phytopathogenic fungi, comprising applying a compound of formula (I), or a composition comprising a compound of formula (I), as described herein to said phytopathogenic fungi, or to the locus of said phytopathogenic fungi, in particular to a plant susceptible to attack by phytopathogenic fungi, in particular oomycetes, or to a propagation material of a plant.

Where a group is indicated as being substituted, e.g. alkyl, this includes those groups that are part of other groups, e.g. the alkyl in alkylthio.

30 Definitions:

- The term "halogen" or "halo" refers to fluorine (fluoro or F), chlorine (chloro or Cl), bromine (bromo or Br) or iodine (iodo or I), preferably fluorine, chlorine or bromine.

- The term "amino" refers to a -NH₂ group.

- The term "Alkyl" as used herein- in isolation or as part of a chemical group – represents straight-chain or branched hydrocarbons, preferably with 1 to 6 carbon atoms, for example methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, s-butyl, t-butyl, pentyl, 1- methylbutyl, 2-methylbutyl, 3-methylbutyl, 1,2-dimethylpropyl, 1,1 -dimethylpropyl, 2,2- dimethylpropyl, 1 -ethylpropyl, hexyl, 1 -methylpentyl, 2-methylpentyl, 3-methylpentyl, 4- methylpentyl, 1,2-dimethylpropyl, 1,3-dimethylbutyl, 1,4-dimethylbutyl, 2,3-dimethylbutyl, 1,1- dimethylbutyl, 2,2-dimethylbutyl, 3,3-dimethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-

trimethylpropyl, 1-ethylbutyl and 2-ethylbutyl. Alkyl groups with 1 to 4 carbon atoms are preferred, for example methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, s-butyl or t-butyl.

- The term "Alkenyl" - in isolation or as part of a chemical group - represents straight-chain or branched hydrocarbons, preferably with 2 to 6 carbon atoms and at least one double bond, for example vinyl, 2-propenyl, 2-butenyl, 3-butenyl, 1-methyl-2-propenyl, 2-methyl-2-propenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 1-methyl-2-butenyl, 2-methyl-2-butenyl, 3-methyl-2-butenyl, 1-methyl-3-butenyl, 2-methyl-3-butenyl, 3-methyl-3-butenyl, 1,1-dimethyl-2-propenyl, 1,2-dimethyl-2-propenyl, 1-ethyl-2-propenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 1-methyl-2-pentenyl, 2-methyl-2-pentenyl, 3-methyl-2-pentenyl, 4-methyl-2-pentenyl, 3-methyl-3-pentenyl, 4-methyl-3-pentenyl, 1-methyl-4-pentenyl, 2-methyl-4-pentenyl, 3-methyl-4-pentenyl, 4-methyl-4-pentenyl, 1,1-dimethyl-2-butenyl, 1,1-dimethyl-3-butenyl, 1,2-dimethyl-2-butenyl, 1,2-dimethyl-3-butenyl, 1,3-dimethyl-2-butenyl, 2,2-dimethyl-3-butenyl, 2,3-dimethyl-2-butenyl, 2,3-dimethyl-3-butenyl, 1-ethyl-2-butenyl, 1-ethyl-3-butenyl, 2-ethyl-2-butenyl, 2-ethyl-3-butenyl, 1,1,2-trimethyl-2-propenyl, 1-ethyl-1-methyl-2-propenyl und 1-ethyl-2-methyl-2-propenyl. Alkenyl groups with 2 to 4 carbon atoms are preferred, for example 2-propenyl, 2-butenyl or 1-methyl-2-propenyl.

- The term "Alkynyl" - in isolation or as part of a chemical group - represents straight-chain or branched hydrocarbons, preferably with 2 to 6 carbon atoms and at least one triple bond, for example 2-propynyl, 2-butyryl, 3-butyryl, 1-methyl-2-propynyl, 2-pentyryl, 3-pentyryl, 4-pentyryl, 1-methyl-3-butyryl, 2-methyl-3-butyryl, 1-methyl-2-butyryl, 1,1-dimethyl-2-propynyl, 1-ethyl-2-propynyl, 2-hexynyl, 3-hexynyl, 4-hexynyl, 5-hexynyl, 1-methyl-2-pentyryl, 1-methyl-3-pentyryl, 1-methyl-4-pentyryl, 2-methyl-3-pentyryl, 2-methyl-4-pentyryl, 3-methyl-4-pentyryl, 4-methyl-2-pentyryl, 1,1-dimethyl-3-butyryl, 1,2-dimethyl-3-butyryl, 2,2-dimethyl-3-butyryl, 1-ethyl-3-butyryl, 2-ethyl-3-butyryl, 1-ethyl-1-methyl-2-propynyl and 2,5-hexadiynyl. Alkynyls with 2 to 4 carbon atoms are preferred, for example ethynyl, 2-propynyl or 2-butyryl-2-propenyl.

- The term "haloalkyl" refers to an alkyl radical as generally defined above substituted by one or more of the same or different halogen atoms, for examples fluoromethyl, fluoroethyl, difluoromethyl, trifluoromethyl, or 2,2,2-trifluoroethyl.

- The term "cyanoalkyl" refers to an alkyl radical as generally defined above substituted by one or more cyano groups.

- The term "cycloalkyl" - in isolation or as part of a chemical group - represents saturated or partially unsaturated mono-, bi- or tricyclic hydrocarbons, preferably with 3 to 10 carbon atoms, for example cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.2]octyl or adamantyl. Cycloalkyls with 3, 4, 5, 6 or 7 carbon atoms are preferred, for example cyclopropyl or cyclobutyl.

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- The term "halocycloalkyl" refers to a cycloalkyl ring as defined above substituted by one or more of the same or different halogen atoms.

- The term "cyanocycloalkyl" refers to a cycloalkyl radical as generally defined above substituted by one or more cyano groups.
- 5 - The term "alkoxy" refers to a radical of the formula $-OR_a$ wherein R_a is an alkyl radical as generally defined above. Examples of alkoxy include, but are not limited to methoxy, ethoxy, propoxy, iso-propoxy, and tert-butoxy. The term "alkoxyalkyl" refers to an alkyl radical (as mentioned above) substituted with said alkoxy group. Examples are methoxymethyl, methoxyethyl, ethoxymethyl and propoxymethyl.
- 10 - The term "alkylsulfanyl" refers to a radical of the formula $-SR_a$ wherein R_a is an alkyl radical as generally defined above.
- The term "alkylsulfinyl" refers to a radical of the formula $-S(O)R_a$ wherein R_a is an alkyl radical as generally defined above.
- 15 - The term "alkylsulfonyl" refers to a radical of the formula $-S(O)_2R_a$ wherein R_a is an alkyl radical as generally defined above.
- The term "alkylcarbonyl" refers to a radical of the formula $R_aC(O)-$ wherein R_a is an alkyl radical as generally defined above.
- 20 - the term "alkoxycarbonyl" refers to a radical of the formula $R_aOC(O)-$, wherein R_a is an alkyl radical as generally defined above.
- 25 - The term "alkylamino" refers to a radical of the formula R_aNH- wherein R_a is an alkyl radical as generally defined above.
- The term "cycloalkylamino" refers to a radical of the formula R_aNH- wherein R_a is a cycloalkyl radical as generally defined above.
- 30 - The term "alkoxyamino" refers to a radical of the formula R_aNH- , wherein R_a is an alkoxy radical as generally defined above.
- The term "alkylaminocarbonyl" refers to a radical of the formula $R_aNHC(O)-$ wherein R_a is an alkyl radical as generally defined above.
- 35 - Hydroxyl or hydroxy stands for a $-OH$ group.

The term "combating", "preventing" or "controlling", and its inflections, within the context of the present invention, mean reducing any undesired effect, such as pathogenic and more particularly phytopathogenic, especially fungi such as oomycetes, infestation or attack of, and pathogenic damage to a plant or to a plant derived product to such a level that an improvement is demonstrated.

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As used herein, the term "effective amount" refers to the amount of the compound, a salt, or N-oxide thereof, which, upon single or multiple applications provides the desired effect.

- 5 An effective amount is readily determined by the skilled person in the art, by the use of known techniques and by observing results obtained under analogous circumstances. In determining the effective amount a number of factors are considered including, but not limited to: the type of plant or derived product to be applied; the pathogen to be controlled & its lifecycle; the particular compound applied; the type of application; and other relevant circumstances.

10

- Compounds of formula (I) which have at least one basic centre can form, for example, acid addition salts, for example with strong inorganic acids such as mineral acids, for example perchloric acid, sulfuric acid, nitric acid, nitrous acid, a phosphorus acid or a hydrohalic acid, with strong organic carboxylic acids, such as C₁₋₄alkanecarboxylic acids which are unsubstituted or substituted, for example by
15 halogen, for example acetic acid, such as saturated or unsaturated dicarboxylic acids, for example oxalic acid, malonic acid, succinic acid, maleic acid, fumaric acid or phthalic acid, such as hydroxycarboxylic acids, for example ascorbic acid, lactic acid, malic acid, tartaric acid or citric acid, or such as benzoic acid, or with organic sulfonic acids, such as C₁₋₄alkane- or arylsulfonic acids which are unsubstituted or substituted, for example by halogen, for example methane- or p-toluenesulfonic acid. Compounds of
20 formula (I) which have at least one acidic group can form, for example, salts with bases, for example mineral salts such as alkali metal or alkaline earth metal salts, for example sodium, potassium or magnesium salts, or salts with ammonia or an organic amine, such as morpholine, piperidine, pyrrolidine, a mono-, di- or tri-lower-alkylamine, for example ethyl-, diethyl-, triethyl- or dimethylpropylamine, or a mono-, di- or trihydroxy-lower-alkylamine, for example mono-, di- or
25 triethanolamine.

- In each case, the compounds of formula (I) according to the invention are in free form, in oxidized form as an N-oxide, in covalently hydrated form, or in salt form, e.g., an agronomically usable or agrochemically acceptable salt form. N-oxides are oxidized forms of tertiary amines or oxidized forms
30 of nitrogen containing heteroaromatic compounds. They are described for instance in the book "Heterocyclic N-oxides" by A. Albini and S. Pietra, CRC Press, Boca Raton 1991. The compounds of formula (I) according to the invention also include hydrates, which may be formed during salt formation.

- The compounds of formula (I) according to the invention also include hydrates which may be formed
35 during the salt formation.

In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, and preferably C₁₋₆alkyl.

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In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^{1b} and R^{1c} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and C_{1-6} alkoxy; and preferably hydrogen.

- 5 In a particular embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^{1a} is selected from hydroxy, halogen, CN, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkoxy, amino, and $NHC(O)C_{1-6}$ alkyl; and R^{1b} and R^{1c} are hydrogen.
- 10 In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^2 are independently selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, di- C_{1-6} alkylaminocarbonyl, and C_{1-6} alkylcarbonyl, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, di- C_{1-6} alkylaminocarbonyl, and
- 15 C_{1-6} alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; preferably R^2 are independently selected from hydrogen, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; and more preferably R^2 are
- 20 independently selected from hydrogen, halogen, CN, C_{1-6} alkyl, and C_{1-6} alkoxy.

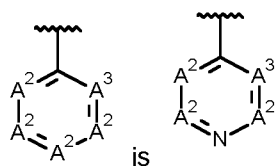
In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^3 is selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, amino, C_{1-6} alkylamino, di- C_{1-6} alkylamino,

25 and C_{3-6} cycloalkylamino, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, amino, C_{1-6} alkylamino, di- C_{1-6} alkylamino and C_{3-6} cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN. In a preferred embodiment, R^3 can be hydrogen.

- 30 In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein four A^2 are CR^2 and A^3 is N.

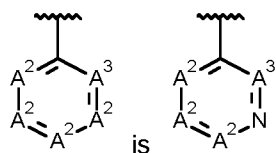
In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein

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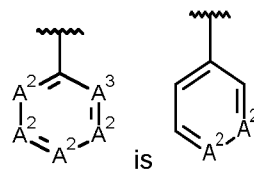
, and preferably the three A^2 are CR^2 and A^3 is CR^3 .

In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein

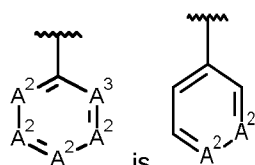


, and preferably the three A^2 are CR^2 and A^3 is CR^3 .

In a further embodiment, there is provided a compound of formula (I) according to the present invention,



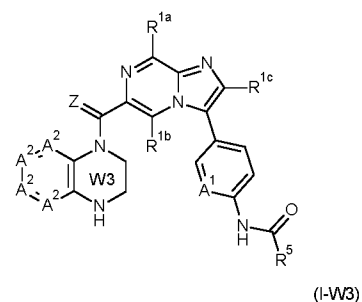
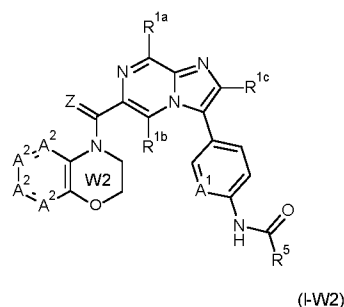
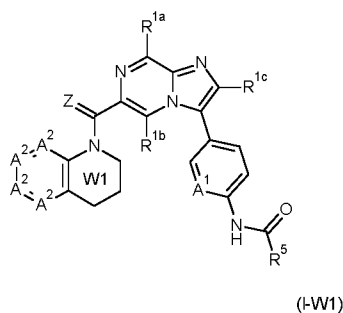
wherein four A^2 are CR^2 and A^3 is CR^3 , and preferably



- 5 In the particular embodiment wherein R^2 is as defined in the present invention; preferably R^2 are independently selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, di- C_{1-6} alkylaminocarbonyl, and C_{1-6} alkylcarbonyl, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkoxycarbonyl, C_{1-6} alkylaminocarbonyl, di- C_{1-6} alkylaminocarbonyl, and C_{1-6} alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; preferably R^2 are independently selected from hydrogen, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; and more preferably R^2 are independently selected from hydrogen, halogen, CN, C_{1-6} alkyl, and C_{1-6} alkoxy.

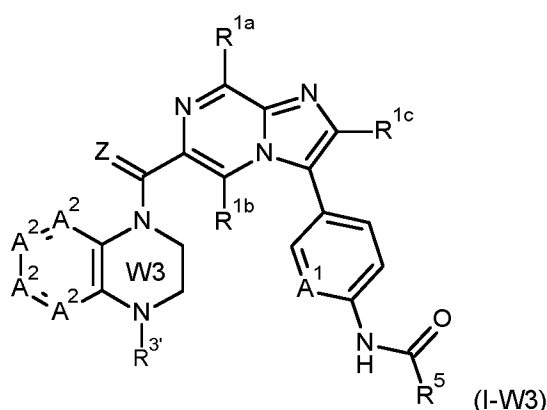
In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^4 is selected from C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{1-6} alkoxy, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{1-6} alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN; preferably R^4 is selected from C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and C_{1-6} alkoxy, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and C_{1-6} alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN; and wherein A^3 and R^4 taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle.

In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein A^3 is CR^3 and wherein R^3 and R^4 taken together form a ring, preferably a 5-8-membered heterocycle, preferably a 6-membered heterocycle, and more preferably one of the rings W1, W2 or W3 as described in the compounds of the formula (I) below:

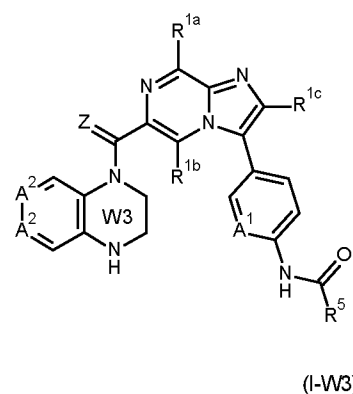
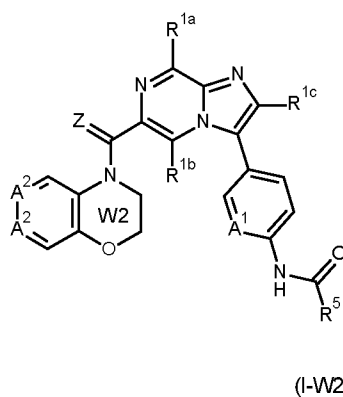
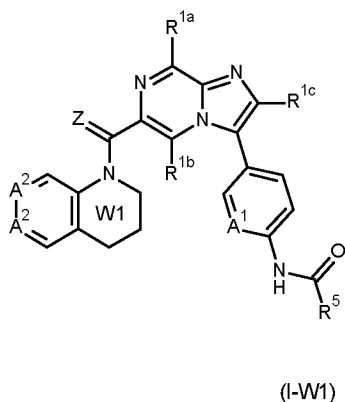


The carbon and/or the nitrogen atoms forming said ring (W1, W2 or W3) can be substituted, especially by a $R^{3'}$ group, wherein $R^{3'}$ is selected from hydrogen, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein each of the C_{1-6} alkyl and C_{3-6} cycloalkyl groups is optionally substituted with one to three substituents independently

5 selected from halogen and CN. For example, the compounds of the formula (I-W3) can be as follows:



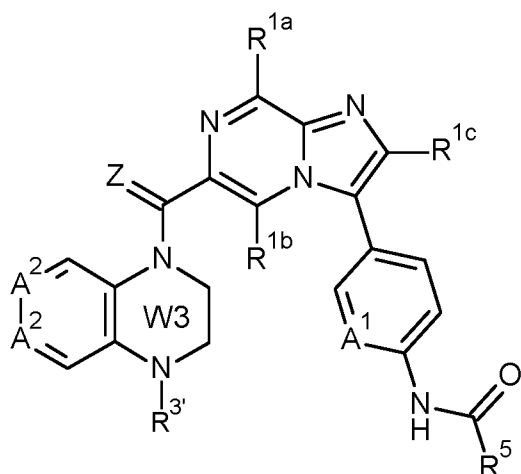
In a preferred embodiment, the compounds of the formula (I-W1), (I-W2) and (I-W3) can be as described below:



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The carbon and/or the nitrogen atoms forming said ring (W1, W2 or W3) can be substituted, especially by a $R^{3'}$ group, wherein $R^{3'}$ is selected from hydrogen, C_{1-6} alkyl, and C_{3-6} cycloalkyl, wherein each of the C_{1-6} alkyl and C_{3-6} cycloalkyl groups is optionally substituted with one to three substituents independently

selected from halogen and CN. For example, the compounds of the formula (I-W3) can be as follows:



(I-W3)

In a further embodiment, there is provided a compound of formula (I) according to the present invention, wherein R^5 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkyl, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN.

In a particular embodiment, there is provided a compound of formula (I) according to the present invention, wherein

10 Z is O;

A^1 is N;

R^{1a} is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and C_{1-6} alkoxy, and preferably C_{1-6} alkyl;

R^{1b} is selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and
15 C_{1-6} alkoxy, and preferably hydrogen;

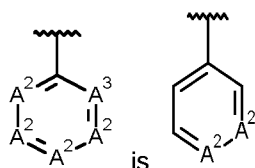
R^{1c} is selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and C_{1-6} alkoxy, and preferably hydrogen;

the four A^2 are CR^2 ; with R^2 being independently selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, and C_{1-6} alkylsulfonyl, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkoxy, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl and C_{1-6} alkylsulfonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; preferably R^2 being independently selected from hydrogen, halogen, CN, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy, wherein each of the C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkoxy- C_{1-6} alkyl, and C_{1-6} alkoxy- C_{1-6} alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; and more preferably R^2 being independently selected from hydrogen, halogen, CN, C_{1-6} alkyl, and C_{1-6} alkoxy;

A³ is CR³ with R³ being independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₃₋₆cycloalkylamino, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆alkylamino and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; and preferably R³ being hydrogen;

R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN; and wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and

R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₁₋₆alkylC₁₋₆alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN, and preferably R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, and C₁₋₆alkoxyC₁₋₆alkyl, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN.



In a preferred embodiment, is , wherein R² is as defined in the present invention; preferably R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; preferably R² are independently selected from hydrogen, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, wherein each of the C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN; and more preferably R² are independently selected from hydrogen, halogen, CN, C₁₋₆alkyl, and C₁₋₆alkoxy.

In a further embodiment, the compound according to the present invention is selected from:

methyl N-[5-[6-[2-cyanoethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;

methyl N-[5-[6-[cyanomethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;

methyl N-[5-[6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;

- methyl N-[5-[6-(6-fluoro-3,4-dihydro-2H-quinoline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-fluoro-3-methyl-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 5 methyl N-[5-[6-[(4-fluorophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-(methoxymethyl)carbamoyl]-8-methyl-imidazo[1,2-
- 10 a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[allyl-(3-fluorophenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-methoxy-2-pyridyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 15 methyl N-[5-[8-methyl-6-[methyl-(3-methylsulfonylphenyl)carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 3-[6-(cyclopropanecarbonylamino)-3-pyridyl]-N-(3,4-difluorophenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- 3-[6-(ethylcarbamoylamino)-3-pyridyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-
- 20 a]pyrazine-6-carboxamide;
- N-(4-fluoro-3-methoxy-phenyl)-3-[4-[(2-methoxyacetyl)amino]phenyl]-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- 3-[4-(cyclopropanecarbonylamino)phenyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- 25 3-[4-(ethylcarbamoylamino)phenyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- 3-(4-acetamidophenyl)-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- 3-(6-acetamido-3-pyridyl)-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-
- 30 carboxamide;
- 3-[6-(cyclopropanecarbonylamino)-3-pyridyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- 3-(6-acetamido-3-pyridyl)-N-(3,4-difluorophenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide;
- methyl N-[5-[8-acetamido-6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-
- 35 pyridyl]carbamate;
- methyl N-[5-[8-acetamido-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[8-cyano-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 40 methyl N-[5-[8-cyclopropyl-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;

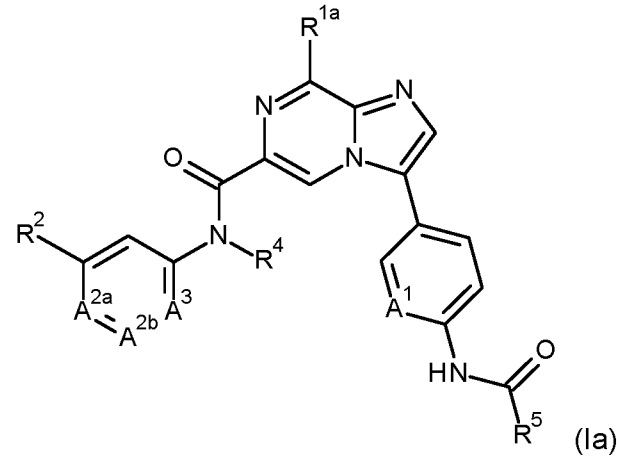
- methyl N-[5-[8-bromo-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[8-ethyl-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 5 methyl N-[5-[6-[(4-chlorophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(3,4-difluorophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-(6-fluoro-4-methyl-2,3-dihydroquinoxaline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 10 methyl N-[5-[6-(7-fluoro-2,3-dihydro-1,4-benzoxazine-4-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-cyano-3-methyl-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 15 methyl N-[5-[6-(6-cyano-3,4-dihydro-2H-quinoline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-cyanophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- methyl N-[5-[6-[(4-cyano-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate;
- 20 methyl N-[4-[6-[(4-cyano-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]phenyl]carbamate;
- methyl N-[4-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]phenyl]carbamate;
- 25 methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate; and
- methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2,8-dimethyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate.

30 The method according to the present invention has advantageous properties for protecting plants against pathogenic, such as phytopathogenic, especially fungi such as oomycetes, attack or infestation, which result in a disease and damage to the plant; particularly in instance of plants, the present invention can control, limit or prevent pathogenic damage on plant, parts of plant, plant propagation material and/or plant grown.

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The compounds in Tables 1.1 to 1.297 below illustrate specific compounds of the invention.

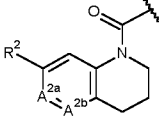
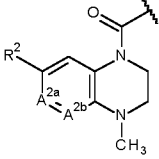
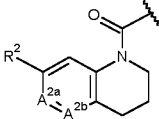
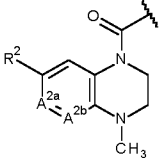
Table 1.1 provides compounds E1.1 to E1.418 of formula (Ia)

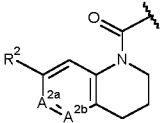
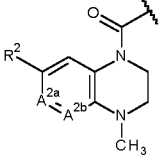
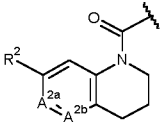
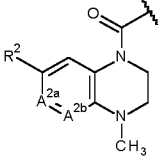


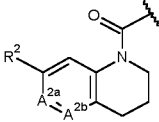
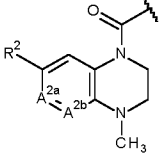
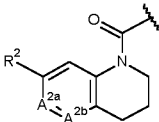
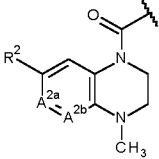
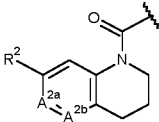
wherein R^{1a} is CH₃, R² is H, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z. More particularly, table Z also includes compounds wherein A³ and R⁴ taken together form a ring. In this case, said ring is depicted in the A³ and R⁴ columns (table Z) merged together, along the amide atom linked to the bicyclic core of the formula (Ia). For example, see the A³ and R⁴ columns of the compound E1.8.

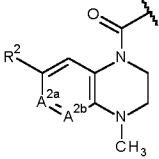
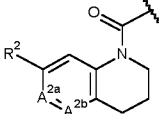
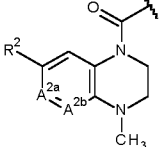
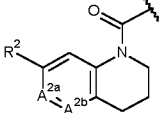
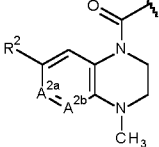
Table Z: Substituent definitions of A¹, A^{2a}, A^{2b}, A³ and R⁴:

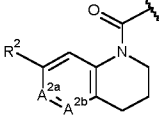
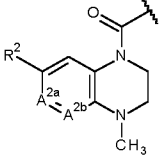
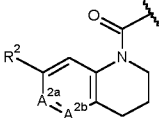
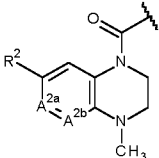
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.1	N	CH	CH	CH ₃	CH
E1.2	N	CH	CH	CH ₂ CH ₃	CH
E1.3	N	CH	CH	CH ₂ OCH ₃	CH
E1.4	N	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.5	N	CH	CH	CH ₂ CN	CH
E1.6	N	CH	CH	CH ₂ CH ₂ CN	CH
E1.7	N	CH	CH	allyl	CH
E1.8	N	CH			CH
E1.9	N	CH			CH
E1.10	CH	CH	CH	CH ₃	CH
E1.11	CH	CH	CH	CH ₂ CH ₃	CH
E1.12	CH	CH	CH	CH ₂ OCH ₃	CH
E1.13	CH	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.14	CH	CH	CH	CH ₂ CN	CH
E1.15	CH	CH	CH	CH ₂ CH ₂ CN	CH
E1.16	CH	CH	CH	allyl	CH
E1.17	CH	CH	N	CH ₃	CH
E1.18	CH	CH	N	CH ₂ CH ₃	CH

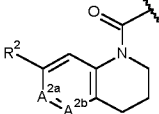
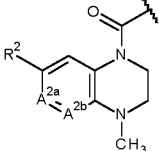
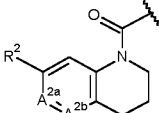
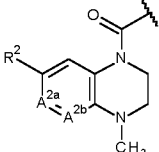
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.19	CH	CH	N	CH ₂ OCH ₃	CH
E1.20	CH	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.21	CH	CH	N	CH ₂ CN	CH
E1.22	CH	CH	N	CH ₂ CH ₂ CN	CH
E1.23	CH	CH	N	allyl	CH
E1.24	CH	CH			CH
E1.25	CH	CH			CH
E1.26	CH	N	CH	CH ₃	CH
E1.27	CH	N	CH	CH ₂ CH ₃	CH
E1.28	CH	N	CH	CH ₂ OCH ₃	CH
E1.29	CH	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.30	CH	N	CH	CH ₂ CN	CH
E1.31	CH	N	CH	CH ₂ CH ₂ CN	CH
E1.32	CH	N	CH	allyl	CH
E1.33	CH	N			CH
E1.34	CH	N			CH
E1.35	CF	CH	CH	CH ₃	CH
E1.36	CF	CH	CH	CH ₂ CH ₃	CH
E1.37	CF	CH	CH	CH ₂ OCH ₃	CH
E1.38	CF	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.39	CF	CH	CH	CH ₂ CN	CH
E1.40	CF	CH	CH	CH ₂ CH ₂ CN	CH
E1.41	CF	CH	CH	allyl	CH
E1.42	CF	CH	N	CH ₃	CH
E1.43	CF	CH	N	CH ₂ CH ₃	CH
E1.44	CF	CH	N	CH ₂ OCH ₃	CH
E1.45	CF	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.46	CF	CH	N	CH ₂ CN	CH
E1.47	CF	CH	N	CH ₂ CH ₂ CN	CH

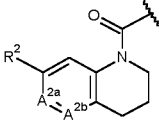
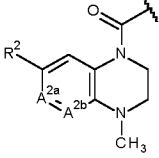
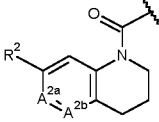
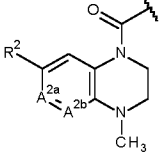
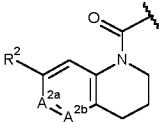
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.48	CF	CH	N	allyl	CH
E1.49	CF	CH			CH
E1.50	CF	CH			CH
E1.51	CF	N	CH	CH ₃	CH
E1.52	CF	N	CH	CH ₂ CH ₃	CH
E1.53	CF	N	CH	CH ₂ OCH ₃	CH
E1.54	CF	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.55	CF	N	CH	CH ₂ CN	CH
E1.56	CF	N	CH	CH ₂ CH ₂ CN	CH
E1.57	CF	N	CH	allyl	CH
E1.58	CF	N			CH
E1.59	CF	N			CH
E1.60	CCl	CH	CH	CH ₃	CH
E1.61	CCl	CH	CH	CH ₂ CH ₃	CH
E1.62	CCl	CH	CH	CH ₂ OCH ₃	CH
E1.63	CCl	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.64	CCl	CH	CH	CH ₂ CN	CH
E1.65	CCl	CH	CH	CH ₂ CH ₂ CN	CH
E1.66	CCl	CH	CH	allyl	CH
E1.67	CCl	CH	N	CH ₃	CH
E1.68	CCl	CH	N	CH ₂ CH ₃	CH
E1.69	CCl	CH	N	CH ₂ OCH ₃	CH
E1.70	CCl	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.71	CCl	CH	N	CH ₂ CN	CH
E1.72	CCl	CH	N	CH ₂ CH ₂ CN	CH
E1.73	CCl	CH	N	allyl	CH

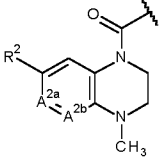
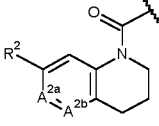
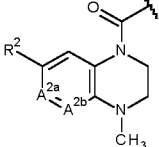
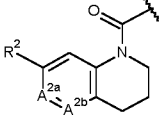
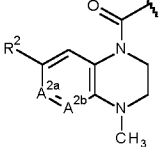
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.74	CCl	CH			CH
E1.75	CCl	CH			CH
E1.76	CCl	N	CH	CH ₃	CH
E1.77	CCl	N	CH	CH ₂ CH ₃	CH
E1.78	CCl	N	CH	CH ₂ OCH ₃	CH
E1.79	CCl	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.80	CCl	N	CH	CH ₂ CN	CH
E1.81	CCl	N	CH	CH ₂ CH ₂ CN	CH
E1.82	CCl	N	CH	allyl	CH
E1.83	CCl	N			CH
E1.84	CCl	N			CH
E1.85	CBr	CH	CH	CH ₃	CH
E1.86	CBr	CH	CH	CH ₂ CH ₃	CH
E1.87	CBr	CH	CH	CH ₂ OCH ₃	CH
E1.88	CBr	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.89	CBr	CH	CH	CH ₂ CN	CH
E1.90	CBr	CH	CH	CH ₂ CH ₂ CN	CH
E1.91	CBr	CH	CH	allyl	CH
E1.92	CBr	CH	N	CH ₃	CH
E1.93	CBr	CH	N	CH ₂ CH ₃	CH
E1.94	CBr	CH	N	CH ₂ OCH ₃	CH
E1.95	CBr	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.96	CBr	CH	N	CH ₂ CN	CH
E1.97	CBr	CH	N	CH ₂ CH ₂ CN	CH
E1.98	CBr	CH	N	allyl	CH
E1.99	CBr	CH			CH

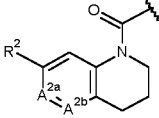
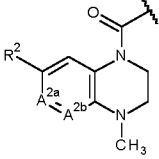
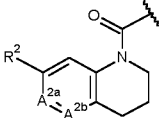
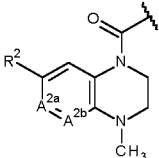
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.100	CBr	CH			CH
E1.101	CBr	N	CH	CH ₃	CH
E1.102	CBr	N	CH	CH ₂ CH ₃	CH
E1.103	CBr	N	CH	CH ₂ OCH ₃	CH
E1.104	CBr	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.105	CBr	N	CH	CH ₂ CN	CH
E1.106	CBr	N	CH	CH ₂ CH ₂ CN	CH
E1.107	CBr	N	CH	allyl	CH
E1.108	CBr	N			CH
E1.109	CBr	N			CH
E1.110	CCH ₃	CH	CH	CH ₃	CH
E1.111	CCH ₃	CH	CH	CH ₂ CH ₃	CH
E1.112	CCH ₃	CH	CH	CH ₂ OCH ₃	CH
E1.113	CCH ₃	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.114	CCH ₃	CH	CH	CH ₂ CN	CH
E1.115	CCH ₃	CH	CH	CH ₂ CH ₂ CN	CH
E1.116	CCH ₃	CH	CH	allyl	CH
E1.117	CCH ₃	CH	N	CH ₃	CH
E1.118	CCH ₃	CH	N	CH ₂ CH ₃	CH
E1.119	CCH ₃	CH	N	CH ₂ OCH ₃	CH
E1.120	CCH ₃	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.121	CCH ₃	CH	N	CH ₂ CN	CH
E1.122	CCH ₃	CH	N	CH ₂ CH ₂ CN	CH
E1.123	CCH ₃	CH	N	allyl	CH
E1.124	CCH ₃	CH			CH
E1.125	CCH ₃	CH			CH

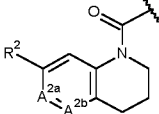
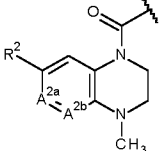
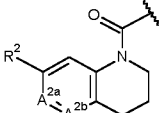
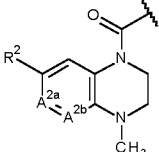
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.126	CCH ₃	N	CH	CH ₃	CH
E1.127	CCH ₃	N	CH	CH ₂ CH ₃	CH
E1.128	CCH ₃	N	CH	CH ₂ OCH ₃	CH
E1.129	CCH ₃	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.130	CCH ₃	N	CH	CH ₂ CN	CH
E1.131	CCH ₃	N	CH	CH ₂ CH ₂ CN	CH
E1.132	CCH ₃	N	CH	allyl	CH
E1.133	CCH ₃	N			CH
E1.134	CCH ₃	N			CH
E1.135	CCH ₂ CH ₃	CH	CH	CH ₃	CH
E1.136	CCH ₂ CH ₃	CH	CH	CH ₂ CH ₃	CH
E1.137	CCH ₂ CH ₃	CH	CH	CH ₂ OCH ₃	CH
E1.138	CCH ₂ CH ₃	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.139	CCH ₂ CH ₃	CH	CH	CH ₂ CN	CH
E1.140	CCH ₂ CH ₃	CH	CH	CH ₂ CH ₂ CN	CH
E1.141	CCH ₂ CH ₃	CH	CH	allyl	CH
E1.142	CCH ₂ CH ₃	CH	N	CH ₃	CH
E1.143	CCH ₂ CH ₃	CH	N	CH ₂ CH ₃	CH
E1.144	CCH ₂ CH ₃	CH	N	CH ₂ OCH ₃	CH
E1.145	CCH ₂ CH ₃	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.146	CCH ₂ CH ₃	CH	N	CH ₂ CN	CH
E1.147	CCH ₂ CH ₃	CH	N	CH ₂ CH ₂ CN	CH
E1.148	CCH ₂ CH ₃	CH	N	allyl	CH
E1.149	CCH ₂ CH ₃	CH			CH
E1.150	CCH ₂ CH ₃	CH			CH
E1.151	CCH ₂ CH ₃	N	CH	CH ₃	CH
E1.152	CCH ₂ CH ₃	N	CH	CH ₂ CH ₃	CH
E1.153	CCH ₂ CH ₃	N	CH	CH ₂ OCH ₃	CH
E1.154	CCH ₂ CH ₃	N	CH	CH ₂ CH ₂ OCH ₃	CH

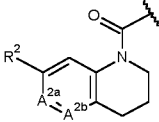
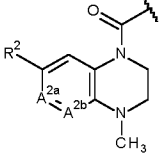
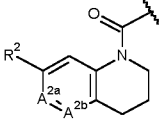
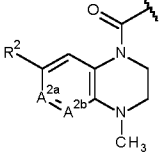
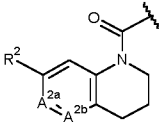
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.155	CCH ₂ CH ₃	N	CH	CH ₂ CN	CH
E1.156	CCH ₂ CH ₃	N	CH	CH ₂ CH ₂ CN	CH
E1.157	CCH ₂ CH ₃	N	CH	allyl	CH
E1.158	CCH ₂ CH ₃	N			CH
E1.159	CCH ₂ CH ₃	N			CH
E1.160	CCN	CH	CH	CH ₃	CH
E1.161	CCN	CH	CH	CH ₂ CH ₃	CH
E1.162	CCN	CH	CH	CH ₂ OCH ₃	CH
E1.163	CCN	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.164	CCN	CH	CH	CH ₂ CN	CH
E1.165	CCN	CH	CH	CH ₂ CH ₂ CN	CH
E1.166	CCN	CH	CH	allyl	CH
E1.167	CCN	CH	N	CH ₃	CH
E1.168	CCN	CH	N	CH ₂ CH ₃	CH
E1.169	CCN	CH	N	CH ₂ OCH ₃	CH
E1.170	CCN	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.171	CCN	CH	N	CH ₂ CN	CH
E1.172	CCN	CH	N	CH ₂ CH ₂ CN	CH
E1.173	CCN	CH	N	allyl	CH
E1.174	CCN	CH			CH
E1.175	CCN	CH			CH
E1.176	CCN	N	CH	CH ₃	CH
E1.177	CCN	N	CH	CH ₂ CH ₃	CH
E1.178	CCN	N	CH	CH ₂ OCH ₃	CH
E1.179	CCN	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.180	CCN	N	CH	CH ₂ CN	CH
E1.181	CCN	N	CH	CH ₂ CH ₂ CN	CH
E1.182	CCN	N	CH	allyl	CH

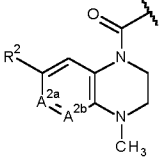
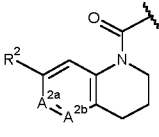
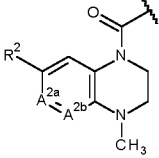
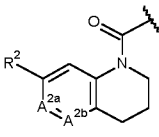
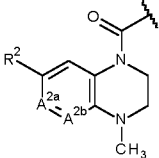
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.183	CCN	N			CH
E1.184	CCN	N			CH
E1.185	COCH ₃	CH	CH	CH ₃	CH
E1.186	COCH ₃	CH	CH	CH ₂ CH ₃	CH
E1.187	COCH ₃	CH	CH	CH ₂ OCH ₃	CH
E1.188	COCH ₃	CH	CH	CH ₂ CH ₂ OCH ₃	CH
E1.189	COCH ₃	CH	CH	CH ₂ CN	CH
E1.190	COCH ₃	CH	CH	CH ₂ CH ₂ CN	CH
E1.191	COCH ₃	CH	CH	allyl	CH
E1.192	COCH ₃	CH	N	CH ₃	CH
E1.193	COCH ₃	CH	N	CH ₂ CH ₃	CH
E1.194	COCH ₃	CH	N	CH ₂ OCH ₃	CH
E1.195	COCH ₃	CH	N	CH ₂ CH ₂ OCH ₃	CH
E1.196	COCH ₃	CH	N	CH ₂ CN	CH
E1.197	COCH ₃	CH	N	CH ₂ CH ₂ CN	CH
E1.198	COCH ₃	CH	N	allyl	CH
E1.199	COCH ₃	CH			CH
E1.200	COCH ₃	CH			CH
E1.201	COCH ₃	N	CH	CH ₃	CH
E1.202	COCH ₃	N	CH	CH ₂ CH ₃	CH
E1.203	COCH ₃	N	CH	CH ₂ OCH ₃	CH
E1.204	COCH ₃	N	CH	CH ₂ CH ₂ OCH ₃	CH
E1.205	COCH ₃	N	CH	CH ₂ CN	CH
E1.206	COCH ₃	N	CH	CH ₂ CH ₂ CN	CH
E1.207	COCH ₃	N	CH	allyl	CH
E1.208	COCH ₃	N			CH

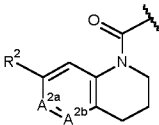
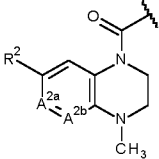
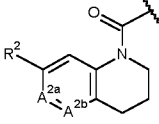
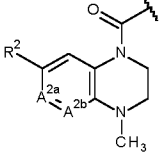
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.209	COCH ₃	N			CH
E1.210	N	CH	CH	CH ₃	N
E1.211	N	CH	CH	CH ₂ CH ₃	N
E1.212	N	CH	CH	CH ₂ OCH ₃	N
E1.213	N	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.214	N	CH	CH	CH ₂ CN	N
E1.215	N	CH	CH	CH ₂ CH ₂ CN	N
E1.216	N	CH	CH	allyl	N
E1.217	N	CH			N
E1.218	N	CH			N
E1.219	CH	CH	CH	CH ₃	N
E1.220	CH	CH	CH	CH ₂ CH ₃	N
E1.221	CH	CH	CH	CH ₂ OCH ₃	N
E1.222	CH	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.223	CH	CH	CH	CH ₂ CN	N
E1.224	CH	CH	CH	CH ₂ CH ₂ CN	N
E1.225	CH	CH	CH	allyl	N
E1.226	CH	CH	N	CH ₃	N
E1.227	CH	CH	N	CH ₂ CH ₃	N
E1.228	CH	CH	N	CH ₂ OCH ₃	N
E1.229	CH	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.230	CH	CH	N	CH ₂ CN	N
E1.231	CH	CH	N	CH ₂ CH ₂ CN	N
E1.232	CH	CH	N	allyl	N
E1.233	CH	CH			N
E1.234	CH	CH			N

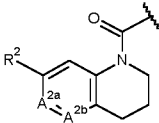
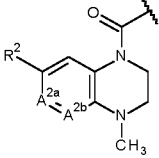
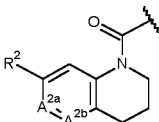
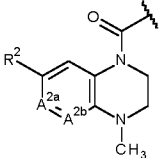
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.235	CH	N	CH	CH ₃	N
E1.236	CH	N	CH	CH ₂ CH ₃	N
E1.237	CH	N	CH	CH ₂ OCH ₃	N
E1.238	CH	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.239	CH	N	CH	CH ₂ CN	N
E1.240	CH	N	CH	CH ₂ CH ₂ CN	N
E1.241	CH	N	CH	allyl	N
E1.242	CH	N			N
E1.243	CH	N			N
E1.244	CF	CH	CH	CH ₃	N
E1.245	CF	CH	CH	CH ₂ CH ₃	N
E1.246	CF	CH	CH	CH ₂ OCH ₃	N
E1.247	CF	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.248	CF	CH	CH	CH ₂ CN	N
E1.249	CF	CH	CH	CH ₂ CH ₂ CN	N
E1.250	CF	CH	CH	allyl	N
E1.251	CF	CH	N	CH ₃	N
E1.252	CF	CH	N	CH ₂ CH ₃	N
E1.253	CF	CH	N	CH ₂ OCH ₃	N
E1.254	CF	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.255	CF	CH	N	CH ₂ CN	N
E1.256	CF	CH	N	CH ₂ CH ₂ CN	N
E1.257	CF	CH	N	allyl	N
E1.258	CF	CH			N
E1.259	CF	CH			N
E1.260	CF	N	CH	CH ₃	N
E1.261	CF	N	CH	CH ₂ CH ₃	N
E1.262	CF	N	CH	CH ₂ OCH ₃	N
E1.263	CF	N	CH	CH ₂ CH ₂ OCH ₃	N

Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.264	CF	N	CH	CH ₂ CN	N
E1.265	CF	N	CH	CH ₂ CH ₂ CN	N
E1.266	CF	N	CH	allyl	N
E1.267	CF	N			N
E1.268	CF	N			N
E1.269	CCl	CH	CH	CH ₃	N
E1.270	CCl	CH	CH	CH ₂ CH ₃	N
E1.271	CCl	CH	CH	CH ₂ OCH ₃	N
E1.272	CCl	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.273	CCl	CH	CH	CH ₂ CN	N
E1.274	CCl	CH	CH	CH ₂ CH ₂ CN	N
E1.275	CCl	CH	CH	allyl	N
E1.276	CCl	CH	N	CH ₃	N
E1.277	CCl	CH	N	CH ₂ CH ₃	N
E1.278	CCl	CH	N	CH ₂ OCH ₃	N
E1.279	CCl	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.280	CCl	CH	N	CH ₂ CN	N
E1.281	CCl	CH	N	CH ₂ CH ₂ CN	N
E1.282	CCl	CH	N	allyl	N
E1.283	CCl	CH			N
E1.284	CCl	CH			N
E1.285	CCl	N	CH	CH ₃	N
E1.286	CCl	N	CH	CH ₂ CH ₃	N
E1.287	CCl	N	CH	CH ₂ OCH ₃	N
E1.288	CCl	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.289	CCl	N	CH	CH ₂ CN	N
E1.290	CCl	N	CH	CH ₂ CH ₂ CN	N
E1.291	CCl	N	CH	allyl	N

Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.292	CCl	N			N
E1.293	CCl	N			N
E1.294	CBr	CH	CH	CH ₃	N
E1.295	CBr	CH	CH	CH ₂ CH ₃	N
E1.296	CBr	CH	CH	CH ₂ OCH ₃	N
E1.297	CBr	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.298	CBr	CH	CH	CH ₂ CN	N
E1.299	CBr	CH	CH	CH ₂ CH ₂ CN	N
E1.300	CBr	CH	CH	allyl	N
E1.301	CBr	CH	N	CH ₃	N
E1.302	CBr	CH	N	CH ₂ CH ₃	N
E1.303	CBr	CH	N	CH ₂ OCH ₃	N
E1.304	CBr	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.305	CBr	CH	N	CH ₂ CN	N
E1.306	CBr	CH	N	CH ₂ CH ₂ CN	N
E1.307	CBr	CH	N	allyl	N
E1.308	CBr	CH			N
E1.309	CBr	CH			N
E1.310	CBr	N	CH	CH ₃	N
E1.311	CBr	N	CH	CH ₂ CH ₃	N
E1.312	CBr	N	CH	CH ₂ OCH ₃	N
E1.313	CBr	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.314	CBr	N	CH	CH ₂ CN	N
E1.315	CBr	N	CH	CH ₂ CH ₂ CN	N
E1.316	CBr	N	CH	allyl	N
E1.317	CBr	N			N

Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.318	CBr	N			N
E1.319	CCH ₃	CH	CH	CH ₃	N
E1.320	CCH ₃	CH	CH	CH ₂ CH ₃	N
E1.321	CCH ₃	CH	CH	CH ₂ OCH ₃	N
E1.322	CCH ₃	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.323	CCH ₃	CH	CH	CH ₂ CN	N
E1.324	CCH ₃	CH	CH	CH ₂ CH ₂ CN	N
E1.325	CCH ₃	CH	CH	allyl	N
E1.326	CCH ₃	CH	N	CH ₃	N
E1.327	CCH ₃	CH	N	CH ₂ CH ₃	N
E1.328	CCH ₃	CH	N	CH ₂ OCH ₃	N
E1.329	CCH ₃	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.330	CCH ₃	CH	N	CH ₂ CN	N
E1.331	CCH ₃	CH	N	CH ₂ CH ₂ CN	N
E1.332	CCH ₃	CH	N	allyl	N
E1.333	CCH ₃	CH			N
E1.334	CCH ₃	CH			N
E1.335	CCH ₃	N	CH	CH ₃	N
E1.336	CCH ₃	N	CH	CH ₂ CH ₃	N
E1.337	CCH ₃	N	CH	CH ₂ OCH ₃	N
E1.338	CCH ₃	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.339	CCH ₃	N	CH	CH ₂ CN	N
E1.340	CCH ₃	N	CH	CH ₂ CH ₂ CN	N
E1.341	CCH ₃	N	CH	allyl	N
E1.342	CCH ₃	N			N
E1.343	CCH ₃	N			N

Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.344	CCH ₂ CH ₃	CH	CH	CH ₃	N
E1.345	CCH ₂ CH ₃	CH	CH	CH ₂ CH ₃	N
E1.346	CCH ₂ CH ₃	CH	CH	CH ₂ OCH ₃	N
E1.347	CCH ₂ CH ₃	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.348	CCH ₂ CH ₃	CH	CH	CH ₂ CN	N
E1.349	CCH ₂ CH ₃	CH	CH	CH ₂ CH ₂ CN	N
E1.350	CCH ₂ CH ₃	CH	CH	allyl	N
E1.351	CCH ₂ CH ₃	CH	N	CH ₃	N
E1.352	CCH ₂ CH ₃	CH	N	CH ₂ CH ₃	N
E1.353	CCH ₂ CH ₃	CH	N	CH ₂ OCH ₃	N
E1.354	CCH ₂ CH ₃	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.355	CCH ₂ CH ₃	CH	N	CH ₂ CN	N
E1.356	CCH ₂ CH ₃	CH	N	CH ₂ CH ₂ CN	N
E1.357	CCH ₂ CH ₃	CH	N	allyl	N
E1.358	CCH ₂ CH ₃	CH			N
E1.359	CCH ₂ CH ₃	CH			N
E1.360	CCH ₂ CH ₃	N	CH	CH ₃	N
E1.361	CCH ₂ CH ₃	N	CH	CH ₂ CH ₃	N
E1.362	CCH ₂ CH ₃	N	CH	CH ₂ OCH ₃	N
E1.363	CCH ₂ CH ₃	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.364	CCH ₂ CH ₃	N	CH	CH ₂ CN	N
E1.365	CCH ₂ CH ₃	N	CH	CH ₂ CH ₂ CN	N
E1.366	CCH ₂ CH ₃	N	CH	allyl	N
E1.367	CCH ₂ CH ₃	N			N
E1.368	CCH ₂ CH ₃	N			N
E1.369	CCN	CH	CH	CH ₃	N
E1.370	CCN	CH	CH	CH ₂ CH ₃	N
E1.371	CCN	CH	CH	CH ₂ OCH ₃	N
E1.372	CCN	CH	CH	CH ₂ CH ₂ OCH ₃	N

Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.373	CCN	CH	CH	CH ₂ CN	N
E1.374	CCN	CH	CH	CH ₂ CH ₂ CN	N
E1.375	CCN	CH	CH	allyl	N
E1.376	CCN	CH	N	CH ₃	N
E1.377	CCN	CH	N	CH ₂ CH ₃	N
E1.378	CCN	CH	N	CH ₂ OCH ₃	N
E1.379	CCN	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.380	CCN	CH	N	CH ₂ CN	N
E1.381	CCN	CH	N	CH ₂ CH ₂ CN	N
E1.382	CCN	CH	N	allyl	N
E1.383	CCN	CH			N
E1.384	CCN	CH			N
E1.385	CCN	N	CH	CH ₃	N
E1.386	CCN	N	CH	CH ₂ CH ₃	N
E1.387	CCN	N	CH	CH ₂ OCH ₃	N
E1.388	CCN	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.389	CCN	N	CH	CH ₂ CN	N
E1.390	CCN	N	CH	CH ₂ CH ₂ CN	N
E1.391	CCN	N	CH	allyl	N
E1.392	CCN	N			N
E1.393	CCN	N			N
E1.394	COCH ₃	CH	CH	CH ₃	N
E1.395	COCH ₃	CH	CH	CH ₂ CH ₃	N
E1.396	COCH ₃	CH	CH	CH ₂ OCH ₃	N
E1.397	COCH ₃	CH	CH	CH ₂ CH ₂ OCH ₃	N
E1.398	COCH ₃	CH	CH	CH ₂ CN	N
E1.399	COCH ₃	CH	CH	CH ₂ CH ₂ CN	N
E1.400	COCH ₃	CH	CH	allyl	N
E1.401	COCH ₃	CH	N	CH ₃	N

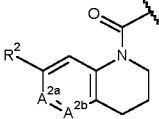
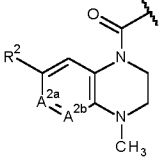
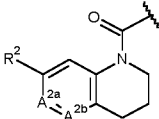
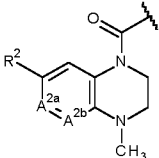
Compound	A ^{2a}	A ^{2b}	A ³	R ⁴	A ¹
E1.402	COCH ₃	CH	N	CH ₂ CH ₃	N
E1.403	COCH ₃	CH	N	CH ₂ OCH ₃	N
E1.404	COCH ₃	CH	N	CH ₂ CH ₂ OCH ₃	N
E1.405	COCH ₃	CH	N	CH ₂ CN	N
E1.406	COCH ₃	CH	N	CH ₂ CH ₂ CN	N
E1.407	COCH ₃	CH	N	allyl	N
E1.408	COCH ₃	CH			N
E1.409	COCH ₃	CH			N
E1.410	COCH ₃	N	CH	CH ₃	N
E1.411	COCH ₃	N	CH	CH ₂ CH ₃	N
E1.412	COCH ₃	N	CH	CH ₂ OCH ₃	N
E1.413	COCH ₃	N	CH	CH ₂ CH ₂ OCH ₃	N
E1.414	COCH ₃	N	CH	CH ₂ CN	N
E1.415	COCH ₃	N	CH	CH ₂ CH ₂ CN	N
E1.416	COCH ₃	N	CH	allyl	N
E1.417	COCH ₃	N			N
E1.418	COCH ₃	N			N

Table 1.2 provides 418 compounds E2.1 to E2.418 of formula (Ia) wherein R^{1a} is CH₃, R² is H, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.3 provides 418 compounds E3.1 to E3.418 of formula (Ia) wherein R^{1a} is CH₃, R² is H, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.4 provides 418 compounds E4.1 to E4.418 of formula (Ia) wherein R^{1a} is CH₃, R² is H, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.5 provides 418 compounds E5.1 to E5.418 of formula (Ia) wherein R^{1a} is CH₃, R² is H, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.6 provides 418 compounds E6.1 to E6.418 of formula (Ia) wherein R^{1a} is CH₃, R² is CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.7 provides 418 compounds E7.1 to E7.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.8 provides 418 compounds E8.1 to E8.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 5 Table 1.9 provides 418 compounds E9.1 to E9.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.10 provides 418 compounds E10.1 to E10.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.11 provides 418 compounds E11.1 to E11.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_2CH_3 ,

- 10 R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.12 provides 418 compounds E12.1 to E12.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_2CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.13 provides 418 compounds E13.1 to E13.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_2CH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 15 Table 1.14 provides 418 compounds E14.1 to E14.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_2CH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.15 provides 418 compounds E15.1 to E15.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is CH_2CH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.16 provides 418 compounds E16.1 to E16.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is F , R^5 is

- 20 CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.17 provides 418 compounds E17.1 to E17.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is F , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.18 provides 418 compounds E18.1 to E18.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is F , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 25 Table 1.19 provides 418 compounds E19.1 to E19.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is F , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.20 provides 418 compounds E20.1 to E20.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is F , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.21 provides 418 compounds E21.1 to E21.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Cl , R^5

- 30 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.22 provides 418 compounds E22.1 to E22.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Cl , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.23 provides 418 compounds E23.1 to E23.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Cl , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 35 Table 1.24 provides 418 compounds E24.1 to E24.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Cl , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.25 provides 418 compounds E25.1 to E25.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Cl , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.26 provides 418 compounds E26.1 to E26.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Br , R^5

- 40 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.27 provides 418 compounds E27.1 to E27.418 of formula (Ia) wherein R^{1a} is CH_3 , R^2 is Br , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.28 provides 418 compounds E28.1 to E28.418 of formula (Ia) wherein R^{1a} is CH₃, R² is Br, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.29 provides 418 compounds E29.1 to E29.418 of formula (Ia) wherein R^{1a} is CH₃, R² is Br, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 5 Table 1.30 provides 418 compounds E30.1 to E30.418 of formula (Ia) wherein R^{1a} is CH₃, R² is Br, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.31 provides 418 compounds E31.1 to E31.418 of formula (Ia) wherein R^{1a} is CH₃, R² is CN, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 10 Table 1.32 provides 418 compounds E32.1 to E32.418 of formula (Ia) wherein R^{1a} is CH₃, R² is CN, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.33 provides 418 compounds E33.1 to E33.418 of formula (Ia) wherein R^{1a} is CH₃, R² is CN, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.34 provides 418 compounds E34.1 to E34.418 of formula (Ia) wherein R^{1a} is CH₃, R² is CN, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 15 Table 1.35 provides 418 compounds E35.1 to E35.418 of formula (Ia) wherein R^{1a} is CH₃, R² is CN, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.36 provides 418 compounds E36.1 to E36.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 20 Table 1.37 provides 418 compounds E37.1 to E37.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.38 provides 418 compounds E38.1 to E38.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.39 provides 418 compounds E39.1 to E39.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 25 Table 1.40 provides 418 compounds E40.1 to E40.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.41 provides 418 compounds E41.1 to E41.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 30 Table 1.42 provides 418 compounds E42.1 to E42.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.43 provides 418 compounds E43.1 to E43.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.44 provides 418 compounds E44.1 to E44.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 35 Table 1.45 provides 418 compounds E45.1 to E45.418 of formula (Ia) wherein R^{1a} is CH₃, R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.46 provides 418 compounds E46.1 to E46.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is H, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 40 Table 1.47 provides 418 compounds E47.1 to E47.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is H, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.48 provides 418 compounds E48.1 to E48.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is H, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- Table 1.49 provides 418 compounds E49.1 to E49.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is H, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.50 provides 418 compounds E50.1 to E50.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is H, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 5 Table 1.51 provides 418 compounds E51.1 to E51.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_3 , R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.52 provides 418 compounds E52.1 to E52.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.53 provides 418 compounds E53.1 to E53.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 10 Table 1.54 provides 418 compounds E54.1 to E54.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.55 provides 418 compounds E55.1 to E55.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 15 Table 1.56 provides 418 compounds E56.1 to E56.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_2CH_3 , R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.57 provides 418 compounds E57.1 to E57.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_2CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.58 provides 418 compounds E58.1 to E58.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_2CH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 20 Table 1.59 provides 418 compounds E59.1 to E59.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_2CH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.60 provides 418 compounds E60.1 to E60.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is CH_2CH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 25 Table 1.61 provides 418 compounds E61.1 to E61.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is F, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.62 provides 418 compounds E62.1 to E62.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is F, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.63 provides 418 compounds E63.1 to E63.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is F, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 30 Table 1.64 provides 418 compounds E64.1 to E64.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is F, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.65 provides 418 compounds E65.1 to E65.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is F, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 35 Table 1.66 provides 418 compounds E66.1 to E66.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is Cl, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.67 provides 418 compounds E67.1 to E67.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is Cl, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.68 provides 418 compounds E68.1 to E68.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is Cl, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 40 Table 1.69 provides 418 compounds E69.1 to E69.418 of formula (Ia) wherein R^{1a} is CH_2CH_3 , R^2 is Cl, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- Table 1.70 provides 418 compounds E70.1 to E70.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is Cl, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.71 provides 418 compounds E71.1 to E71.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is Br, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 5 Table 1.72 provides 418 compounds E72.1 to E72.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is Br, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.73 provides 418 compounds E73.1 to E73.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is Br, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.74 provides 418 compounds E74.1 to E74.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is Br, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 10 Table 1.75 provides 418 compounds E75.1 to E75.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is Br, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.76 provides 418 compounds E76.1 to E76.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is CN, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 15 Table 1.77 provides 418 compounds E77.1 to E77.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is CN, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.78 provides 418 compounds E78.1 to E78.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is CN, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.79 provides 418 compounds E79.1 to E79.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is CN, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 20 Table 1.80 provides 418 compounds E80.1 to E80.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is CN, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.81 provides 418 compounds E81.1 to E81.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 25 Table 1.82 provides 418 compounds E82.1 to E82.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.83 provides 418 compounds E83.1 to E83.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.84 provides 418 compounds E84.1 to E84.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 30 Table 1.85 provides 418 compounds E85.1 to E85.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.86 provides 418 compounds E86.1 to E86.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 35 Table 1.87 provides 418 compounds E87.1 to E87.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.88 provides 418 compounds E88.1 to E88.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.89 provides 418 compounds E89.1 to E89.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 40 Table 1.90 provides 418 compounds E90.1 to E90.418 of formula (Ia) wherein R^{1a} is CH₂CH₃, R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.91 provides 418 compounds E91.1 to E91.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is H, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.92 provides 418 compounds E92.1 to E92.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is H, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 5 Table 1.93 provides 418 compounds E93.1 to E93.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is H, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.94 provides 418 compounds E94.1 to E94.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is H, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- Table 1.95 provides 418 compounds E95.1 to E95.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is H, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.96 provides 418 compounds E96.1 to E96.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_3 , R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.97 provides 418 compounds E97.1 to E97.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 15 Table 1.98 provides 418 compounds E98.1 to E98.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.99 provides 418 compounds E99.1 to E99.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- Table 1.100 provides 418 compounds E100.1 to E100.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.101 provides 418 compounds E101.1 to E101.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_2CH_3 , R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.102 provides 418 compounds E102.1 to E102.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_2CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 25 Table 1.103 provides 418 compounds E103.1 to E103.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_2CH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.104 provides 418 compounds E104.1 to E104.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_2CH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- Table 1.105 provides 418 compounds E105.1 to E105.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CH_2CH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.106 provides 418 compounds E106.1 to E106.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is F, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.107 provides 418 compounds E107.1 to E107.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is F, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- 35 Table 1.108 provides 418 compounds E108.1 to E108.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is F, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.109 provides 418 compounds E109.1 to E109.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is F, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- Table 1.110 provides 418 compounds E110.1 to E110.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is F, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.111 provides 418 compounds E111.1 to E111.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Cl, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

- Table 1.112 provides 418 compounds E112.1 to E112.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Cl, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.113 provides 418 compounds E113.1 to E113.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Cl, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 5 Table 1.114 provides 418 compounds E114.1 to E114.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Cl, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.115 provides 418 compounds E115.1 to E115.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Cl, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.116 provides 418 compounds E116.1 to E116.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Br, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 10 Table 1.117 provides 418 compounds E117.1 to E117.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Br, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.118 provides 418 compounds E118.1 to E118.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Br, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 15 Table 1.119 provides 418 compounds E119.1 to E119.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Br, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.120 provides 418 compounds E120.1 to E120.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is Br, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.121 provides 418 compounds E121.1 to E121.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CN, R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 20 Table 1.122 provides 418 compounds E122.1 to E122.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CN, R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.123 provides 418 compounds E123.1 to E123.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CN, R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 25 Table 1.124 provides 418 compounds E124.1 to E124.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CN, R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.125 provides 418 compounds E125.1 to E125.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is CN, R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.126 provides 418 compounds E126.1 to E126.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_3 , R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 30 Table 1.127 provides 418 compounds E127.1 to E127.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.128 provides 418 compounds E128.1 to E128.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_3 , R^5 is cyclopropyl and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 35 Table 1.129 provides 418 compounds E129.1 to E129.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_3 , R^5 is CH_2OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.130 provides 418 compounds E130.1 to E130.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_3 , R^5 is $NHCH_2CH_3$ and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- Table 1.131 provides 418 compounds E131.1 to E131.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_2CH_3 , R^5 is CH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.
- 40 Table 1.132 provides 418 compounds E132.1 to E132.418 of formula (Ia) wherein R^{1a} is CH_2OCH_3 , R^2 is OCH_2CH_3 , R^5 is OCH_3 and A^1 , A^{2a} , A^{2b} , A^3 , R^4 are as defined in table Z.

Table 1.133 provides 418 compounds E133.1 to E133.418 of formula (Ia) wherein R^{1a} is CH₂OCH₃, R² is OCH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.134 provides 418 compounds E134.1 to E134.418 of formula (Ia) wherein R^{1a} is CH₂OCH₃, R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 5 Table 1.135 provides 418 compounds E135.1 to E135.418 of formula (Ia) wherein R^{1a} is CH₂OCH₃, R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.136 provides 418 compounds E136.1 to E136.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is H, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 10 Table 1.137 provides 418 compounds E137.1 to E137.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is H, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.138 provides 418 compounds E138.1 to E138.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is H, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.139 provides 418 compounds E139.1 to E139.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is H, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 15 Table 1.140 provides 418 compounds E140.1 to E140.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.141 provides 418 compounds E141.1 to E141.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 20 Table 1.142 provides 418 compounds E142.1 to E142.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.143 provides 418 compounds E143.1 to E143.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.144 provides 418 compounds E144.1 to E144.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 25 Table 1.145 provides 418 compounds E145.1 to E145.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.146 provides 418 compounds E146.1 to E146.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 30 Table 1.147 provides 418 compounds E147.1 to E147.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.148 provides 418 compounds E148.1 to E148.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is F, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.149 provides 418 compounds E149.1 to E149.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is F, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 35 Table 1.150 provides 418 compounds E150.1 to E150.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is F, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.151 provides 418 compounds E151.1 to E151.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is F, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 40 Table 1.152 provides 418 compounds E152.1 to E152.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Cl, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.153 provides 418 compounds E153.1 to E153.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Cl, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.154 provides 418 compounds E154.1 to E154.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Cl, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.155 provides 418 compounds E155.1 to E155.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Cl, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

5 Table 1.156 provides 418 compounds E156.1 to E156.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Br, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.157 provides 418 compounds E157.1 to E157.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Br, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.158 provides 418 compounds E158.1 to E158.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Br, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.159 provides 418 compounds E159.1 to E159.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is Br, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.160 provides 418 compounds E160.1 to E160.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CN, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

15 Table 1.161 provides 418 compounds E161.1 to E161.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CN, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.162 provides 418 compounds E162.1 to E162.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CN, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.163 provides 418 compounds E163.1 to E163.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is CN, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.164 provides 418 compounds E164.1 to E164.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.165 provides 418 compounds E165.1 to E165.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

25 Table 1.166 provides 418 compounds E166.1 to E166.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.167 provides 418 compounds E167.1 to E167.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

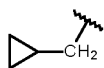
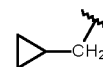
Table 1.168 provides 418 compounds E168.1 to E168.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.169 provides 418 compounds E169.1 to E169.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.170 provides 418 compounds E170.1 to E170.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

35 Table 1.171 provides 418 compounds E171.1 to E171.418 of formula (Ia) wherein R^{1a} is cyclopropyl, R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.172 provides 418 compounds E172.1 to E172.418 of formula (Ia) wherein R^{1a} is



, R² is H, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.173 provides 418 compounds E173.1 to E173.418 of formula (Ia) wherein R^{1a} is , R² is H, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.174 provides 418 compounds E174.1 to E174.418 of formula (Ia) wherein R^{1a} is , R² is H, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

5 Table 1.175 provides 418 compounds E175.1 to E175.418 of formula (Ia) wherein R^{1a} is , R² is H, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.176 provides 418 compounds E176.1 to E176.418 of formula (Ia) wherein R^{1a} is , R² is CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

10 Table 1.177 provides 418 compounds E177.1 to E177.418 of formula (Ia) wherein R^{1a} is , R² is CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.178 provides 418 compounds E178.1 to E178.418 of formula (Ia) wherein R^{1a} is , R² is CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.179 provides 418 compounds E179.1 to E179.418 of formula (Ia) wherein R^{1a} is , R² is CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

15 Table 1.180 provides 418 compounds E180.1 to E180.418 of formula (Ia) wherein R^{1a} is , R² is CH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.181 provides 418 compounds E181.1 to E181.418 of formula (Ia) wherein R^{1a} is , R² is CH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

20 Table 1.182 provides 418 compounds E182.1 to E182.418 of formula (Ia) wherein R^{1a} is , R² is CH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.183 provides 418 compounds E183.1 to E183.418 of formula (Ia) wherein R^{1a} is , R² is CH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.184 provides 418 compounds E184.1 to E184.418 of formula (Ia) wherein R^{1a} is , R² is F, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

25 Table 1.185 provides 418 compounds E185.1 to E185.418 of formula (Ia) wherein R^{1a} is , R² is F, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.186 provides 418 compounds E186.1 to E186.418 of formula (Ia) wherein R^{1a} is , R² is F, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.187 provides 418 compounds E187.1 to E187.418 of formula (Ia) wherein R^{1a} is , R² is F, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

5 Table 1.188 provides 418 compounds E188.1 to E188.418 of formula (Ia) wherein R^{1a} is , R² is Cl, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.189 provides 418 compounds E189.1 to E189.418 of formula (Ia) wherein R^{1a} is , R² is Cl, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.190 provides 418 compounds E190.1 to E190.418 of formula (Ia) wherein R^{1a} is , R² is Cl, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.191 provides 418 compounds E191.1 to E191.418 of formula (Ia) wherein R^{1a} is , R² is Cl, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.192 provides 418 compounds E192.1 to E192.418 of formula (Ia) wherein R^{1a} is , R² is Br, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

15 Table 1.193 provides 418 compounds E193.1 to E193.418 of formula (Ia) wherein R^{1a} is , R² is Br, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.194 provides 418 compounds E194.1 to E194.418 of formula (Ia) wherein R^{1a} is , R² is Br, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.195 provides 418 compounds E195.1 to E195.418 of formula (Ia) wherein R^{1a} is , R² is Br, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.196 provides 418 compounds E196.1 to E196.418 of formula (Ia) wherein R^{1a} is , R² is CN, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.197 provides 418 compounds E197.1 to E197.418 of formula (Ia) wherein R^{1a} is , R² is CN, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

25 Table 1.198 provides 418 compounds E198.1 to E198.418 of formula (Ia) wherein R^{1a} is , R² is CN, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

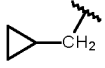
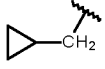
Table 1.199 provides 418 compounds E199.1 to E199.418 of formula (Ia) wherein R^{1a} is , R² is CN, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.200 provides 418 compounds E200.1 to E200.418 of formula (Ia) wherein R^{1a} is , R² is OCH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

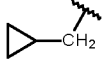
5 Table 1.201 provides 418 compounds E201.1 to E201.418 of formula (Ia) wherein R^{1a} is , R² is OCH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

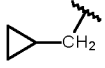
Table 1.202 provides 418 compounds E202.1 to E202.418 of formula (Ia) wherein R^{1a} is , R² is OCH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

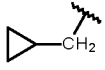
Table 1.203 provides 418 compounds E203.1 to E203.418 of formula (Ia) wherein R^{1a} is , R² is OCH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

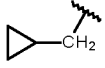
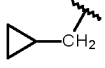
Table 1.204 provides 418 compounds E204.1 to E204.418 of formula (Ia) wherein R^{1a} is , R² is OCH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.205 provides 418 compounds E205.1 to E205.418 of formula (Ia) wherein R^{1a} is , R² is OCH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

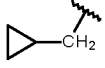
15 Table 1.206 provides 418 compounds E206.1 to E206.418 of formula (Ia) wherein R^{1a} is , R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

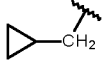
Table 1.207 provides 418 compounds E207.1 to E207.418 of formula (Ia) wherein R^{1a} is , R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.208 provides 418 compounds E208.1 to E208.418 of formula (Ia) wherein R^{1a} is NHAc, R² is H, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.209 provides 418 compounds E209.1 to E209.418 of formula (Ia) wherein R^{1a} is NHAc, R² is H, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.210 provides 418 compounds E210.1 to E210.418 of formula (Ia) wherein R^{1a} is NHAc, R² is H, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

25 Table 1.211 provides 418 compounds E211.1 to E211.418 of formula (Ia) wherein R^{1a} is NHAc, R² is H, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.212 provides 418 compounds E212.1 to E212.418 of formula (Ia) wherein R^{1a} is NHAc, R² is H, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.213 provides 418 compounds E213.1 to E213.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

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- Table 1.214 provides 418 compounds E214.1 to E214.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.215 provides 418 compounds E215.1 to E215.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 5 Table 1.216 provides 418 compounds E216.1 to E216.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.217 provides 418 compounds E217.1 to E217.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.218 provides 418 compounds E218.1 to E218.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 10 Table 1.219 provides 418 compounds E219.1 to E219.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.220 provides 418 compounds E220.1 to E220.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 15 Table 1.221 provides 418 compounds E221.1 to E221.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.222 provides 418 compounds E222.1 to E222.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.223 provides 418 compounds E223.1 to E223.418 of formula (Ia) wherein R^{1a} is NHAc, R² is F, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 20 Table 1.224 provides 418 compounds E224.1 to E224.418 of formula (Ia) wherein R^{1a} is NHAc, R² is F, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.225 provides 418 compounds E225.1 to E225.418 of formula (Ia) wherein R^{1a} is NHAc, R² is F, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 25 Table 1.226 provides 418 compounds E226.1 to E226.418 of formula (Ia) wherein R^{1a} is NHAc, R² is F, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.227 provides 418 compounds E227.1 to E227.418 of formula (Ia) wherein R^{1a} is NHAc, R² is F, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.228 provides 418 compounds E228.1 to E228.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Cl, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 30 Table 1.229 provides 418 compounds E229.1 to E229.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Cl, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.230 provides 418 compounds E230.1 to E230.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Cl, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 35 Table 1.231 provides 418 compounds E231.1 to E231.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Cl, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.232 provides 418 compounds E232.1 to E232.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Cl, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.233 provides 418 compounds E233.1 to E233.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Br, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 40 Table 1.234 provides 418 compounds E234.1 to E234.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Br, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- Table 1.235 provides 418 compounds E235.1 to E235.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Br, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.236 provides 418 compounds E236.1 to E236.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Br, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 5 Table 1.237 provides 418 compounds E237.1 to E237.418 of formula (Ia) wherein R^{1a} is NHAc, R² is Br, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.238 provides 418 compounds E238.1 to E238.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CN, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.239 provides 418 compounds E239.1 to E239.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CN, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 10 Table 1.240 provides 418 compounds E240.1 to E240.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CN, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.241 provides 418 compounds E241.1 to E241.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CN, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 15 Table 1.242 provides 418 compounds E242.1 to E242.418 of formula (Ia) wherein R^{1a} is NHAc, R² is CN, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.243 provides 418 compounds E243.1 to E243.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.244 provides 418 compounds E244.1 to E244.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 20 Table 1.245 provides 418 compounds E245.1 to E245.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.246 provides 418 compounds E246.1 to E246.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 25 Table 1.247 provides 418 compounds E247.1 to E247.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.248 provides 418 compounds E248.1 to E248.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.249 provides 418 compounds E249.1 to E249.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 30 Table 1.250 provides 418 compounds E250.1 to E250.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.251 provides 418 compounds E251.1 to E251.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 35 Table 1.252 provides 418 compounds E252.1 to E252.418 of formula (Ia) wherein R^{1a} is NHAc, R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.253 provides 418 compounds E253.1 to E253.418 of formula (Ia) wherein R^{1a} is CN, R² is H, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.254 provides 418 compounds E254.1 to E254.418 of formula (Ia) wherein R^{1a} is CN, R² is H, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 40 Table 1.255 provides 418 compounds E255.1 to E255.418 of formula (Ia) wherein R^{1a} is CN, R² is H, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- Table 1.256 provides 418 compounds E256.1 to E256.418 of formula (Ia) wherein R^{1a} is CN, R² is H, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.257 provides 418 compounds E257.1 to E257.418 of formula (Ia) wherein R^{1a} is CN, R² is H, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 5 Table 1.258 provides 418 compounds E258.1 to E258.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.259 provides 418 compounds E259.1 to E259.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.260 provides 418 compounds E260.1 to E260.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 10 Table 1.261 provides 418 compounds E261.1 to E261.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.262 provides 418 compounds E262.1 to E262.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 15 Table 1.263 provides 418 compounds E263.1 to E263.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.264 provides 418 compounds E264.1 to E264.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.265 provides 418 compounds E265.1 to E265.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 20 Table 1.266 provides 418 compounds E266.1 to E266.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.267 provides 418 compounds E267.1 to E267.418 of formula (Ia) wherein R^{1a} is CN, R² is CH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 25 Table 1.268 provides 418 compounds E268.1 to E268.418 of formula (Ia) wherein R^{1a} is CN, R² is F, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.269 provides 418 compounds E269.1 to E269.418 of formula (Ia) wherein R^{1a} is CN, R² is F, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.270 provides 418 compounds E270.1 to E270.418 of formula (Ia) wherein R^{1a} is CN, R² is F, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 30 Table 1.271 provides 418 compounds E271.1 to E271.418 of formula (Ia) wherein R^{1a} is CN, R² is F, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.272 provides 418 compounds E272.1 to E272.418 of formula (Ia) wherein R^{1a} is CN, R² is F, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 35 Table 1.273 provides 418 compounds E273.1 to E273.418 of formula (Ia) wherein R^{1a} is CN, R² is Cl, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.274 provides 418 compounds E274.1 to E274.418 of formula (Ia) wherein R^{1a} is CN, R² is Cl, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- Table 1.275 provides 418 compounds E275.1 to E275.418 of formula (Ia) wherein R^{1a} is CN, R² is Cl, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.
- 40 Table 1.276 provides 418 compounds E276.1 to E276.418 of formula (Ia) wherein R^{1a} is CN, R² is Cl, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.277 provides 418 compounds E277.1 to E277.418 of formula (Ia) wherein R^{1a} is CN, R² is Cl, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.278 provides 418 compounds E278.1 to E278.418 of formula (Ia) wherein R^{1a} is CN, R² is Br, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 5 Table 1.279 provides 418 compounds E279.1 to E279.418 of formula (Ia) wherein R^{1a} is CN, R² is Br, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.280 provides 418 compounds E280.1 to E280.418 of formula (Ia) wherein R^{1a} is CN, R² is Br, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- Table 1.281 provides 418 compounds E281.1 to E281.418 of formula (Ia) wherein R^{1a} is CN, R² is Br, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.282 provides 418 compounds E282.1 to E282.418 of formula (Ia) wherein R^{1a} is CN, R² is Br, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.283 provides 418 compounds E283.1 to E283.418 of formula (Ia) wherein R^{1a} is CN, R² is CN, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 15 Table 1.284 provides 418 compounds E284.1 to E284.418 of formula (Ia) wherein R^{1a} is CN, R² is CN, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.285 provides 418 compounds E285.1 to E285.418 of formula (Ia) wherein R^{1a} is CN, R² is CN, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- Table 1.286 provides 418 compounds E286.1 to E286.418 of formula (Ia) wherein R^{1a} is CN, R² is CN, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.287 provides 418 compounds E287.1 to E287.418 of formula (Ia) wherein R^{1a} is CN, R² is CN, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.288 provides 418 compounds E288.1 to E288.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 25 Table 1.289 provides 418 compounds E289.1 to E289.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.290 provides 418 compounds E290.1 to E290.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- Table 1.291 provides 418 compounds E291.1 to E291.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.292 provides 418 compounds E292.1 to E292.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.293 provides 418 compounds E293.1 to E293.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₂CH₃, R⁵ is CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

- 35 Table 1.294 provides 418 compounds E294.1 to E294.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₂CH₃, R⁵ is OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.295 provides 418 compounds E295.1 to E295.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₂CH₃, R⁵ is cyclopropyl and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

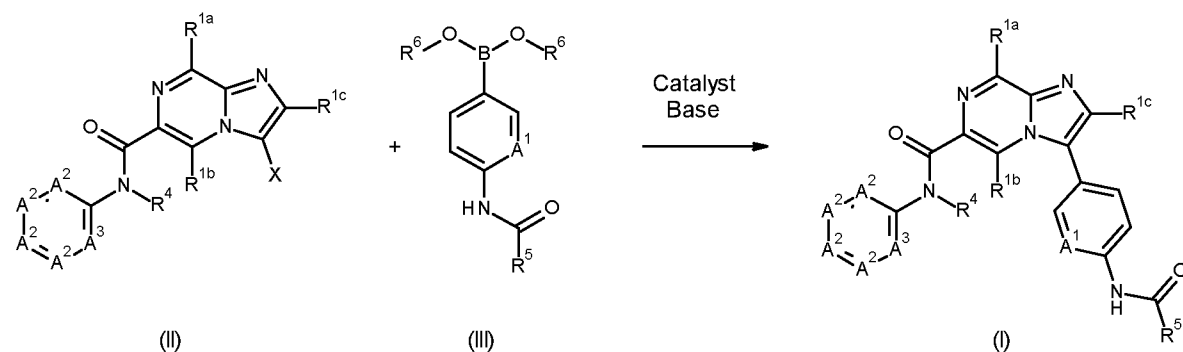
- Table 1.296 provides 418 compounds E296.1 to E296.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₂CH₃, R⁵ is CH₂OCH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Table 1.297 provides 418 compounds E297.1 to E297.418 of formula (Ia) wherein R^{1a} is CN, R² is OCH₂CH₃, R⁵ is NHCH₂CH₃ and A¹, A^{2a}, A^{2b}, A³, R⁴ are as defined in table Z.

Compounds according to the invention may possess any number of benefits including, *inter alia*, advantageous levels of biological activity for protecting plants against diseases that are caused by fungi or superior properties for use as agrochemical active ingredients (for example, greater biological activity, an advantageous spectrum of activity, an increased safety profile, improved physico-chemical properties, or increased biodegradability). Compounds according to the invention have particularly advantageous levels of biological activity for protecting plants against oomycetes such as *Phytophthora*, *Plasmopara* and *Pythium*.

- 10 Compounds of formula (I), wherein Z is O, can be made as shown in the following schemes 1 to 18, in which, unless otherwise stated, the definition of each variable is as defined in the present invention.

Compounds of formula (I) can be prepared via Suzuki cross coupling of compounds of formula (II), wherein X is Cl, Br or I, and a compound of formula (III), wherein either R⁶ is independently from each other hydrogen, C₁₋₆alkyl or wherein two R⁶ together can form a C₃₋₈cycloalkyl, in the presence of a base, such as Cs₂CO₃, K₂CO₃ or NaOtBu, and a suitable palladium catalyst, such as tetrakis(triphenylphosphine)palladium, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), bis(diphenylphosphine)palladium(II) chloride, palladium dichloride or palladium acetate, in a suitable solvent, such as dimethylformamide, dioxane, tetrahydrofuran, ethanol or water. Compounds of formula (III), wherein either R⁶ is independently from each other hydrogen, C₁₋₆alkyl or wherein two R⁶ together can form a C₃₋₈cycloalkyl are prepared by known methods or are commercially available. This transformation is depicted in Scheme 1.

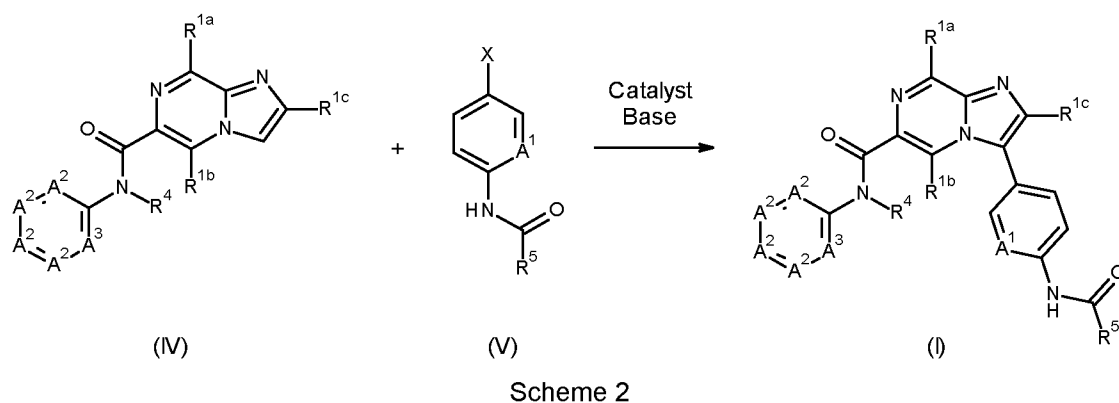


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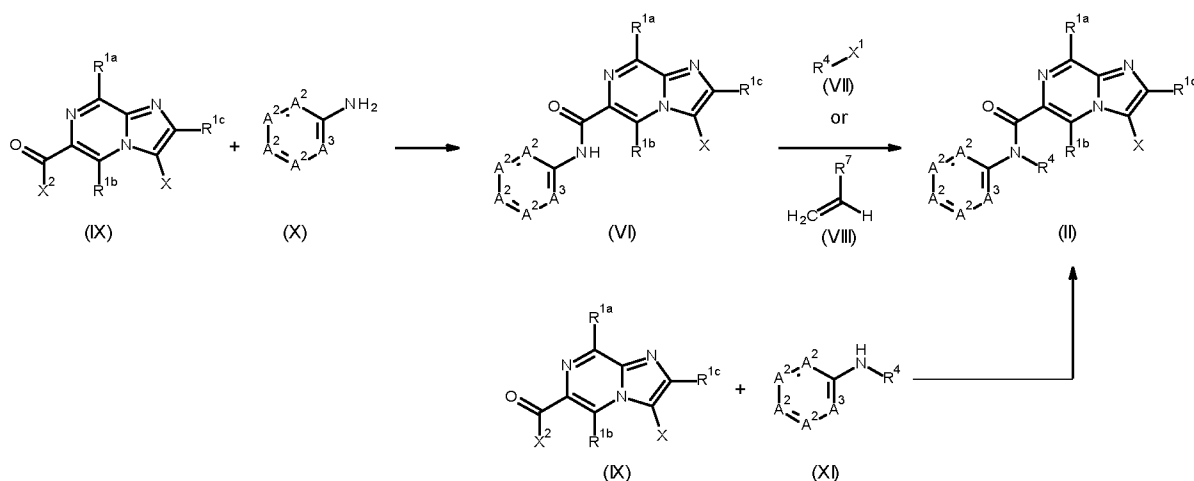
Scheme 1

Alternatively, compounds of formula (I) can be prepared by direct arylation of compounds of formula (IV) with compounds of formula (V), wherein X is Cl, Br or I, in the presence of a catalyst such as palladium diacetate, a ligand such as triphenylphosphine or (dicyclohexylphosphino)biphenyl, and a base such as cesium carbonate or potassium carbonate. Compounds of formula (V), wherein X is Cl, Br or I, are prepared by known methods or are commercially available. This coupling reaction is depicted in Scheme 2.

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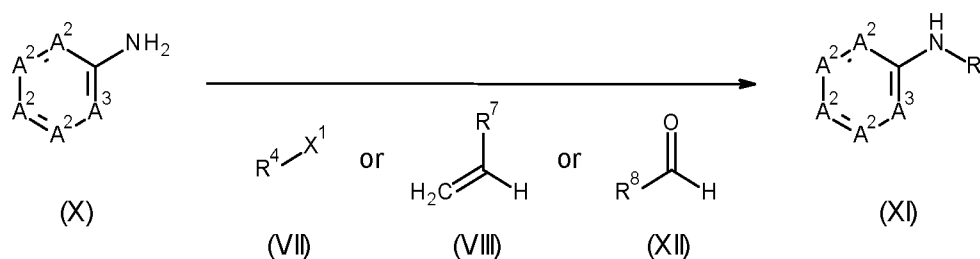


Compounds of formula (II), wherein X is Cl, Br or I, can be prepared by reacting compounds of formula (VI), wherein X is Cl, Br or I, with an reagent of formula (VII), wherein X¹ is a good leaving group such as Cl, Br, I, triflate, tosyl or mesyl, in the presence of a base such as Cs₂CO₃, K₂CO₃, NaH or NaOtBu. A compound of formula (VIII), wherein R⁷ is an electron-withdrawing group such as a cyano or an ester, can alternatively be used to functionalize the amide nitrogen, optionally in the presence of a base such as triethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene. Compounds of formula (VI), wherein X is Cl, Br or I, can be prepared by a peptide-coupling reaction between a compound of formula (IX), wherein X is Cl, Br or I, and X² is OH, and amines of formula (X), and by activating the carboxylic acid function of the compounds of formula (IX), a process that usually takes place by converting the -OH of the carboxylic acid into a good leaving group, such as a chloride group, for example by using (COCl)₂ or SOCl₂, prior to treatment with amines of formula (X), preferably in a suitable solvent (e.g., N-methylpyrrolidone, acetonitrile, dimethylacetamide, dichloromethane or tetrahydrofuran), preferably at temperatures between 25°C and 60°C, and optionally in the presence of a base such as triethylamine or N,N-diisopropylethylamine; or alternatively under conditions described in the literature for an amide coupling such as 1-propanephosphonic acid cyclic anhydride (T3P) in suitable solvent (e.g., acetonitrile) optionally in the presence of a base (e.g., triethylamine or N,N-diisopropylethylamine). For examples, see *Chem. Soc. Rev.* **2009**, 38, 606 and *Chem. Soc. Rev.* **2011**, 40, 5084. Alternatively, compounds of formula (II), wherein X is Cl, Br or I, can be obtained by an amide-coupling transformation between compounds of formula (IX), wherein X is Cl, Br or I, and X² is OH, and amines of formula (XI) using the conditions described above. These transformations are depicted in Scheme 3.



Scheme 3

Compounds of formula (XI) are commercially available or can be obtained by reaction of compounds of formula (X) with a compound of formula (VII) wherein X^1 is a good leaving group such as Cl, Br, I, triflate, tosyl or mesyl, in the presence of a base such as Cs_2CO_3 , K_2CO_3 , NaH or NaOtBu. Alternatively, compounds of formula (XI) can also be synthesized by reacting compounds of formula (X) with compounds of formula (VIII), wherein R^7 is an electron-withdrawing group such as cyano or ester, optionally in the presence of a base such as triethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene. Alternatively, compounds of formula (XI) can be obtained from amines of formula (X) by a reductive amination with aldehydes of formula (XII), wherein R^8 is selected from C_{1-5} alkyl, C_{1-6} alkoxy- C_{1-5} alkyl, C_{3-6} cycloalkyl- C_{1-3} alkyl, C_{1-5} alkenyl, C_{1-5} alkynyl, C_{1-5} alkoxy, C_{1-6} alkylsulfanyl- C_{1-5} alkyl, C_{1-6} alkylsulfinyl- C_{1-5} alkyl, C_{1-6} alkylsulfonyl- C_{1-5} alkyl, C_{1-6} alkoxycarbonyl- C_{1-5} alkyl, C_{1-6} alkylaminocarbonyl- C_{1-5} alkyl, di- C_{1-6} alkylaminocarbonyl- C_{1-5} alkyl, e.g. in the presence of $\text{NaBH}(\text{OAc})_3$ or NaBH_3CN , in a suitable solvent, optionally in the presence of a Brønsted or Lewis acid such as acetic acid. Alternatively, another reagent system for the reductive amination uses a combination of titanium isopropoxide and NaBH_4 . The synthesis of compounds of formula (XI) from amines of formula (X) is depicted in Scheme 4.

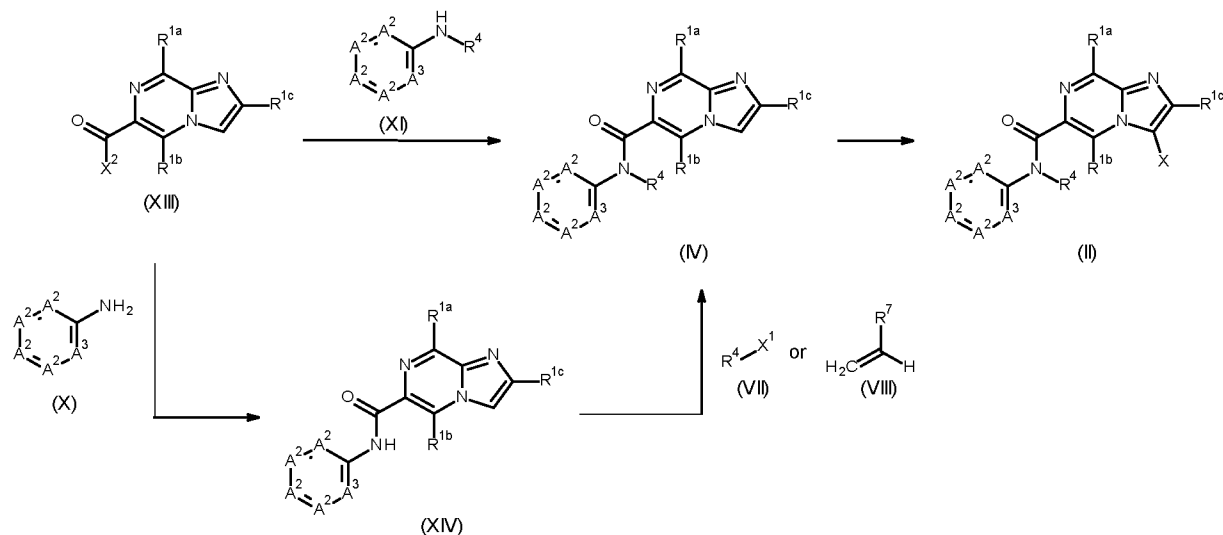


Scheme 4

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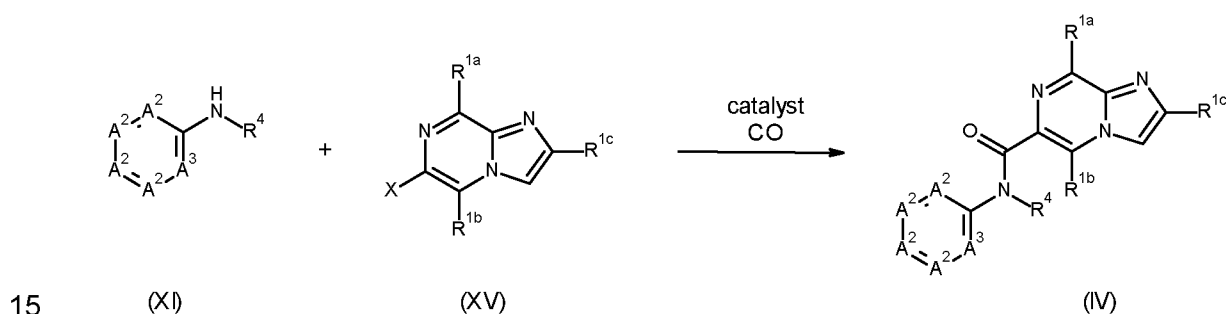
Alternatively, compounds of formula (II), wherein X is Cl, Br or I, can be prepared from the reaction of a compound of formula (IV) and a halogenating agent, such as N-chlorosuccinimide, N-bromosuccinimide, N-iodosuccinimide or bromine in a suitable solvent, such as dichloromethane, chloroform, tetrahydrofuran or acetonitrile. Compounds of formula (IV) can be obtained by an amide-coupling transformation of amines of formula (XI) with compounds of formula (XIII), wherein X^2 is OH, and by activating the carboxylic acid function of the compounds of formula (XIII), a process that usually takes place by converting the -OH of the carboxylic acid into a good leaving group, such as a chloride group, for example by using $(\text{COCl})_2$ or SOCl_2 , prior to treatment with amines of formula (XI), preferably in a suitable solvent (e.g., N-methylpyrrolidone, acetonitrile, dimethylacetamide, dichloromethane or tetrahydrofuran), preferably at temperatures between 25 °C and 60 °C, and optionally in the presence of a base such as triethylamine or N,N-diisopropylethylamine; or alternatively under conditions described in the literature for an amide coupling such as 1-propanephosphonic acid cyclic anhydride (T3P) in suitable solvent (e.g., acetonitrile) optionally in the presence of a base (e.g., triethylamine or N,N-diisopropylethylamine). Alternatively, compounds of formula (IV) can be obtained by alkylation of compounds of formula (XIV) with compounds of formula (VII), wherein X^1 is a good leaving group such as Cl, Br, I, triflate, tosyl or mesyl, in the presence of a base such as Cs_2CO_3 , K_2CO_3 , NaH or NaOtBu. Alternatively, compounds of formula (IV) can also be synthesized by reacting compounds of formula

(XIV) with compounds of formula (VIII), wherein R^7 is an electron-withdrawing group such as cyano or ester, optionally in the presence of a base such as triethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene. Compounds of formula (XIV) can be prepared by a peptide-coupling transformation from compounds of formula (XIII), wherein X^2 is OH, with amines of formula (X) using the conditions described 5 above. These transformations are depicted in Scheme 5.



Scheme 5

10 Alternatively, compounds of formula (IV) can be synthesized by reacting compounds of formula (XV), wherein X is Cl, Br or I, with amines of formula (XI) and carbon monoxide in the presence of a catalyst such as [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), and, optionally, a base such as triethylamine. This transformation is depicted in Scheme 6.

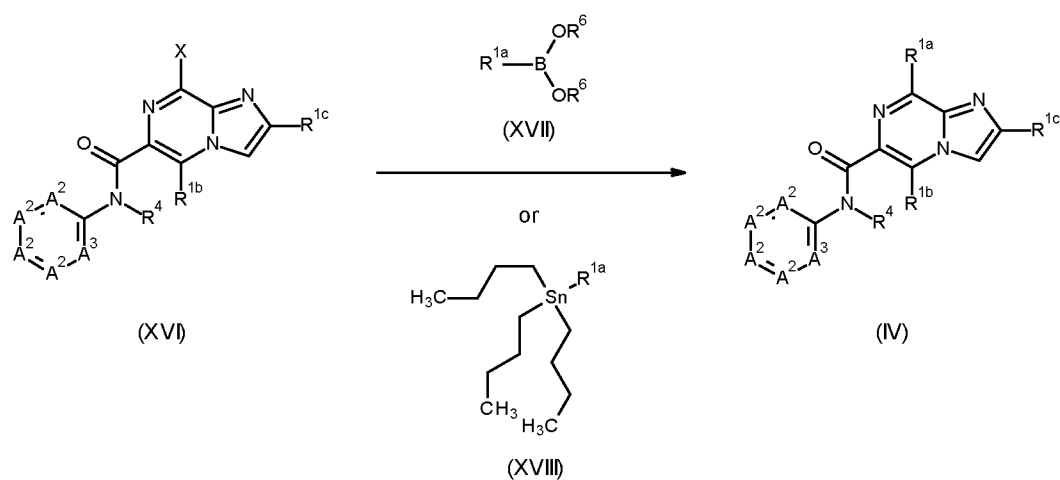


Scheme 6

Alternatively, compounds of formula (IV) can be obtained from compounds of formula (XVI), wherein X is Cl, Br or I, by a cross-coupling transformation with a compound of formula (XVII), wherein either R^6 is 20 independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl (Suzuki cross-coupling), or a compound of formula (XVIII) (Stille coupling), or by a palladium catalyzed cyanation reaction. Suzuki cross-couplings can be achieved by using a suitable palladium catalyst, such as tetrakis(triphenylphosphine)palladium, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), bis(diphenylphosphine)palladium(II) chloride, palladium dichloride or palladium acetate, in the presence 25 of a base, such as Cs_2CO_3 , K_2CO_3 or $NaOtBu$, in a suitable solvent, such as dimethylformamide,

dioxane, tetrahydrofuran, ethanol or water. Stille couplings can be achieved a suitable palladium catalyst such as tetrakis(triphenylphosphine)palladium, tris(dibenzylideneacetone)dipalladium, palladium dichloride or palladium acetate in the presence of a base, such as Cs_2CO_3 or sodium acetate, in a suitable solvent, such as dimethylformamide, dioxane or acetonitrile. Palladium-catalyzed cyanation can be achieved by using a suitable catalyst such as tris(dibenzylidenacetone)dipalladium(0) or palladium acetate, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), optionally with suitable ligands such as 5-diphenylphosphanyl-9,9-dimethylxanthene-4-yl)-diphenyl-phosphane (Xantphos), 2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (XPhos), and a cyanating reagent such as zinc cyanide, potassium cyanide or potassium hexacyanoferrate(II) trihydrate optionally in the presence of a base such as potassium acetate or cesium carbonate, in a suitable solvent such as dimethyl formamide, dioxane, tetrahydrofuran with or without the presence of water as a co-solvent. Compounds of formula (XVII), wherein either R^6 is independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl, and compounds of formula (XVIII) are prepared by known methods or are commercially available. These transformations are depicted in Scheme 7.

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Scheme 7

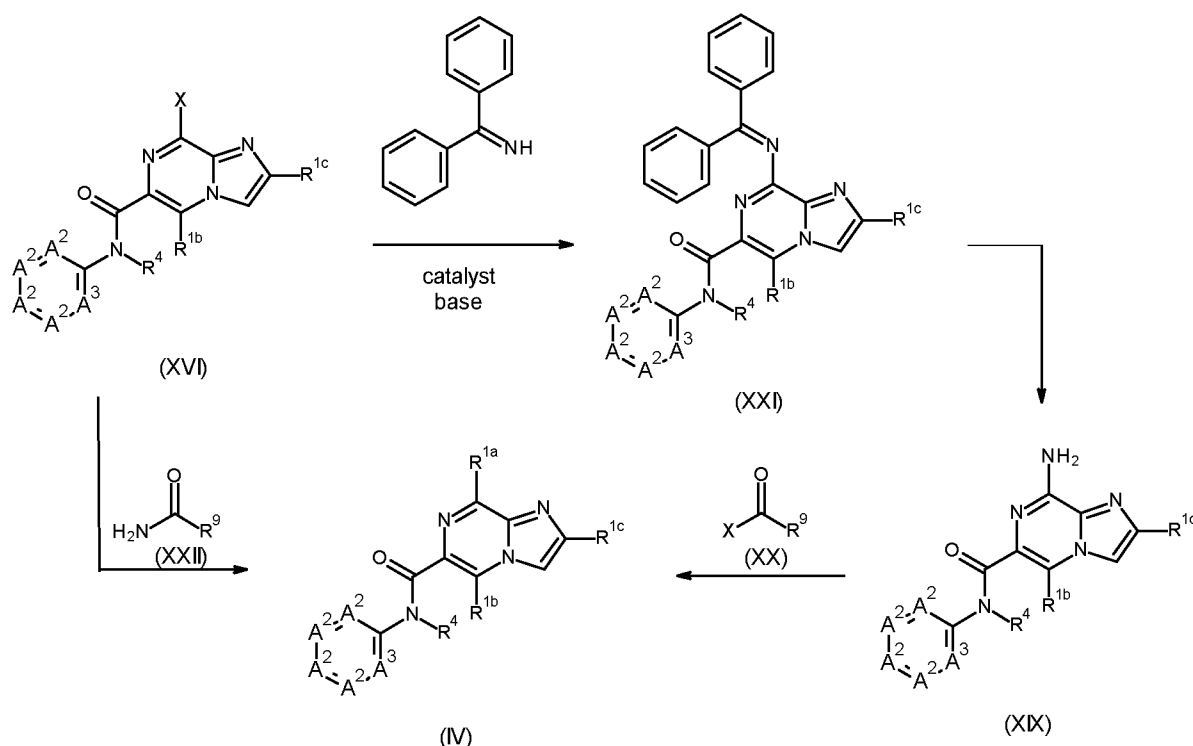
Alternatively, compounds of formula (IV) can be obtained from compounds of formula (XIX) by reaction with a compound of formula (XX), wherein X is Cl or Br, and R^9 is C_{1-6} alkyl, in the presence of a base such as pyridine or diisopropylethylamine. Amines of formula (XIX) can be prepared by treatment of compounds of formula (XXI) with an acid, typically hydrochloric acid, or with sodium acetate and hydroxyamine hydrochloride in a protic solvent such as methanol. Compounds of formula (XXI) can be synthesized by reaction of compounds of formula (XVI), wherein X is Cl, Br or I, with diphenylmethanimine (CAS number 1013-88-3) in the presence of a catalyst, such as palladium acetate or tris(dibenzylideneacetone)dipalladium, optionally a ligand such as 1,1'-[1,1'-binaphthalene]-2,2'-diylbis[1,1-diphenylphosphine] or (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane), and in the presence of a base such as cesium carbonate or sodium tert-butoxide. Alternatively, compounds of formula (IV) may be obtained directly by reacting compounds of formula (XVI) with compounds of formula (XXII), wherein R^9 is C_{1-6} alkyl, by a palladium catalyzed coupling reaction (Buchwald-Hartwig reaction). This reaction can be achieved by using a suitable catalyst such as Xantphos-Pd-G2 (CAS 1375325-77-1), XantPhos Pd G3 (Cas 1445085-97-1) or [1,1'-

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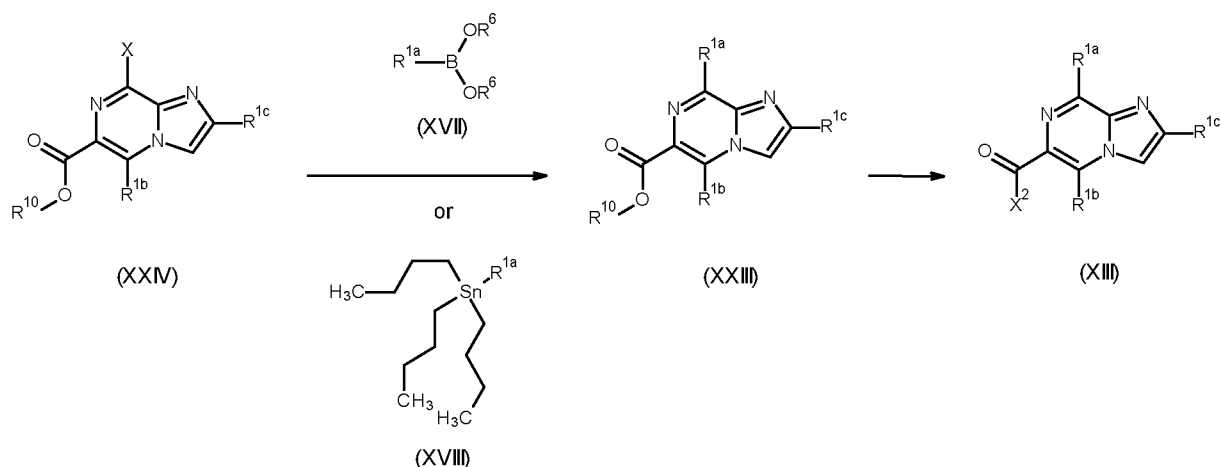
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Bis(diphenylphosphino)ferrocen]dichloropalladium(II), in the presence of a base such as cesium carbonate, sodium tert-butoxide or potassium phosphate in a suitable solvent such as dioxane, tetrahydrofuran or toluene. These transformations are depicted in Scheme 8.



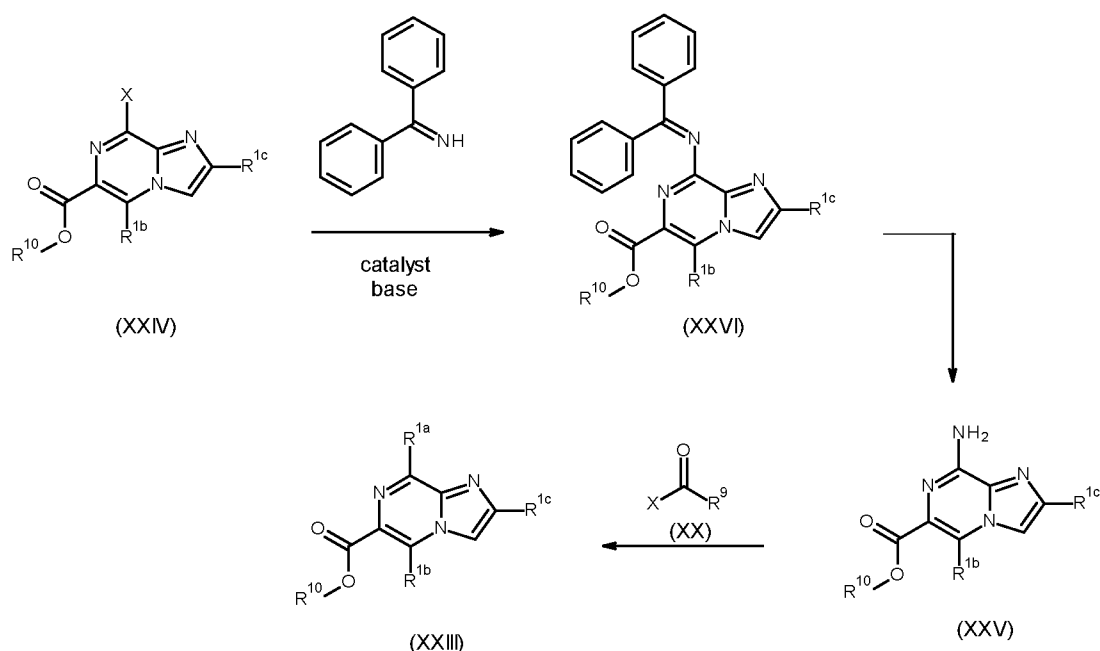
Scheme 8

Compounds of formula (XIV), wherein X² is OH, can be synthesized from compounds of formula (XXIII), wherein R⁹ is C₁₋₆alkyl, by treatment with an acid or a base. This transformation is well known to those skilled in the art. Compounds of formula (XXIII), wherein R¹⁰ is C₁₋₆alkyl, can be obtained from compounds of formula (XXIV), wherein X is Cl, Br or I and R¹⁰ is C₁₋₆alkyl, by a cross-coupling transformation with a compound of formula (XVII) (Suzuki cross-coupling) or a compound of formula (XVIII) (Stille coupling), using the conditions described above. These transformations are depicted in Scheme 9.



Scheme 9

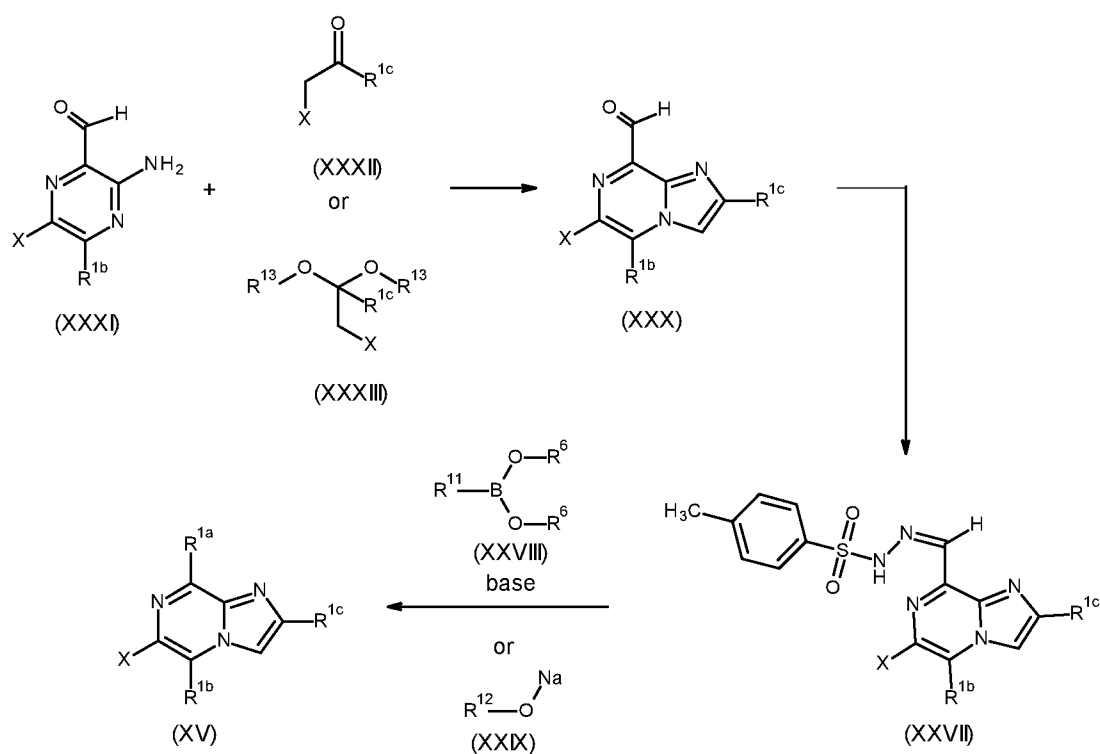
Alternatively, compounds of formula (XXIII), wherein R^{10} is C_{1-6} alkyl, can be obtained from compounds of formula (XXV), wherein R^{10} is C_{1-6} alkyl, by reaction with a compound of formula (XX), wherein X is Cl or Br and R^9 is C_{1-6} alkyl, in the presence of a base such as pyridine or diisopropylethylamine. Amines of formula (XXV), wherein R^{10} is C_{1-6} alkyl, can be prepared by treatment of compounds of formula (XXVI), wherein R^{10} is C_{1-6} alkyl, with an acid, typically hydrochloric acid, or with sodium acetate and hydroxyamine hydrochloride in a protic solvent such as methanol. Compounds of formula (XXVI), wherein R^{10} is C_{1-6} alkyl, can be synthesized by reaction of compounds of formula (XXIV), wherein X is Cl, Br or I, and R^{10} is C_{1-6} alkyl, with diphenylmethanimine (CAS number 1013-88-3) in the presence of a catalyst, such as palladium acetate or tris(dibenzylideneacetone)dipalladium, optionally a ligand such as 1,1'-[1,1'-binaphthalene]-2,2'-diylbis[1,1-diphenylphosphine] or (9,9-dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane), and in the presence of a base such as cesium carbonate or sodium tert-butoxide. These transformations are depicted in Scheme 10.



Scheme 10

Compounds of formula (XV), wherein X is Cl, Br or I, can be prepared by cross-coupling of hydrazones of formula (XXVII), wherein X is Cl, Br or I, with a compound of formula (XXVIII), wherein either R^6 is independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl and R^{11} is selected from C_{1-5} alkyl, C_{1-6} alkoxy- C_{1-5} alkyl and C_{3-6} cycloalkyl- C_{1-3} alkyl, in the presence of a base, such as Cs_2CO_3 , K_2CO_3 or 1,8-diazabicyclo[5.4.0]undec-7-ene. Such transformations are described in the literature, for instance in *Org. Lett.* **2020**, 22, 2271. Alternatively, a compound of formula (XV), wherein X is Cl, Br or I, can be obtained by reacting hydrazone of formula (XXVII), wherein X is Cl, Br or I, with an alkoxide of formula (XXIX), wherein R^{12} is C_{1-5} alkyl, in a protic solvent such as methanol or tert-butanol. Compounds of formula (XXVIII), wherein either R^6 is independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl and R^{11} is selected from C_{1-5} alkyl, C_{1-6} alkoxy- C_{1-5} alkyl and C_{3-6} cycloalkyl- C_{1-3} alkyl, and compounds of formula (XXIX), wherein

R^{12} is C_{1-8} alkyl, are commercially available or can be prepared by known methods. Hydrazones of formula (XXVII), wherein X is Cl, Br or I, can be prepared by condensation of p-toluenesulfonylhydrazide (CAS 1576-35-8) with aldehydes of formula (XXX), wherein X is Cl, Br or I. Aldehydes of formula (XXX), wherein X is Cl, Br or I, are commercially available or, alternatively, can be prepared by the condensation of a compound of formula (XXXI), wherein X is Cl, Br or I, with a compound of formula (XXXII), wherein X is Cl, Br or I, or its corresponding acetal of formula (XXXIII), wherein X is Cl, Br or I and either R^{13} is independently from each other C_{1-8} alkyl or wherein two R^{13} together can form a C_{3-8} cycloalkyl, in a solvent, such as water, ethanol, acetone or acetonitrile. In some instance, the outcome of the reaction can be improved by using a base, such as sodium bicarbonate or potassium carbonate, or by using an acid, such as p-toluenesulfonic acid or hydrogen bromide. Compounds of formula (XXXI), wherein X is Cl, Br or I, compounds of formula (XXXII), wherein X is Cl, Br or I, and compounds of formula (XXXIII) wherein X is Cl, Br or I, are commercially available or prepared using known methods by those skilled in the art. These transformations are depicted in Scheme 11.

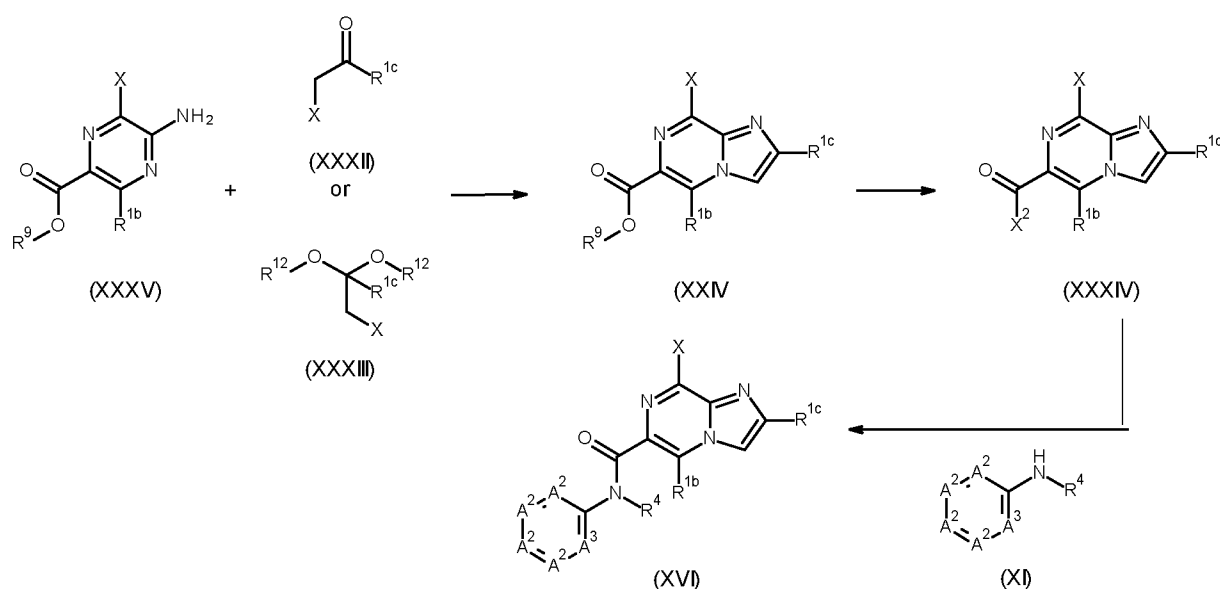


Scheme 11

Compounds of formula (XVI), wherein X is Cl, Br or I, can be obtained by an amide-coupling transformation of amines of formula (XI) with compounds of formula (XXXIV), wherein X is Cl, Br or I, and X^2 is OH, and by activating the carboxylic acid function of the compounds of formula (XXXIV), a process that usually takes place by converting the -OH of the carboxylic acid into a good leaving group, such as a chloride group, for example by using $(COCl)_2$ or $SOCl_2$, prior to treatment with amines of formula (XI), preferably in a suitable solvent (e.g., N-methylpyrrolidone, acetonitrile, dimethylacetamide, dichloromethane or tetrahydrofuran), preferably at temperatures between 25 °C and 60 °C, and optionally in the presence of a base such as triethylamine or N,N-diisopropylethylamine; or alternatively under conditions described in the literature for an amide coupling such as 1-propanephosphonic acid cyclic anhydride (T3P) in suitable solvent (e.g., acetonitrile) optionally in the presence of a base (e.g.,

triethylamine or N,N-diisopropylethylamine). Compounds of formula (XXXIV), wherein X is Cl, Br or I, and X² is OH, can be prepared by hydrolysis of the ester function of compounds of formula (XXIV), wherein X is Cl, Br or I, and R¹⁰ is C₁₋₆alkyl, which in turn can be synthesized by condensation of compounds of formula (XXXV), wherein X is Cl, Br or I, and R¹⁰ is C₁₋₆alkyl, with a compound of formula (XXXII), wherein X is Cl, Br or I, or its corresponding acetal of formula (XXXIII), wherein X is Cl, Br or I and either R¹³ is independently from each other C₁₋₆alkyl or wherein two R¹³ together can form a C₃-cycloalkyl, using the conditions described above. Compounds of formula (XXXV) wherein X is Cl, Br or I, and R¹⁰ is C₁₋₆alkyl, are commercially available or prepared using known methods by those skilled in the art. These transformations are depicted in Scheme 12.

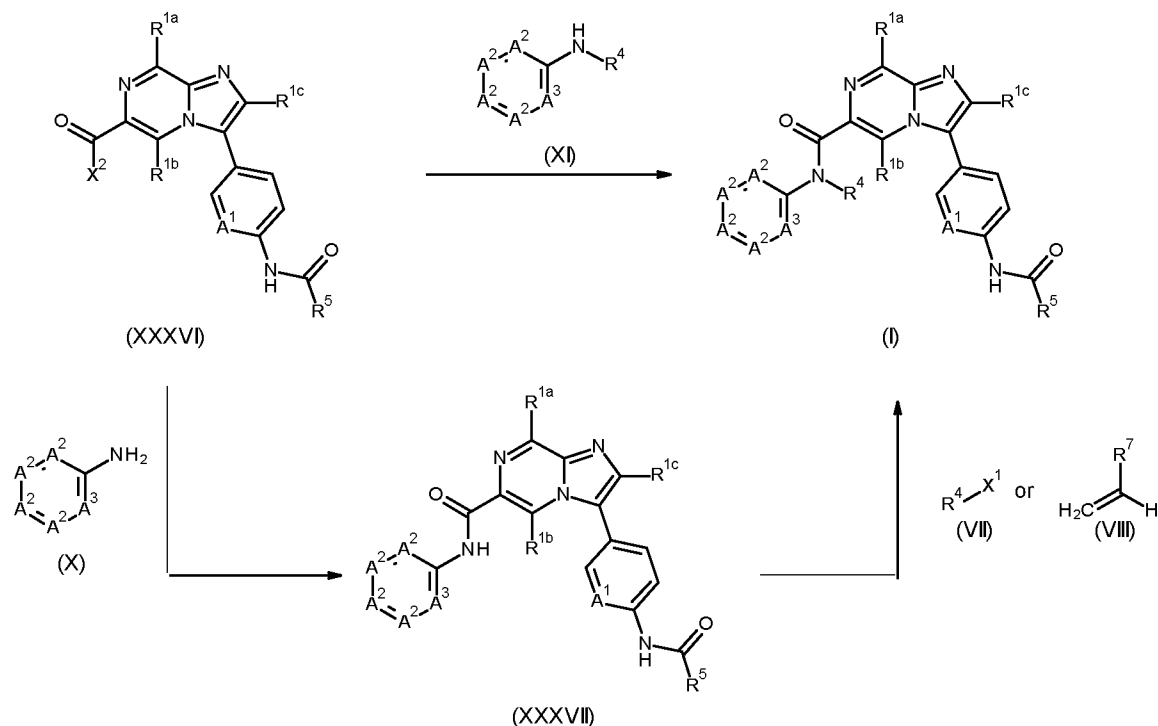
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Scheme 12

Alternatively, compounds of formula (I) can be prepared by an amide-coupling transformation of amines of formula (XI) with compounds of formula (XXXVI), wherein X is Cl, Br or I, and X² is OH, and by activating the carboxylic acid function of the compounds of formula (XXXVI), a process that usually takes place by converting the -OH of the carboxylic acid into a good leaving group, such as a chloride group, for example by using (COCl)₂ or SOCl₂, prior to treatment with amines of formula (XI), preferably in a suitable solvent (e.g., N-methylpyrrolidone, acetonitrile, dimethylacetamide, dichloromethane or tetrahydrofuran), preferably at temperatures between 25 °C and 60 °C, and optionally in the presence of a base such as triethylamine or N,N-diisopropylethylamine; or alternatively under conditions described in the literature for an amide coupling such as 1-propanephosphonic acid cyclic anhydride (T3P) in suitable solvent (e.g., acetonitrile) optionally in the presence of a base (e.g., triethylamine or N,N-diisopropylethylamine). Compounds of formula (I) can alternatively be prepared by alkylation of compounds of formula (XXXVII) with compounds of formula (VII), wherein X¹ is a good leaving group such as Cl, Br, I, triflate, tosyl or mesyl, in the presence of a base such as Cs₂CO₃, K₂CO₃, NaH or NaOtBu. Alternatively, compounds of formula (I) can also be synthesized by reacting compounds of formula (XXXVII) with compounds of formula (VIII), wherein R⁷ is an electron-withdrawing group such as cyano or ester, optionally in the presence of a base such as triethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene. Compounds of formula (XXXVII) can be synthesized by a peptide-

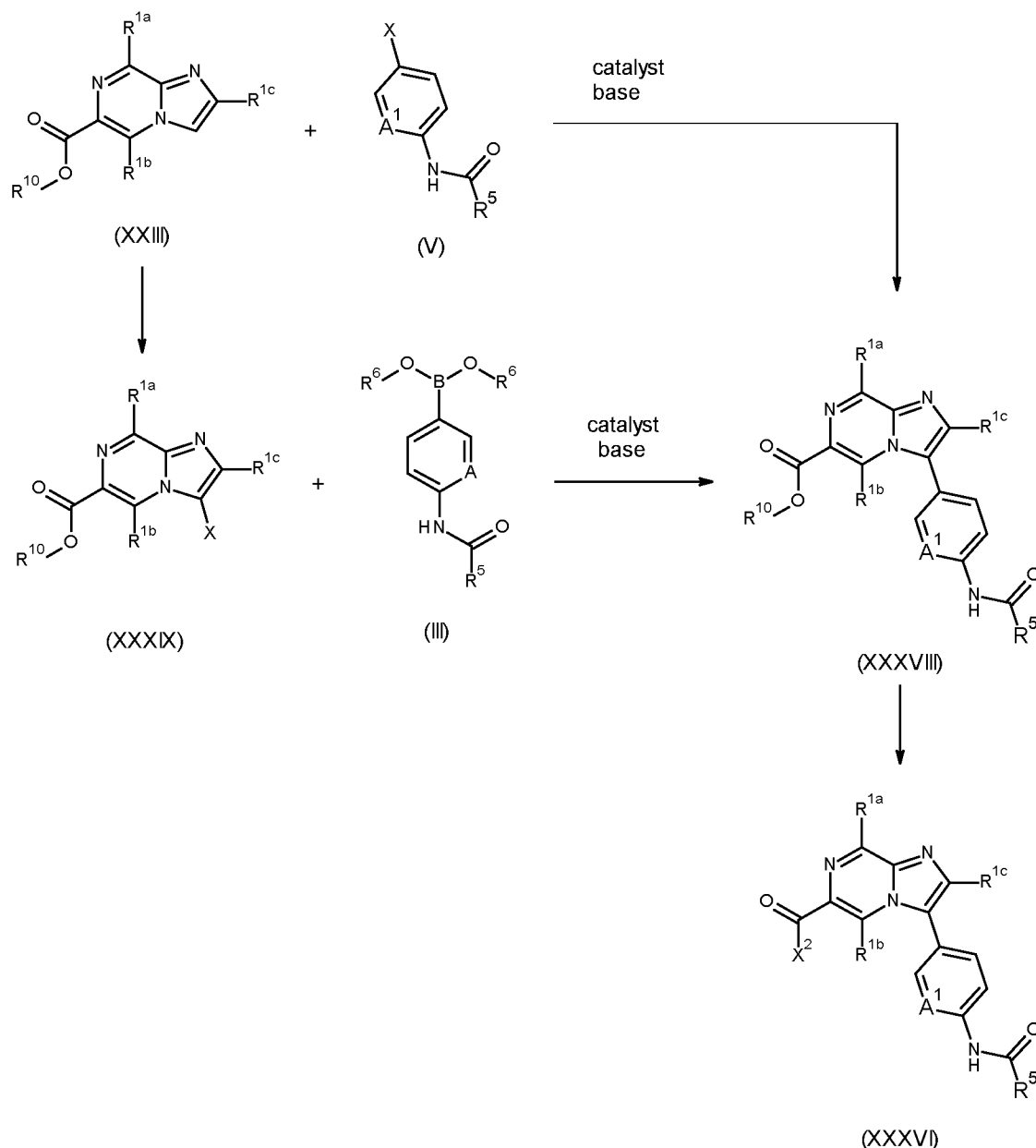
coupling transformation from compounds of formula (XXXVI), wherein X^2 is OH, and amines of formula (X) using the conditions described above. These transformations are depicted in Scheme 13.



Scheme 13

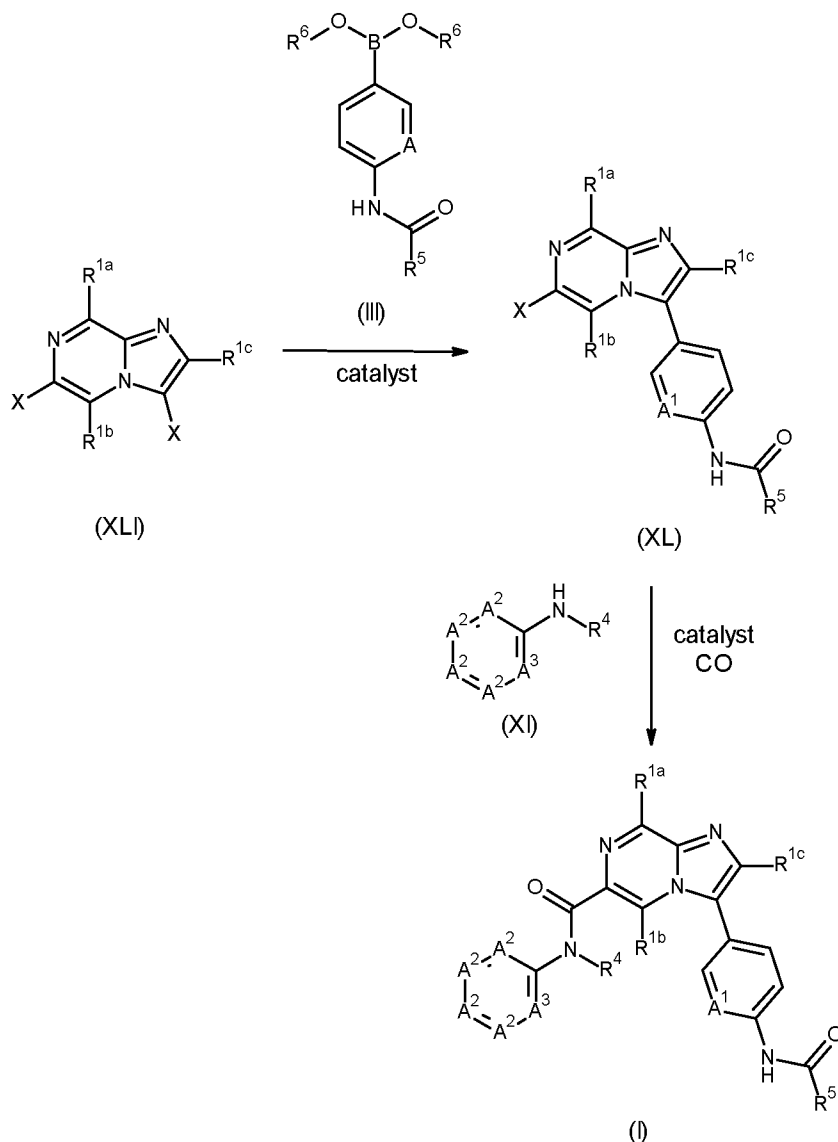
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Compounds of formula (XXXVI), wherein X^2 is OH, can be obtained by hydrolysis of the ester moiety of compounds of formula (XXXVIII), wherein R^{10} is C_{1-6} alkyl. Compounds of formula (XXXVIII), wherein R^{10} is C_{1-6} alkyl, can be prepared by direct arylation of compounds of formula (XXIII), wherein R^{10} is C_{1-6} alkyl, with compounds of formula (V), wherein X is Cl, Br or I, in the presence of a catalyst such as palladium diacetate, a ligand such as triphenylphosphine or (dicyclohexylphosphino)biphenyl, and a base such as cesium carbonate or potassium carbonate. Alternatively, compounds of formula (XXXVIII), wherein R^{10} is C_{1-6} alkyl, can result from a Suzuki cross-coupling reaction between compounds of formula (XXXIX), wherein X is Cl, Br or I, and R^{10} is C_{1-6} alkyl, and compounds of formula (III), wherein either R^6 is independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl, in the presence of a base, such as Cs_2CO_3 , K_2CO_3 or $NaOtBu$, and a suitable palladium catalyst, such as tetrakis(triphenylphosphine)palladium, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), bis(diphenylphosphine)palladium(II) chloride, palladium dichloride or palladium acetate, in a suitable solvent, such as dimethylformamide, dioxane, tetrahydrofuran, ethanol or water. Compounds of formula (XXXIX), wherein X is Cl, Br or I, and R^{10} is C_{1-6} alkyl, can be synthesized by the reaction of a compound of formula (XXIII), wherein R^{10} is C_{1-6} alkyl, and a halogenating agent, such as N-chlorosuccinimide, N-bromosuccinimide, N-iodosuccinimide or bromine in a suitable solvent, such as dichloromethane, chloroform, tetrahydrofuran or acetonitrile. These transformations are depicted in Scheme 14.



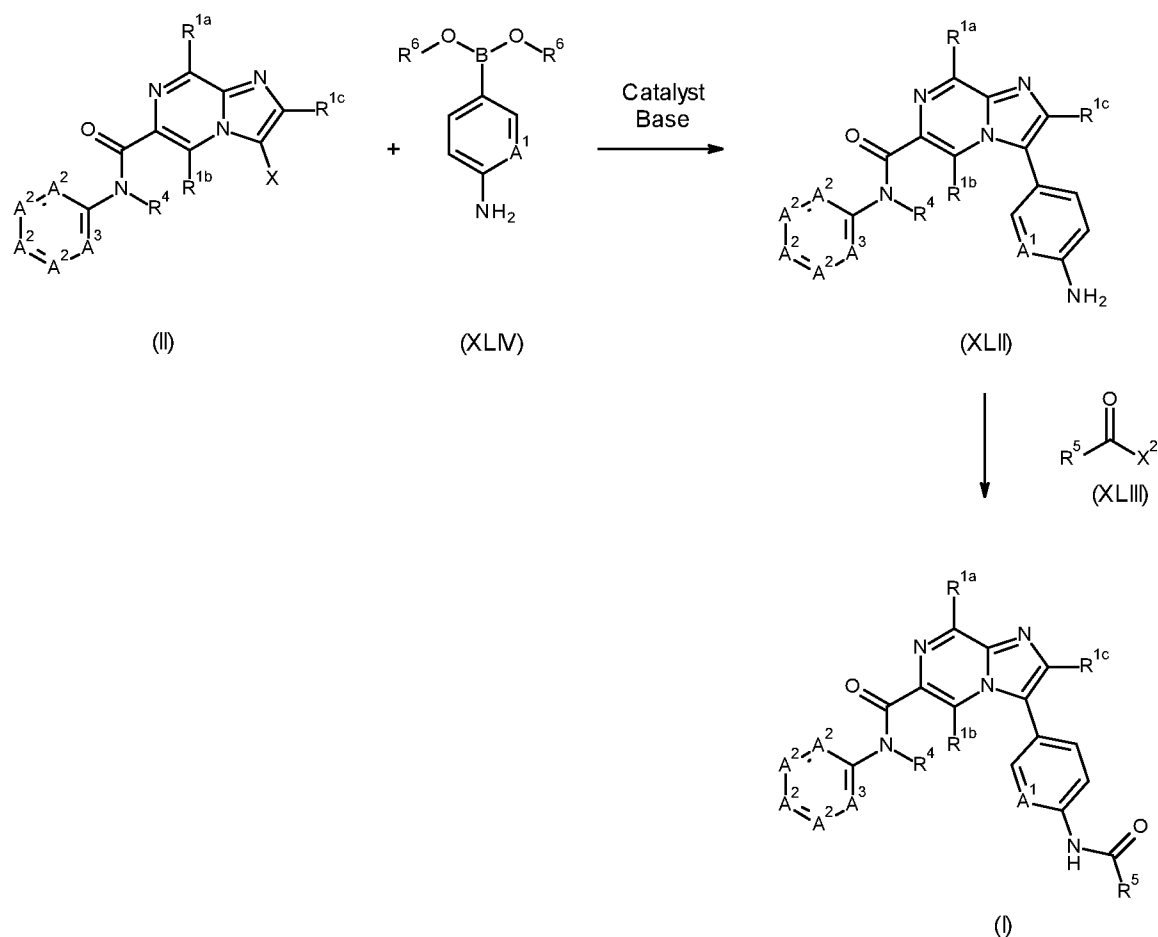
Scheme 14

Alternatively, compounds of formula (I) can be synthesized by reacting compounds of formula (XL),
 5 wherein X is Cl, Br or I, with amines of formula (XI) and carbon monoxide in the presence of a catalyst
 such as [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), and, optionally, a base such as
 triethylamine. Compounds of formula (XL), wherein X is Cl, Br or I, can be prepared from compounds of
 formula (XLI), wherein either X is independently from each other Cl, Br or I, through a Suzuki cross-
 coupling with compounds of formula (III), wherein either R^6 is independently from each other hydrogen,
 10 C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl, in the presence of a base, such as
 CS_2CO_3 , K_2CO_3 or $NaOtBu$, and a suitable palladium catalyst, such as
 tetrakis(triphenylphosphine)palladium, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II),
 bis(diphenylphosphine)palladium(II) chloride, palladium dichloride or palladium acetate, in a suitable
 solvent, such as dimethylformamide, dioxane, tetrahydrofuran, ethanol or water. These transformations
 15 are depicted in Scheme 15.



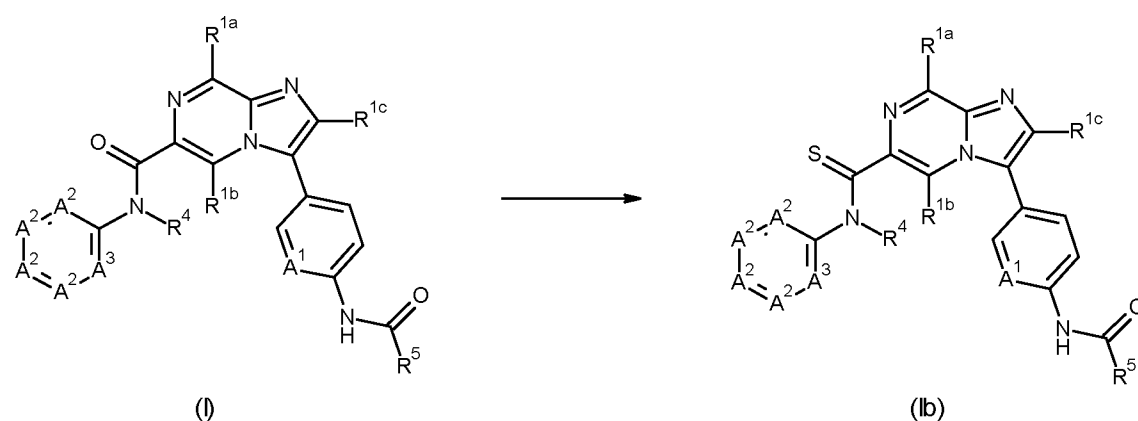
Scheme 15

- 5 Alternatively, compounds of formula (I) can be prepared by the reaction of a compound of formula (XLII) with compounds of formula (XLIII), wherein X^2 is OH, in a peptide-coupling transformation, using the conditions described above. Compounds of formula (XLII) can be prepared via Suzuki cross coupling of a compound of formula (II), wherein X is Cl, Br or I, and a compound of formula (XLIV), wherein either R^6 is independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl, in the presence of a base, such as Cs_2CO_3 , K_2CO_3 or $NaOtBu$, and a suitable palladium catalyst, such as tetrakis(triphenylphosphine)palladium, [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II), bis(diphenylphosphine)palladium(II) chloride, palladium dichloride or palladium acetate, in a suitable solvent, such as dimethylformamide, dioxane, tetrahydrofuran, ethanol or water. Compounds of formula (XLIV), wherein either R^6 is independently from each other hydrogen, C_{1-6} alkyl or wherein two R^6 together can form a C_{3-8} cycloalkyl are prepared by known methods or are commercially available. These transformations are depicted in Scheme 16.



Scheme 16

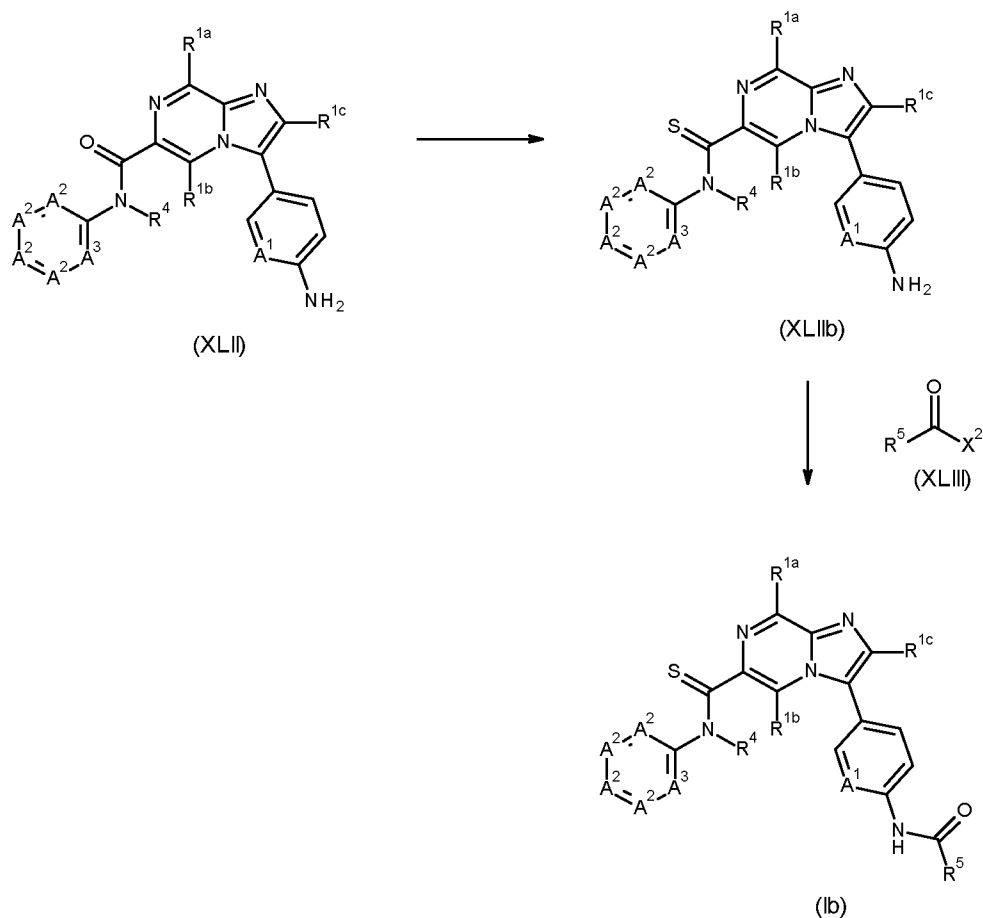
Compounds of formula (Ib), wherein Z is S, can be prepared by the reaction of a compound of formula 5 (I), wherein Z is O, with phosphorus pentasulfide or Lawesson's reagent (CAS: 19172-47-5) in a suitable solvent such as toluene, xylene or dichloromethane. This transformation is depicted in Scheme 17.



Scheme 17

Alternatively, compounds of formula (Ib), wherein Z is S, can be prepared by the reaction of a compound of formula (XLIb) with compounds of formula (XLIII), wherein X^2 is OH, in a peptide-coupling transformation, using the conditions described above. Compounds of formula (XLIb) can be prepared by the reaction of a compound of formula (XLII), with phosphorus pentasulfide or Lawesson's reagent

(CAS: 19172-47-5) in a suitable solvent such as toluene, xylene or dichloromethane. This transformation is depicted in Scheme 18.



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Scheme 18

It is understood by the person skilled in the art that the amide coupling reactions described above between an acid, an amine and a coupling agent could also be performed using the corresponding acid chloride and amine. The transformation of an acid into its corresponding acid chloride is well known by the person skilled in the art.

When the term "compound/compounds according to the invention" is used, then this refers to compounds according to the present invention.

15

Alternatively, the compounds according to the present invention can be obtained by using standard synthesis techniques known to the person skilled in the art. Non-exhaustive examples include oxidation reactions, reduction reactions, hydrolysis reactions, coupling reactions, aromatic nucleophilic or electrophilic substitution reactions, nucleophilic substitution reactions, nucleophilic addition reactions, olefination reactions, oxime formation, alkylation and halogenation reactions.

20

A compound according to the present invention can be converted in a manner known per se into another compound according to the present invention by replacing one or more substituents of the starting compound according to the present invention in the customary manner by (an)other substituent(s) according to the invention.

5

Depending on the choice of the reaction conditions and starting materials which are suitable in each case, it is possible, for example, in one reaction step only to replace one substituent by another substituent according to the invention, or a plurality of substituents can be replaced by other substituents according to the invention in the same reaction step.

10

Salts of the compounds according to the present invention can be prepared in a manner known per se. Thus, for example, acid addition salts of the compounds according to the present invention are obtained by treatment with a suitable acid or a suitable ion exchanger reagent and salts with bases are obtained by treatment with a suitable base or with a suitable ion exchanger reagent.

15

Salts of compounds the compounds according to the present invention can be converted in the customary manner into the free compounds, acid addition salts, for example, by treatment with a suitable basic compound or with a suitable ion exchanger reagent and salts with bases, for example, by treatment with a suitable acid or with a suitable ion exchanger reagent.

20

Salts of the compounds according to the present invention can be converted in a manner known per se into other salts of the compounds according to the present invention, acid addition salts, for example, into other acid addition salts, for example by treatment of a salt of inorganic acid such as hydrochloride with a suitable metal salt such as a sodium, barium or silver salt, of an acid, for example with silver acetate, in a suitable solvent in which an inorganic salt which forms, for example silver chloride, is insoluble and thus precipitates from the reaction mixture.

25

Depending on the procedure or the reaction conditions, the compounds according to the present invention, which have salt-forming properties can be obtained in free form or in the form of salts.

30

The compounds according to the present invention and, where appropriate, the tautomers thereof, in each case in free form or in salt form, can be present in the form of one of the stereoisomers which are possible or as a mixture of these, for example in the form of pure stereoisomers, such as antipodes and/or diastereomers, or as stereoisomer mixtures, such as enantiomer mixtures, for example racemates, diastereomer mixtures or racemate mixtures, depending on the number, absolute and relative configuration of asymmetric carbon atoms which occur in the molecule and/or depending on the configuration of non-aromatic double bonds which occur in the molecule; the invention relates to the pure stereoisomers and also to all stereoisomer mixtures which are possible and is to be understood in each case in this sense hereinabove and hereinbelow, even when stereochemical details are not

40

mentioned specifically in each case.

Diastereomer mixtures or racemate mixtures of the compounds according to the present invention, in free form or in salt form, which can be obtained depending on which starting materials and procedures have been chosen can be separated in a known manner into the pure diastereomers or racemates on the basis of the physicochemical differences of the components, for example by fractional crystallization,
5 distillation and/or chromatography.

Enantiomer mixtures, such as racemates, which can be obtained in a similar manner can be resolved into the optical antipodes by known methods, for example by recrystallization from an optically active solvent, by chromatography on chiral adsorbents, for example high-performance liquid chromatography
10 (HPLC) on acetyl cellulose, with the aid of suitable microorganisms, by cleavage with specific, immobilized enzymes, via the formation of inclusion compounds, for example using chiral crown ethers, where only one enantiomer is complexed, or by conversion into diastereomeric salts, for example by reacting a basic end-product racemate with an optically active acid, such as a carboxylic acid, for example camphor, tartaric or malic acid, or sulfonic acid, for example camphorsulfonic acid, and
15 separating the diastereomer mixture which can be obtained in this manner, for example by fractional crystallization based on their differing solubilities, to give the diastereomers, from which the desired enantiomer can be set free by the action of suitable agents, for example basic agents.

Pure diastereomers or enantiomers can be obtained according to the invention not only by separating
20 suitable stereoisomer mixtures, but also by generally known methods of diastereoselective or enantioselective synthesis, for example by carrying out the process according to the invention with starting materials of a suitable stereochemistry.

N-oxides can be prepared by reacting a compound according to the present invention with a suitable oxidizing agent, for example the H₂O₂/urea adduct in the presence of an acid anhydride, e.g.
25 trifluoroacetic anhydride. Such oxidations are known from the literature, for example from J. Med. Chem., 32 (12), 2561-73, 1989 or WO 00/15615.

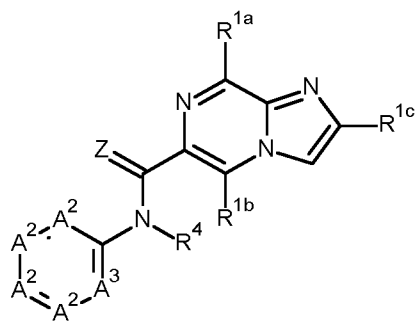
It is advantageous to isolate or synthesize in each case the biologically more effective stereoisomer, for example enantiomer or diastereomer, or stereoisomer mixture, for example enantiomer mixture or diastereomer mixture, if the individual components have a different biological activity.
30 The compounds according to the present invention and, where appropriate, the tautomers thereof, in each case in free form or in salt form, can, if appropriate, also be obtained in the form of hydrates and/or include other solvents, for example those which may have been used for the crystallization of compounds which are present in solid form.

The following Examples illustrate, but do not limit, the invention.
35

The present invention also provides intermediates useful for the preparation of compounds according to the present invention.

The below intermediates form a further aspect of the invention.
40

A compound of formula (IV)



(IV)

wherein Z is O or S, and preferably Z is O;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl,

5 and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

10 A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R² are independently selected

20 from hydrogen, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

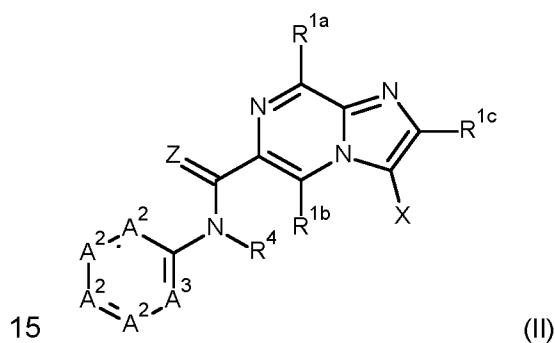
A³ is independently CR³ or N;

R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋

- 6alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN; and preferably R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN; and
- 10 wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; or a salt or N-oxide thereof.

A compound of formula (II)



- wherein Z is O or S, and preferably Z is O;
- R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;
- 20 R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;
- A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;
- 25 R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy;
- 30
- 35

is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

A³ is independently CR³ or N;

R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

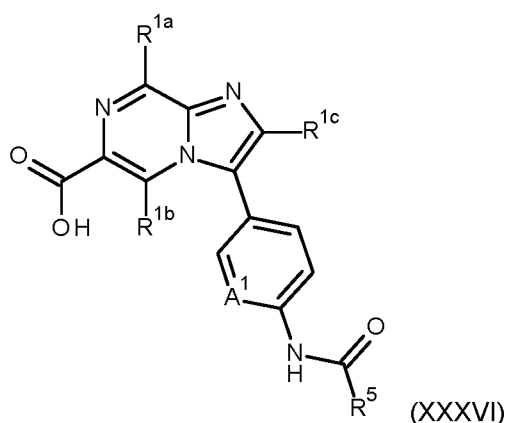
R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN; and preferably R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN;

wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and

X is Cl, Br or I;

or a salt or N-oxide thereof.

A compound of formula (XXXVI)

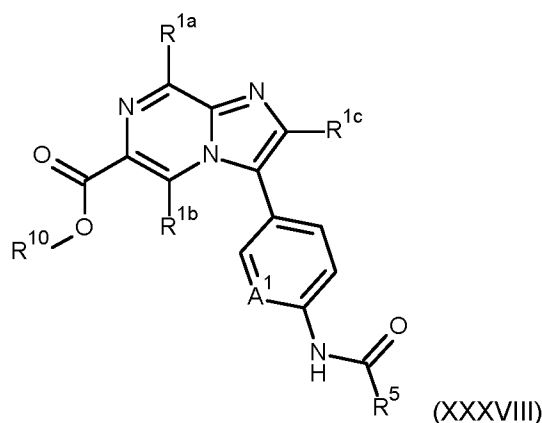


wherein A¹ is CH or N, and preferably N;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;

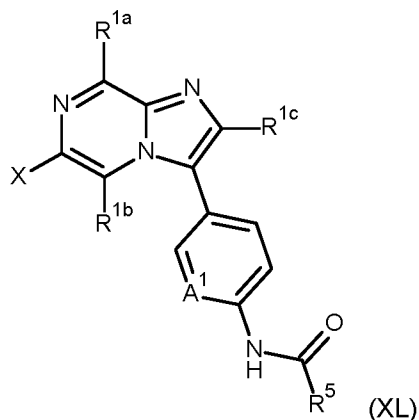
- 5 R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen; and
- R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₁₋₆alkylC₁₋₆alkoxyamino, wherein each of said groups is optionally
- 10 substituted with one to three substituents independently selected from halogen and CN; or a salt or N-oxide thereof.

A compound of formula (XXXVIII)



- 15 wherein A¹ is CH or N, and preferably N;
- R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;
- 20 R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;
- R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₁₋₆alkylC₁₋₆alkoxyamino, wherein each of said groups is optionally
- 25 substituted with one to three substituents independently selected from halogen and CN; and
- R¹⁰ is a C₁₋₆ alkyl; or a salt or N-oxide thereof.

A compound of formula (XL)



wherein A¹ is CH or N, and preferably N;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;

5 and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

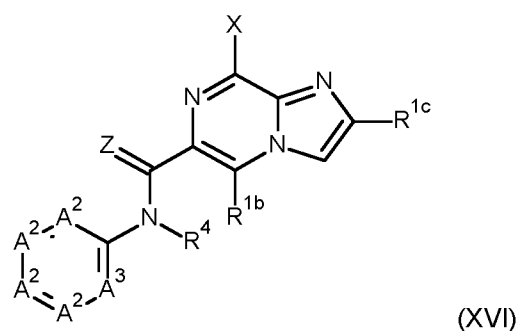
10 R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₁₋₆alkylC₁₋₆alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN; and

X is Cl, Br or I;

or a salt or N-oxide thereof.

15

A compound of formula (XVI)



wherein Z is O or S, and preferably Z is O;

20 R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

25 R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋

- alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R² are independently selected from hydrogen, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;
- 10 A³ is independently CR³ or N;
R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;
- 15 R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN; and preferably R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN;
- 20 wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and
X is Cl, Br or I;
- 25 or a salt or N-oxide thereof.

The compounds of formula (I) as defined in the present invention can be used in the agricultural sector and related fields of use e.g. as active ingredients for controlling plant pathogens or on non-living materials for control of spoilage microorganisms or organisms potentially harmful to man. The novel compounds are distinguished by excellent activity at low rates of application, by being well tolerated by plants and by being environmentally safe. They have very useful curative, preventive and systemic properties and may be used for protecting numerous cultivated plants. The compounds of formula (I) as

defined in the present invention can be used to inhibit or destroy the pathogens that occur on plants or parts of plants (fruit, blossoms, leaves, stems, tubers, roots) of different crops of useful plants, while at the same time protecting also those parts of the plants that grow later e.g. from phytopathogenic microorganisms.

5

It is also possible to use compounds of formula (I) as defined in the present invention as fungicide. The term "fungicide" as used herein means a compound that controls, modifies, or prevents the growth of fungi. The term "fungicidally effective amount" means the quantity of such a compound or combination of such compounds that is capable of producing an effect on the growth of fungi. Controlling or modifying effects include all deviation from natural development, such as killing, retardation and the like, and prevention includes barrier or other defensive formation in or on a plant to prevent fungal infection.

It is also possible to use compounds of formula (I) as defined in the present invention as dressing agents for the treatment of plant propagation material, e.g., seed, such as fruits, tubers or grains, or plant cuttings (for example rice), for the protection against fungal infections as well as against phytopathogenic fungi occurring in the soil. The propagation material can be treated with a composition comprising a compound of formula (I) as defined in the present invention before planting: seed, for example, can be dressed before being sown. The compounds of formula (I) as defined in the present invention can also be applied to grains (coating), either by impregnating the seeds in a liquid formulation or by coating them with a solid formulation. The composition can also be applied to the planting site when the propagation material is being planted, for example, to the seed furrow during sowing. The invention relates also to such methods of treating plant propagation material and to the plant propagation material so treated.

Furthermore the compounds of formula (I) as defined in the present invention can be used for controlling fungi in related areas, for example in the protection of technical materials, including wood and wood related technical products, in food storage, in hygiene management.

In addition, the invention could be used to protect non-living materials from fungal attack, e.g. lumber, wall boards and paint.

Compounds of formula (I) as defined in the present invention and fungicidal compositions containing them may be used to control plant diseases caused by a broad spectrum of fungal plant pathogens. They are effective in controlling a broad spectrum of plant diseases, such as foliar pathogens of ornamental, turf, vegetable, field, cereal, and fruit crops.

These fungi and fungal vectors of disease, as well as phytopathogenic bacteria and viruses, which may be controlled are for example:

Absidia corymbifera, *Alternaria* spp, *Aphanomyces* spp, *Ascochyta* spp, *Aspergillus* spp. including *A. flavus*, *A. fumigatus*, *A. nidulans*, *A. niger*, *A. terreus*, *Aureobasidium* spp. including *A. pullulans*, *Blastomyces dermatitidis*, *Blumeria graminis*, *Bremia lactucae*, *Botryosphaeria* spp. including *B. dothidea*, *B. obtusa*, *Botrytis* spp. including *B. cinerea*, *Candida* spp. including *C. albicans*, *C. glabrata*,

- C. krusei, C. lusitanae, C. parapsilosis, C. tropicalis, Cephaloascus fragrans, Ceratocystis spp, Cercospora spp. including C. arachidicola, Cercosporidium personatum, Cladosporium spp, Claviceps purpurea, Coccidioides immitis, Cochliobolus spp, Colletotrichum spp. including C. musae,
- 5 Cryptococcus neoformans, Diaporthe spp, Didymella spp, Drechslera spp, Elsinoe spp, Epidermophyton spp, Erwinia amylovora, Erysiphe spp. including E. cichoracearum, Eutypa lata, Fusarium spp. including F. culmorum, F. graminearum, F. langsethiae, F. moniliforme, F. oxysporum, F. proliferatum, F. subglutinans, F. solani, Gaeumannomyces graminis, Gibberella fujikuroi, Gloeodes pomigena, Gloeosporium musarum, Glomerella cingulate, Guignardia bidwellii,
- 10 Gymnosporangium juniperi-virginianae, Helminthosporium spp, Hemileia spp, Histoplasma spp. including H. capsulatum, Laetisaria fuciformis, Leptographium lindbergi, Leveillula taurica, Lophodermium seditiosum, Microdochium nivale, Microsporum spp, Monilinia spp, Mucor spp, Mycosphaerella spp. including M. graminicola, M. pomi, Oncobasidium theobromaeon, Ophiostoma piceae, Paracoccidioides spp, Penicillium spp. including P. digitatum, P. italicum, Petriellidium spp,
- 15 Peronosclerospora spp. Including P. maydis, P. philippinensis and P. sorghi, Peronospora spp, Phaeosphaeria nodorum, Phakopsora pachyrhizi, Phellinus igniarius, Phialophora spp, Phoma spp, Phomopsis viticola, Phytophthora spp. including P. infestans, Plasmopara spp. including P. halstedii, P. viticola, Pleospora spp., Podosphaera spp. including P. leucotricha, Polymyxa graminis, Polymyxa betae, Pseudocercospora herpotrichoides, Pseudomonas spp, Pseudoperonospora spp. including P.
- 20 cubensis, P. humuli, Pseudopeziza tracheiphila, Puccinia Spp. including P. hordei, P. recondita, P. striiformis, P. tritici, Pyrenopeziza spp, Pyrenophora spp, Pyricularia spp. including P. oryzae, Pythium spp. including P. ultimum, Ramularia spp, Rhizoctonia spp, Rhizomucor pusillus, Rhizopus arrhizus, Rhynchosporium spp, Scedosporium spp. including S. apiospermum and S. prolificans, Schizothyrium pomi,
- 25 Sclerotinia spp, Sclerotium spp, Septoria spp, including S. nodorum, S. tritici, Sphaerotheca macularis, Sphaerotheca fusca (Sphaerotheca fuliginea), Sporothrix spp, Stagonospora nodorum, Stemphylium spp., Stereum hirsutum, Thanatephorus cucumeris, Thielaviopsis basicola, Tilletia spp, Trichoderma spp. including T. harzianum, T. pseudokoningii, T. viride,
- Trichophyton spp, Typhula spp, Uncinula necator, Urocystis spp, Ustilago spp, Venturia spp. including
- 30 V. inaequalis, Verticillium spp, and Xanthomonas spp.

In particular, compounds of formula (I) as defined in the present invention and fungicidal compositions containing them may be used to control plant diseases caused by a broad spectrum of fungal plant pathogens in the Basidiomycete, Ascomycete, Oomycete and/or Deuteromycete, Blasocladiomycete,

- 35 Chytridiomycete, Glomeromycete and/or Mucoromycete classes. More particularly, the compounds of formula (I) as defined in the present invention may be used to control oomycetes.

These pathogens may include:

- Oomycetes, including Phytophthora diseases such as those caused by *Phytophthora capsici*,
- 40 *Phytophthora infestans*, *Phytophthora sojae*, *Phytophthora fragariae*, *Phytophthora nicotianae*, *Phytophthora cinnamomi*, *Phytophthora citricola*, *Phytophthora citrophthora* and *Phytophthora erythroseptica*; Pythium diseases such as those caused by *Pythium aphanidermatum*, *Pythium*

arrhenomanes, *Pythium graminicola*, *Pythium irregulare*, *Pythium sylvaticum* and *Pythium ultimum*; diseases caused by Peronosporales such as *Peronospora destructor*, *Peronospora parasitica*, *Plasmopara viticola*, *Plasmopara halstedii*, *Pseudoperonospora cubensis*, *Albugo candida*, *Sclerophthora macrospora* and *Bremia lactucae*; and others such as *Aphanomyces cochlioides*,
5 *Labyrinthula zosterae*, *Peronosclerospora sorghi* and *Sclerospora graminicola*.
Ascomycetes, including blotch, spot, blast or blight diseases and/or rots for example those caused by Pleosporales such as *Stemphylium solani*, *Stagonospora tainanensis*, *Spilocaea oleaginea*, *Setosphaeria turcica*, *Pyrenochaeta lycopersici*, *Pleospora herbarum*, *Phoma destructiva*, *Phaeosphaeria herpotrichoides*, *Phaeocryptocus gaeumannii*, *Ophiosphaerella graminicola*,
10 *Ophiobolus graminis*, *Leptosphaeria maculans*, *Hendersonia creberrima*, *Helminthosporium tritici-repentis*, *Setosphaeria turcica*, *Drechslera glycines*, *Didymella bryoniae*, *Cycloconium oleagineum*, *Corynespora cassicola*, *Cochliobolus sativus*, *Bipolaris cactivora*, *Venturia inaequalis*, *Pyrenophora teres*, *Pyrenophora tritici-repentis*, *Alternaria alternata*, *Alternaria brassicicola*, *Alternaria solani* and *Alternaria tomatophila*, Capnodiales such as *Septoria tritici*, *Septoria nodorum*, *Septoria glycines*,
15 *Cercospora arachidicola*, *Cercospora soijina*, *Cercospora zeae-maydis*, *Cercospora capsellae* and *Cercospora herpotrichoides*, *Cladosporium carpophilum*, *Cladosporium effusum*, *Passalora fulva*, *Cladosporium oxysporum*, *Dothistroma septosporium*, *Isariopsis clavispora*, *Mycosphaerella fijiensis*, *Mycosphaerella graminicola*, *Mycovellosiella koepkei*, *Phaeoisariopsis bataticola*, *Pseudocercospora vitis*, *Pseudocercospora herpotrichoides*, *Ramularia beticola*, *Ramularia collo-cygni*, Magnaporthales
20 such as *Gaeumannomyces graminis*, *Magnaporthe grisea*, *Pyricularia oryzae*, Diaporthales such as *Anisogramma anomala*, *Apiognomonina errabunda*, *Cytospora platani*, *Diaporthe phaseolorum*, *Discula destructiva*, *Gnomonia fructicola*, *Greeneria uvicola*, *Melanconium juglandinum*, *Phomopsis viticola*, *Sirococcus clavigignenti-juglandacearum*, *Tubakia dryina*, *Dicarpella* spp., *Valsa ceratosperma*, and others such as *Actinothyrium graminis*, *Ascochyta pisi*, *Aspergillus flavus*, *Aspergillus fumigatus*,
25 *Aspergillus nidulans*, *Asperisporium caricae*, *Blumeriella jaapii*, *Candida* spp., *Capnodium ramosum*, *Cephalosporium* spp., *Cephalosporium gramineum*, *Ceratocystis paradoxa*, *Chaetomium* spp., *Hymenoscyphus pseudoalbidus*, *Coccidioides* spp., *Cylindrosporium padi*, *Diplocarpon malae*, *Drepanopeziza campestris*, *Elsinoe ampelina*, *Epicoecum nigrum*, *Epidermophyton* spp., *Eutypa lata*, *Geotrichum candidum*, *Gibellina cerealis*, *Gloeocercospora sorghi*, *Gloeodes pomigena*, *Gloeosporium*
30 *perennans*, *Gloeotinia temulenta*, *Griphosphaeria corticola*, *Kabatiella lini*, *Leptographium microsporum*, *Leptosphaerulina crassiasca*, *Lophodermium seditiosum*, *Marssonina graminicola*, *Microdochium nivale*, *Monilinia fructicola*, *Monographella albescens*, *Monosporascus cannonballus*, *Naemacyclus* spp., *Ophiostoma novo-ulmi*, *Paracoccidioides brasiliensis*, *Penicillium expansum*, *Pestalotia rhododendri*, *Petriellidium* spp., *Pezicula* spp., *Phialophora gregata*, *Phyllachora pomigena*,
35 *Phymatotrichum omnivora*, *Physalospora abdita*, *Plectosporium tabacinum*, *Polyscytalum pustulans*, *Pseudopeziza medicaginis*, *Pyrenopeziza brassicae*, *Ramulispora sorghi*, *Rhabdocline pseudotsugae*, *Rhynchosporium secalis*, *Sacrocladium oryzae*, *Scedosporium* spp., *Schizothyrium pomi*, *Sclerotinia sclerotiorum*, *Sclerotinia minor*, *Sclerotium* spp., *Typhula ishikariensis*, *Seimatosporium mariae*, *Lepteutypa cupressi*, *Septocytia ruborum*, *Sphaeloma perseae*, *Sporonema phacidoides*, *Stigmia*
40 *palmivora*, *Tapesia yallundae*, *Taphrina bullata*, *Thielviopsis basicola*, *Trichoseptoria fructigena*, *Zygophiala jamaicensis*; powdery mildew diseases for example those caused by Erysiphales such as *Blumeria graminis*, *Erysiphe polygoni*, *Uncinula necator*, *Sphaerotheca fuligena*, *Podosphaera*

leucotricha, *Podospaera macularis* *Golovinomyces cichoracearum*, *Leveillula taurica*, *Microsphaera diffusa*, *Oidiopsis gossypii*, *Phyllactinia guttata* and *Oidium arachidis*; molds for example those caused by Botryosphaerales such as *Dothiorella aromatica*, *Diplodia seriata*, *Guignardia bidwellii*, *Botrytis cinerea*, *Botryotinia allii*, *Botryotinia fabae*, *Fusicoccum amygdali*, *Lasiodiplodia theobromae*,
5 *Macrophoma theicola*, *Macrophomina phaseolina*, *Phyllosticta cucurbitacearum*; anthracnoses for example those caused by Glomerellales such as *Colletotrichum gloeosporioides*, *Colletotrichum lagenarium*, *Colletotrichum gossypii*, *Glomerella cingulata*, and *Colletotrichum graminicola*; and wilts or blights for example those caused by Hypocreales such as *Acremonium strictum*, *Claviceps purpurea*, *Fusarium culmorum*, *Fusarium graminearum*, *Fusarium virguliforme*, *Fusarium oxysporum*, *Fusarium*
10 *subglutinans*, *Fusarium oxysporum* f.sp. *cubense*, *Gerlachia nivale*, *Gibberella fujikuroi*, *Gibberella zeae*, *Gliocladium* spp., *Myrothecium verrucaria*, *Nectria ramulariae*, *Trichoderma viride*, *Trichothecium roseum*, and *Verticillium theobromae*.

Basidiomycetes, including smuts for example those caused by Ustilaginales such as *Ustilagoidea virens*, *Ustilago nuda*, *Ustilago tritici*, *Ustilago zeae*, rusts for example those caused by Pucciniales such
15 as *Cerotelium fici*, *Chrysomyxa arctostaphyli*, *Coleosporium ipomoeae*, *Hemileia vastatrix*, *Puccinia arachidis*, *Puccinia cacabata*, *Puccinia graminis*, *Puccinia recondita*, *Puccinia sorghi*, *Puccinia hordei*, *Puccinia striiformis* f.sp. *Hordei*, *Puccinia striiformis* f.sp. *Secalis*, *Pucciniastrum coryli*, or Uredinales such as *Cronartium ribicola*, *Gymnosporangium juniperi-viginianae*, *Melampsora medusae*, *Phakopsora pachyrhizi*, *Phragmidium mucronatum*, *Physopella ampeloidis*, *Tranzschelia discolor* and *Uromyces*
20 *viciae-fabae*; and other rots and diseases such as those caused by *Cryptococcus* spp., *Exobasidium vexans*, *Marasmiellus inoderma*, *Mycena* spp., *Sphacelotheca reiliana*, *Typhula ishikariensis*, *Urocystis agropyri*, *Uromyces perplexans*, *Corticium invisum*, *Laetisaria fuciformis*, *Waitea circinata*, *Rhizoctonia solani*, *Thanetophorus cucurmeris*, *Entyloma dahliae*, *Entylomella microspora*, *Neovossia molinae* and *Tilletia caries*.

25 Blastocladiomycetes, such as *Physoderma maydis*.

Mucoromycetes, such as *Choanephora cucurbitarum*.; *Mucor* spp.; *Rhizopus arrhizus*.

As well as diseases caused by other species and genera closely related to those listed above.

In addition to their fungicidal activity, the compounds and compositions comprising compounds of
30 formula (I) as defined in the present invention may also have activity against bacteria such as *Erwinia amylovora*, *Erwinia caratovora*, *Xanthomonas campestris*, *Pseudomonas syringae*, *Streptomyces scabies* and other related species as well as certain protozoa.

Within the scope of the present invention, target crops and/or useful plants to be protected typically
35 comprise perennial and annual crops, such as berry plants for example blackberries, blueberries, cranberries, raspberries and strawberries; cereals for example barley, maize (corn), millet, oats, rice, rye, sorghum tritcale and wheat; fibre plants for example cotton, flax, hemp, jute and sisal; field crops for example sugar and fodder beet, coffee, hops, mustard, oilseed rape (canola), poppy, sugar cane, sunflower, tea and tobacco; fruit trees for example apple, apricot, avocado, banana, cherry, citrus,
40 nectarine, peach, pear and plum; grasses for example Bermuda grass, bluegrass, bentgrass, centipede grass, fescue, ryegrass, St. Augustine grass and Zoysia grass; herbs such as basil, borage, chives, coriander, lavender, lovage, mint, oregano, parsley, rosemary, sage and thyme; legumes for example

beans, lentils, peas and soya beans; nuts for example almond, cashew, ground nut, hazelnut, peanut, pecan, pistachio and walnut; palms for example oil palm; ornamentals for example flowers, shrubs and trees; other trees, for example cacao, coconut, olive and rubber; vegetables for example asparagus, aubergine, broccoli, cabbage, carrot, cucumber, garlic, lettuce, marrow, melon, okra, onion, pepper, 5 potato, pumpkin, rhubarb, spinach and tomato; and vines for example grapes.

The useful plants and / or target crops in accordance with the invention include conventional as well as genetically enhanced or engineered varieties such as, for example, insect resistant (e.g. Bt. and VIP varieties) as well as disease resistant, herbicide tolerant (e.g. glyphosate- and glufosinate-resistant 10 maize varieties commercially available under the trade names RoundupReady® and LibertyLink®) and nematode tolerant varieties. By way of example, suitable genetically enhanced or engineered crop varieties include the Stoneville 5599BR cotton and Stoneville 4892BR cotton varieties.

The term "useful plants" and/or "target crops" is to be understood as including also useful plants that 15 have been rendered tolerant to herbicides like bromoxynil or classes of herbicides (such as, for example, HPPD inhibitors, ALS inhibitors, for example primisulfuron, prosulfuron and trifloxysulfuron, EPSPS (5-enol-pyrovyl-shikimate-3-phosphate-synthase) inhibitors, GS (glutamine synthetase) inhibitors or PPO (protoporphyrinogen-oxidase) inhibitors) as a result of conventional methods of breeding or genetic engineering. An example of a crop that has been rendered tolerant to imidazolinones, e.g. imazamox, 20 by conventional methods of breeding (mutagenesis) is Clearfield® summer rape (Canola). Examples of crops that have been rendered tolerant to herbicides or classes of herbicides by genetic engineering methods include glyphosate- and glufosinate-resistant maize varieties commercially available under the trade names RoundupReady®, Herculex I® and LibertyLink®.

25 The term "useful plants" and/or "target crops" is to be understood as including those which naturally are or have been rendered resistant to harmful insects. This includes plants transformed by the use of recombinant DNA techniques, for example, to be capable of synthesising one or more selectively acting toxins, such as are known, for example, from toxin-producing bacteria. Examples of toxins which can be expressed include δ -endotoxins, vegetative insecticidal proteins (Vip), insecticidal proteins of 30 bacteria colonising nematodes, and toxins produced by scorpions, arachnids, wasps and fungi. An example of a crop that has been modified to express the *Bacillus thuringiensis* toxin is the Bt maize KnockOut® (Syngenta Seeds). An example of a crop comprising more than one gene that codes for insecticidal resistance and thus expresses more than one toxin is VipCot® (Syngenta Seeds). Crops or seed material thereof can also be resistant to multiple types of pests (so-called stacked transgenic 35 events when created by genetic modification). For example, a plant can have the ability to express an insecticidal protein while at the same time being herbicide tolerant, for example Herculex I® (Dow AgroSciences, Pioneer Hi-Bred International).

The term "useful plants" and/or "target crops" is to be understood as including also useful plants which 40 have been so transformed by the use of recombinant DNA techniques that they are capable of synthesising antipathogenic substances having a selective action, such as, for example, the so-called

"pathogenesis-related proteins" (PRPs, see e.g. EP-A-0 392 225). Examples of such antipathogenic substances and transgenic plants capable of synthesising such antipathogenic substances are known, for example, from EP-A-0 392 225, WO 95/33818, and EP-A-0 353 191. The methods of producing such transgenic plants are generally known to the person skilled in the art and are described, for example, in
5 the publications mentioned above.

Toxins that can be expressed by transgenic plants include, for example, insecticidal proteins from *Bacillus cereus* or *Bacillus popilliae*; or insecticidal proteins from *Bacillus thuringiensis*, such as δ -endotoxins, e.g. Cry1Ab, Cry1Ac, Cry1F, Cry1Fa2, Cry2Ab, Cry3A, Cry3Bb1 or Cry9C, or vegetative
10 insecticidal proteins (Vip), e.g. Vip1, Vip2, Vip3 or Vip3A; or insecticidal proteins of bacteria colonising nematodes, for example *Photorhabdus* spp. or *Xenorhabdus* spp., such as *Photorhabdus luminescens*, *Xenorhabdus nematophilus*; toxins produced by animals, such as scorpion toxins, arachnid toxins, wasp toxins and other insect-specific neurotoxins; toxins produced by fungi, such as *Streptomyces* toxins, plant lectins, such as pea lectins, barley lectins or snowdrop lectins; agglutinins; proteinase inhibitors,
15 such as trypsin inhibitors, serine protease inhibitors, patatin, cystatin, papain inhibitors; ribosome-inactivating proteins (RIP), such as ricin, maize-RIP, abrin, luffin, saporin or bryodin; steroid metabolism enzymes, such as 3-hydroxysteroidoxidase, ecdysteroid-UDP-glycosyl-transferase, cholesterol oxidases, ecdysone inhibitors, HMG-COA-reductase, ion channel blockers, such as blockers of sodium or calcium channels, juvenile hormone esterase, diuretic hormone receptors, stilbene synthase, bibenzyl
20 synthase, chitinases and glucanases.

Further, in the context of the present invention there are to be understood by δ -endotoxins, for example Cry1Ab, Cry1Ac, Cry1F, Cry1Fa2, Cry2Ab, Cry3A, Cry3Bb1 or Cry9C, or vegetative insecticidal proteins (Vip), for example Vip1, Vip2, Vip3 or Vip3A, expressly also hybrid toxins, truncated toxins and modified
25 toxins. Hybrid toxins are produced recombinantly by a new combination of different domains of those proteins (see, for example, WO 02/15701). Truncated toxins, for example a truncated Cry1Ab, are known. In the case of modified toxins, one or more amino acids of the naturally occurring toxin are replaced. In such amino acid replacements, preferably non-naturally present protease recognition sequences are inserted into the toxin, such as, for example, in the case of Cry3A055, a cathepsin-G-
30 recognition sequence is inserted into a Cry3A toxin (see WO03/018810).

More examples of such toxins or transgenic plants capable of synthesising such toxins are disclosed, for example, in EP-A-0 374 753, WO93/07278, WO95/34656, EP-A-0 427 529, EP-A-451 878 and WO03/052073.

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The processes for the preparation of such transgenic plants are generally known to the person skilled in the art and are described, for example, in the publications mentioned above. CryI-type deoxyribonucleic acids and their preparation are known, for example, from WO 95/34656, EP-A-0 367 474, EP-A-0 401 979 and WO 90/13651.

40

The toxin contained in the transgenic plants imparts to the plants tolerance to harmful insects. Such insects can occur in any taxonomic group of insects, but are especially commonly found in the beetles (Coleoptera), two-winged insects (Diptera) and butterflies (Lepidoptera).

5 Transgenic plants containing one or more genes that code for an insecticidal resistance and express one or more toxins are known and some of them are commercially available. Examples of such plants are: YieldGard® (maize variety that expresses a Cry1Ab toxin); YieldGard Rootworm® (maize variety that expresses a Cry3Bb1 toxin); YieldGard Plus® (maize variety that expresses a Cry1Ab and a Cry3Bb1 toxin); Starlink® (maize variety that expresses a Cry9C toxin); Herculex I® (maize variety that
10 expresses a Cry1Fa2 toxin and the enzyme phosphinothricine N-acetyltransferase (PAT) to achieve tolerance to the herbicide glufosinate ammonium); NuCOTN 33B® (cotton variety that expresses a Cry1Ac toxin); Bollgard I® (cotton variety that expresses a Cry1Ac toxin); Bollgard II® (cotton variety that expresses a Cry1Ac and a Cry2Ab toxin); VipCot® (cotton variety that expresses a Vip3A and a Cry1Ab toxin); NewLeaf® (potato variety that expresses a Cry3A toxin); NatureGard®, Agrisure® GT
15 Advantage (GA21 glyphosate-tolerant trait), Agrisure® CB Advantage (Bt11 corn borer (CB) trait) and Protecta®.

Further examples of such transgenic crops are:

1. **Bt11 Maize** from Syngenta Seeds SAS, Chemin de l'Hobit 27, F-31 790 St. Sauveur, France,
20 registration number C/FR/96/05/10. Genetically modified *Zea mays* which has been rendered resistant to attack by the European corn borer (*Ostrinia nubilalis* and *Sesamia nonagrioides*) by transgenic expression of a truncated Cry1Ab toxin. Bt11 maize also transgenically expresses the enzyme PAT to achieve tolerance to the herbicide glufosinate ammonium.
2. **Bt176 Maize** from Syngenta Seeds SAS, Chemin de l'Hobit 27, F-31 790 St. Sauveur, France,
25 registration number C/FR/96/05/10. Genetically modified *Zea mays* which has been rendered resistant to attack by the European corn borer (*Ostrinia nubilalis* and *Sesamia nonagrioides*) by transgenic expression of a Cry1Ab toxin. Bt176 maize also transgenically expresses the enzyme PAT to achieve tolerance to the herbicide glufosinate ammonium.
3. **MIR604 Maize** from Syngenta Seeds SAS, Chemin de l'Hobit 27, F-31 790 St. Sauveur, France,
30 registration number C/FR/96/05/10. Maize which has been rendered insect-resistant by transgenic expression of a modified Cry3A toxin. This toxin is Cry3A055 modified by insertion of a cathepsin-G-protease recognition sequence. The preparation of such transgenic maize plants is described in WO 03/018810.
4. **MON 863 Maize** from Monsanto Europe S.A. 270-272 Avenue de Tervuren, B-1150 Brussels,
35 Belgium, registration number C/DE/02/9. MON 863 expresses a Cry3Bb1 toxin and has resistance to certain Coleoptera insects.
5. **IPC 531 Cotton** from Monsanto Europe S.A. 270-272 Avenue de Tervuren, B-1150 Brussels, Belgium, registration number C/ES/96/02.
6. **1507 Maize** from Pioneer Overseas Corporation, Avenue Tedesco, 7 B-1160 Brussels, Belgium,
40 registration number C/NL/00/10. Genetically modified maize for the expression of the protein Cry1F for

achieving resistance to certain Lepidoptera insects and of the PAT protein for achieving tolerance to the herbicide glufosinate ammonium.

7. **NK603 × MON 810 Maize** from Monsanto Europe S.A. 270-272 Avenue de Tervuren, B-1150 Brussels, Belgium, registration number C/GB/02/M3/03. Consists of conventionally bred hybrid maize varieties by crossing the genetically modified varieties NK603 and MON 810. NK603 × MON 810 Maize transgenically expresses the protein CP4 EPSPS, obtained from *Agrobacterium* sp. strain CP4, which imparts tolerance to the herbicide Roundup® (contains glyphosate), and also a Cry1Ab toxin obtained from *Bacillus thuringiensis subsp. kurstaki* which brings about tolerance to certain Lepidoptera, include the European corn borer.

10

The term "locus" as used herein means fields in or on which plants are growing, or where seeds of cultivated plants are sown, or where seed will be placed into the soil. It includes soil, seeds, and seedlings, as well as established vegetation.

15 The term "plants" refers to all physical parts of a plant, including seeds, seedlings, saplings, roots, tubers, stems, stalks, foliage, and fruits.

The term "plant propagation material" is understood to denote generative parts of the plant, such as seeds, which can be used for the multiplication of the latter, and vegetative material, such as cuttings or tubers, for example potatoes. There may be mentioned for example seeds (in the strict sense), roots, fruits, tubers, bulbs, rhizomes and parts of plants. Germinated plants and young plants which are to be transplanted after germination or after emergence from the soil, may also be mentioned. These young plants may be protected before transplantation by a total or partial treatment by immersion. Preferably "plant propagation material" is understood to denote seeds.

25 Pesticidal agents referred to herein using their common name are known, for example, from "The Pesticide Manual", 19th Ed., British Crop Protection Council 2021.

The compounds of formula (I) as defined in the present invention may be used in unmodified form or, preferably, together with the adjuvants conventionally employed in the art of formulation. To this end they may be conveniently formulated in known manner to emulsifiable concentrates, coatable pastes, directly sprayable or dilutable solutions or suspensions, dilute emulsions, wettable powders, soluble powders, dusts, granulates, and also encapsulations e.g. in polymeric substances. As with the type of the compositions, the methods of application, such as spraying, atomising, dusting, scattering, coating or pouring, are chosen in accordance with the intended objectives and the prevailing circumstances.

35 The compositions may also contain further adjuvants such as stabilizers, antifoams, viscosity regulators, binders or tackifiers as well as fertilizers, micronutrient donors or other formulations for obtaining special effects.

Suitable carriers and/or adjuvants, e.g. for agricultural use, can be solid or liquid and are substances useful in formulation technology, e.g. natural or regenerated mineral substances, solvents, dispersants, wetting agents, tackifiers, thickeners, binders or fertilizers. Such carriers are for example described in WO 97/33890.

40

Suspension concentrates are aqueous formulations in which finely divided solid particles of the active compound are suspended. Such formulations include anti-settling agents and dispersing agents and may further include a wetting agent to enhance activity as well an anti-foam and a crystal growth inhibitor. In use, these concentrates are diluted in water and normally applied as a spray to the area to be treated. The amount of active ingredient may range from 0.5% to 95% of the concentrate.

Wettable powders are in the form of finely divided particles which disperse readily in water or other liquid carriers. The particles contain the active ingredient retained in a solid matrix. Typical solid matrices include fuller's earth, kaolin clays, silicas and other readily wet organic or inorganic solids. Wettable powders normally contain from 5% to 95% of the active ingredient plus a small amount of wetting, dispersing or emulsifying agent.

Emulsifiable concentrates are homogeneous liquid compositions dispersible in water or other liquid and may consist entirely of the active compound with a liquid or solid emulsifying agent, or may also contain a liquid carrier, such as xylene, heavy aromatic naphthas, isophorone and other non-volatile organic solvents. In use, these concentrates are dispersed in water or other liquid and normally applied as a spray to the area to be treated. The amount of active ingredient may range from 0.5% to 95% of the concentrate.

Granular formulations include both extrudates and relatively coarse particles and are usually applied without dilution to the area in which treatment is required. Typical carriers for granular formulations include sand, fuller's earth, attapulgite clay, bentonite clays, montmorillonite clay, vermiculite, perlite, calcium carbonate, brick, pumice, pyrophyllite, kaolin, dolomite, plaster, wood flour, ground corn cobs, ground peanut hulls, sugars, sodium chloride, sodium sulphate, sodium silicate, sodium borate, magnesia, mica, iron oxide, zinc oxide, titanium oxide, antimony oxide, cryolite, gypsum, diatomaceous earth, calcium sulphate and other organic or inorganic materials which absorb or which can be coated with the active compound. Granular formulations normally contain 5% to 25% of active ingredients which may include surface-active agents such as heavy aromatic naphthas, kerosene and other petroleum fractions, or vegetable oils; and/or stickers such as dextrans, glue or synthetic resins.

Dusts are free-flowing admixtures of the active ingredient with finely divided solids such as talc, clays, flours and other organic and inorganic solids which act as dispersants and carriers.

Microcapsules are typically droplets or granules of the active ingredient enclosed in an inert porous shell which allows escape of the enclosed material to the surroundings at controlled rates. Encapsulated droplets are typically 1 to 50 microns in diameter. The enclosed liquid typically constitutes 50 to 95% of the weight of the capsule and may include solvent in addition to the active compound. Encapsulated granules are generally porous granules with porous membranes sealing the granule pore openings, retaining the active species in liquid form inside the granule pores. Granules typically range from 1 millimetre to 1 centimetre and preferably 1 to 2 millimetres in diameter. Granules are formed by extrusion, agglomeration or prilling, or are naturally occurring. Examples of such materials are

vermiculite, sintered clay, kaolin, attapulgite clay, sawdust and granular carbon. Shell or membrane materials include natural and synthetic rubbers, cellulosic materials, styrene-butadiene copolymers, polyacrylonitriles, polyacrylates, polyesters, polyamides, polyureas, polyurethanes and starch xanthates.

5

Other useful formulations for agrochemical applications include simple solutions of the active ingredient in a solvent in which it is completely soluble at the desired concentration, such as acetone, alkylated naphthalenes, xylene and other organic solvents. Pressurised sprayers, wherein the active ingredient is dispersed in finely-divided form as a result of vaporisation of a low boiling dispersant solvent carrier, may also be used.

10

Suitable agricultural adjuvants and/or carriers that are useful in formulating the compositions of the invention in the formulation types described above are well known to those skilled in the art.

15 Liquid carriers that can be employed include, for example, water, toluene, xylene, petroleum naphtha, crop oil, acetone, methyl ethyl ketone, cyclohexanone, acetic anhydride, acetonitrile, acetophenone, amyl acetate, 2-butanone, chlorobenzene, cyclohexane, cyclohexanol, alkyl acetates, diacetonalcohol, 1,2-dichloropropane, diethanolamine, p-diethylbenzene, diethylene glycol, diethylene glycol abietate, diethylene glycol butyl ether, diethylene glycol ethyl ether, diethylene glycol methyl ether, N,N-dimethyl
20 formamide, dimethyl sulfoxide, 1,4-dioxane, dipropylene glycol, dipropylene glycol methyl ether, dipropylene glycol dibenzoate, diproxitol, alkyl pyrrolidinone, ethyl acetate, 2-ethyl hexanol, ethylene carbonate, 1,1,1-trichloroethane, 2-heptanone, alpha pinene, d-limonene, ethylene glycol, ethylene glycol butyl ether, ethylene glycol methyl ether, gamma-butyrolactone, glycerol, glycerol diacetate, glycerol monoacetate, glycerol triacetate, hexadecane, hexylene glycol, isoamyl acetate, isobornyl
25 acetate, isooctane, isophorone, isopropyl benzene, isopropyl myristate, lactic acid, laurylamine, mesityl oxide, methoxy-propanol, methyl isoamyl ketone, methyl isobutyl ketone, methyl laurate, methyl octanoate, methyl oleate, methylene chloride, m-xylene, n-hexane, n-octylamine, octadecanoic acid, octyl amine acetate, oleic acid, oleylamine, o-xylene, phenol, polyethylene glycol (PEG400), propionic acid, propylene glycol, propylene glycol monomethyl ether, p-xylene, toluene, triethyl phosphate,
30 triethylene glycol, xylene sulfonic acid, paraffin, mineral oil, trichloroethylene, perchloroethylene, ethyl acetate, amyl acetate, butyl acetate, methanol, ethanol, isopropanol, and higher molecular weight alcohols such as amyl alcohol, tetrahydrofurfuryl alcohol, hexanol, octanol, etc., ethylene glycol, propylene glycol, glycerine and N-methyl-2-pyrrolidinone. Water is generally the carrier of choice for the dilution of concentrates.

35

Suitable solid carriers include, for example, talc, titanium dioxide, pyrophyllite clay, silica, attapulgite clay, kieselguhr, chalk, diatomaceous earth, lime, calcium carbonate, bentonite clay, fuller's earth, cotton seed hulls, wheat flour, soybean flour, pumice, wood flour, walnut shell flour and lignin.

40 A broad range of surface-active agents are advantageously employed in both said liquid and solid compositions, especially those designed to be diluted with carrier before application. These agents, when used, normally comprise from 0.1% to 15% by weight of the formulation. They can be anionic,

cationic, non-ionic or polymeric in character and can be employed as emulsifying agents, wetting agents, suspending agents or for other purposes. Typical surface active agents include salts of alkyl sulfates, such as diethanolammonium lauryl sulphate; alkylarylsulfonate salts, such as calcium dodecylbenzenesulfonate; alkylphenol-alkylene oxide addition products, such as nonylphenol-C.sub. 18
5 ethoxylate; alcohol-alkylene oxide addition products, such as tridecyl alcohol-C.sub. 16 ethoxylate; soaps, such as sodium stearate; alkylnaphthalenesulfonate salts, such as sodium dibutylnaphthalenesulfonate; dialkyl esters of sulfosuccinate salts, such as sodium di(2-ethylhexyl) sulfosuccinate; sorbitol esters, such as sorbitol oleate; quaternary amines, such as lauryl trimethylammonium chloride; polyethylene glycol esters of fatty acids, such as polyethylene glycol
10 stearate; block copolymers of ethylene oxide and propylene oxide; and salts of mono and dialkyl phosphate esters.

Other adjuvants commonly utilized in agricultural compositions include crystallisation inhibitors, viscosity modifiers, suspending agents, spray droplet modifiers, pigments, antioxidants, foaming agents, anti-
15 foaming agents, light-blocking agents, compatibilizing agents, antifoam agents, sequestering agents, neutralising agents and buffers, corrosion inhibitors, dyes, odorants, spreading agents, penetration aids, micronutrients, emollients, lubricants and sticking agents.

In addition, further, other biocidally active ingredients or compositions may be combined with the
20 compositions of the invention and used in the methods of the invention and applied simultaneously or sequentially with the compositions of the invention. When applied simultaneously, these further active ingredients may be formulated together with the compositions of the invention or mixed in, for example, the spray tank. These further biocidally active ingredients may be fungicides, herbicides, insecticides, bactericides, acaricides, nematocides, plant growth regulators, and/or biologicals.

25 The following combinations of a compound of formula I with another active substance in a weight ratio of 1:1 are preferred (where the abbreviation "TX" means "one compound selected from the compounds defined in the Tables 1.1 to 1.297 and Table A):

(7E,9Z)-dodeca-7,9-dien-1-yl acetate + TX, (9Z,11E)-tetradeca-9,11-dien-1-yl acetate + TX, (9Z,12E)-tetradeca-9,12-dien-1-yl acetate + TX, (E)-6-methylhept-2-en-4-ol + TX, (E)-dec-5-en-1-yl acetate with (E)-dec-5-en-1-ol + TX, (E)-tridec-4-en-1-yl acetate + TX, (E,Z)-tetradeca-4,10-dien-1-yl acetate + TX, (Z)-dodec-7-en-1-yl acetate + TX, (Z)-hexadec-11-en-1-yl acetate + TX, (Z)-hexadec-11-enal + TX, (Z)-hexadec-13-en-11-yn-1-yl acetate + TX, (Z)-icos-13-en-10-one + TX, (Z)-tetradec-7-en-1-yl acetate + TX, (Z)-tetradec-9-en-1-yl acetate + TX, 1,2-dibromo-3-chloropropane + TX, 1,2-dichloropropane + TX, 1,2-dichloropropane with 1,3-dichloropropene + TX, 1,3-dichloropropene + TX, 14-methyloctadec-1-ene + TX, 1-hydroxy-1H-pyridine-2-thione + TX, 2-(octylthio)ethanol + TX, 2-chlorophenyl N-methylcarbamate (CPMC) + TX, 3-(4-chlorophenyl)-5-methylrhodanine + TX, 3,4-dichlorotetrahydrothiophene 1,1-dioxide + TX, 4-(quinoxalin-2-ylamino)benzenesulfonamide + TX, 4-methylnonan-5-ol with 4-methylnonan-5-one + TX, 5-methyl-6-thioxo-1,3,5-thiadiazinan-3-ylacetic acid + TX, 6-isopentenylaminopurine + TX, 8-hydroxyquinoline sulfate + TX, abamectin + TX, acequinocyl + TX, acetamiprid + TX, acetoprole + TX, acrinathrin + TX, acynonapyr + TX, Adoxophyes orana GV + TX, afidopyropen + TX, afoxolaner + TX, Agrobacterium radiobacter + TX, AKD-3088 + TX, alanycarb

+ TX, aldicarb + TX, aldoxycarb + TX, allethrin + TX, alpha-cypermethrin + TX, alphamethrin + TX, alpha-multistriatin + TX, Amblyseius spp. + TX, amidoflumet + TX, amino acids + TX, aminocarb + TX, Anagrapta falcifera NPV + TX, Anagrus atomus + TX, Aphelinus abdominalis + TX, Aphidius colemani + TX, Aphidoletes aphidimyza + TX, apholate + TX, Autographa californica NPV + TX, AZ 60541 + TX, azadirachtin + TX, azocyclotin + TX, Bacillus aizawai + TX, Bacillus chitosporus AQ746 (NRRL Accession No B-21 618) + TX, Bacillus firmus + TX, Bacillus kurstaki + TX, Bacillus mycoides AQ726 (NRRL Accession No. B-21664) + TX, Bacillus pumilus (NRRL Accession No B-30087) + TX, Bacillus pumilus AQ717 (NRRL Accession No. B-21662) + TX, Bacillus sp. AQ175 (ATCC Accession No. 55608) + TX, Bacillus sp. AQ177 (ATCC Accession No. 55609) + TX, Bacillus sp. AQ178 (ATCC Accession No. 53522) + TX, Bacillus sphaericus Neide + TX, Bacillus subtilis AQ153 (ATCC Accession No. 55614) + TX, Bacillus subtilis AQ30002 (NRRL Accession No. B-50421) + TX, Bacillus subtilis AQ30004 (NRRL Accession No. B- 50455) + TX, Bacillus subtilis AQ713 (NRRL Accession No. B-21661) + TX, Bacillus subtilis AQ743 (NRRL Accession No. B-21665) + TX, Bacillus subtilis unspecified + TX, Bacillus thuringiensis AQ52 (NRRL Accession No. B-21619) + TX, Bacillus thuringiensis BD#32 (NRRL Accession No B-21530) + TX, Bacillus thuringiensis Berliner + TX, Bacillus thuringiensis subsp. Aizawai + TX, Bacillus thuringiensis subsp. Israelensis + TX, Bacillus thuringiensis subsp. Japonensis + TX, Bacillus thuringiensis subsp. Kurstaki + TX, Bacillus thuringiensis subsp. Tenebrionis + TX, Bacillus thuringiensis subspec. kurstaki BMP 123 + TX, Beauveria bassiana + TX, Beauveria brongniartii + TX, benclothiaz + TX, benomyl + TX, bensultap + TX, benzoximate + TX, benzpyrimoxan + TX, betacyfluthrin + TX, beta-cypermethrin + TX, bethoxazin + TX, bifenazate + TX, bifenthrin + TX, binapacryl + TX, bioallethrin + TX, bioresmethrin + TX, bis(tributyltin) oxide + TX, bisazir + TX, bistrifluron + TX, bisulflufen + TX, brevicomin + TX, broflanilide + TX, brofluthrin + TX, bromoacetamide + TX, bromophos-ethyl + TX, bronopol + TX, busulfan + TX, butocarboxim + TX, butopyronoxyl + TX, butoxy(polypropylene glycol) + TX, butylpyridaben + TX, cadusafos + TX, calcium arsenate + TX, carbaryl + TX, carbofuran + TX, carbon disulfide + TX, carbosulfan + TX, cartap + TX, CAS number: 1594624-87-9 + TX, CAS number: 1922957-47-8 + TX, CAS number: 1255091-74-7 + TX, CAS number: 1365070-72-9 + TX, CAS number: 1445683-71-5 + TX, CAS number: 1445684-82-1 + TX, CAS number: 1594626-19-3 + TX, CAS number: 1594637-65-6 + TX, CAS number: 1632218-00-8 + TX, CAS number: 1808115-49-2 + TX, CAS number: 1922957-46-7 + TX, CAS number: 1922957-48-9 + TX, CAS number: 1956329-03-5 + TX, CAS number: 1990457-52-7 + TX, CAS number: 1990457-55-0 + TX, CAS number: 1990457-57-2 + TX, CAS number: 1990457-66-3 + TX, CAS number: 1990457-77-6 + TX, CAS number: 1990457-85-6 + TX, CAS number: 2032403-97-5 + TX, CAS number: 2044701-44-0 + TX, CAS number: 2095470-94-1 + TX, CAS Number: 2128706-04-5 + TX, CAS number: 2128706-05-6 + TX, CAS number: 2133042-31-4 + TX, CAS number: 2133042-44-9 + TX, CAS number: 2171099-09-3 + TX, CAS number: 2220132-55-6 + TX, CAS number: 2396747-83-2 + TX, CAS number: 2408220-91-5 + TX, CAS number: 2408220-94-8 + TX, CAS number: 2415706-16-8 + TX, Piperflanilide (CAS number: 2615135-05-0) + TX, CAS number: 2719848-60-7 + TX, CAS number: RNA (Leptinotarsa decemlineata-specific recombinant double-stranded interfering GS2) + TX, chlorantraniliprole + TX, chlordane + TX, chlorfenapyr + TX, chloropicrin + TX, chloroprallethrin + TX, chlorpyrifos + TX, chromafenozide + TX, Chrysoperla carnea + TX, clenpirin + TX, cloethocarb + TX, clothianidin + TX, codlelure + TX, codlemone + TX, copper acetoarsenite + TX, copper dioctanoate + TX, copper hydroxide + TX, copper sulfate + TX, cresol + TX, cruformate + TX, Cryptolaemus

montrouzieri + TX, cuelure + TX, cyanofenphos + TX, cyantraniliprole + TX, cybutryne + TX, cyclaniliprole + TX, cyclobutrifluram + TX, cycloprothrin + TX, cycloxaprid + TX, Cydia pomonella GV + TX, cyenopyrafen + TX, cyetpyrafen + TX, cyflumetofen + TX, cyfluthrin + TX, cyhalodiamide + TX, cylohalothrin + TX, cypermethrin + TX, cyphenothrin + TX, cyproflanilide + TX, cyromazine + TX, cytokinins + TX, Dacnusa sibirica + TX, dazomet + TX, DBCP + TX, DCIP + TX, deltamethrin + TX, diafenthiuron + TX, dialifos + TX, diamidafos + TX, dibrom + TX, dibutyl adipate + TX, dibutyl phthalate + TX, dibutyl succinate + TX, dichlofenthion + TX, dichlone + TX, dichlorophen + TX, dicliphos + TX, dicloromezotiaz + TX, diethyltoluamide + TX, diflubenzuron + TX, Diglyphus isaea + TX, dimatif + TX, dimethoate + TX, dimethyl carbate + TX, dimethyl phthalate + TX, dimpropyridaz + TX, dinactin + TX, dinocap + TX, dinotefuran + TX, dioxabenzofos + TX, dipyrithione + TX, disparlure + TX, D-limonene + TX, dodec-8-en-1-yl acetate + TX, dodec-9-en-1-yl acetate + TX, dodeca-8,10-dien-1-yl acetate + TX, dodicin + TX, dominicalure + TX, doramectin + TX, emamectin + TX, emamectin benzoate + TX, empenthrin + TX, Encarsia formosa + TX, endothal + TX, endrin + TX, eprinomectin + TX, epsilon - momfluorothrin + TX, epsilon-metofluthrin + TX, Eretmocerus eremicus + TX, esfenvalerate + TX, ethion + TX, ethiprole + TX, ethoprophos + TX, ethyl 4-methyloctanoate + TX, ethyl hexanediol + TX, ethylene dibromide + TX, etofenprox + TX, etoxazole + TX, etpyrafen + TX, eugenol + TX, Extract of seaweed and fermentation product derived from melasse + TX, Extract of seaweed and fermentation product derived from melasse comprising urea + TX, Extract of seaweed and fermented plant products + TX, Extract of seaweed and fermented plant products comprising phytohormones, vitamins, EDTA-chelated copper, zinc, and iron + TX, famphur + TX, fenaminosulf + TX, fenamiphos + TX, fenazaquin + TX, fenfluthrin + TX, fenitrothion + TX, fenmezoditiaz + TX, fenobucarb + TX, fenothiocarb + TX, fenoxycarb + TX, fenpropathrin + TX, fenpyrad + TX, fenpyroximate + TX, fensulfothion + TX, fenthion + TX, fentin + TX, fentinacetate + TX, fenvalerate + TX, ferric phosphate + TX, fipronil + TX, flometoquin + TX, flonicamid + TX, fluacrypyrim + TX, fluazaindolizine + TX, fluazuron + TX, flubendiamide + TX, flubenzimine + TX, fluchlordiniliprole + TX, flucitrate + TX, flucycloxuron + TX, flucythrinate + TX, fluensulfone [318290-98-1] + TX, fluensulfone + TX, flufenerim + TX, flufenprox + TX, flufiprole + TX, fluhexafon + TX, flumethrin + TX, fluopyram + TX, flupyradifurone + TX, flupyrimin + TX, flupyroxystrobin + TX, fluralaner + TX, fluvalinate + TX, fluxametamide + TX, formaldehyde + TX, fosthiazate + TX, fosthietan + TX, frontaline + TX, furfural + TX, gamma-cyhalothrin + TX, Gossypure® (1:1 mixture of the (Z,E) and (Z,Z) isomers of hexadeca-7,11-dien-1-yl-acetate) + TX, grandlure + TX, grandlure I + TX, grandlure II + TX, grandlure III + TX, grandlure IV + TX, Granulovirus + TX, guadiapyr + TX, GY-81 + TX, halfenprox + TX, halofenozide + TX, Harpin + TX, Helicoverpa armigera Nucleopolyhedrovirus + TX, Helicoverpa zea NPV + TX, Helicoverpa zea Nucleopolyhedrovirus + TX, Heliothis punctigera Nucleopolyhedrovirus + TX, Heliothis virescens Nucleopolyhedrovirus + TX, hemel + TX, hempa + TX, heptafluthrin + TX, heterophos + TX, Heterorhabditis bacteriophora and H. megidis + TX, hexalure + TX, hexamide + TX, hexythiazox + TX, Hippodamia convergens + TX, hydramethylnon + TX, hydrargaphen + TX, hydrated lime + TX, imicyafos + TX, imidacloprid + TX, imiprothrin + TX, Indazaproxamet + TX, indoxacarb + TX, iodomethane + TX, iprodione + TX, ipsdienol + TX, ipsenol + TX, isamidofos + TX, isazofos + TX, isocycloseram + TX, Isoflualanin (CAS number: 2892524-05-7) + TX, isothioate + TX, ivermectin + TX, japonilure + TX, kappa-bifenthrin + TX, kappa-tefluthrin + TX, kasugamycin + TX, kasugamycin hydrochloride hydrate + TX, kinetin + TX, lambda-cyhalothrin + TX, ledprona + TX, lepimectin + TX, Leptomastix dactylopii + TX, lineatin + TX, litlure + TX, looplure + TX,

lotilaner + TX, lufenuron + TX, *Macrolophus caliginosus* + TX, *Mamestra brassicae* NPV + TX, mecarphon + TX, medlure + TX, megatomoic acid + TX, metaflumizone + TX, metaldehyde + TX, metam + TX, metam-potassium + TX, metam-sodium + TX, *Metaphycus helvolus* + TX, *Metarhizium anisopliae* var. *acridum* + TX, *Metarhizium anisopliae* var. *anisopliae* + TX, *Metarhizium* spp. + TX, metepa + TX, methiocarb + TX, methiotepa + TX, methomyl + TX, methoquin-butyl + TX, methoxyfenozide + TX, methyl apholate + TX, methyl bromide + TX, methyl eugenol + TX, methyl isothiocyanate + TX, methylneodecanamide + TX, metofluthrin + TX, metolcarb + TX, mexacarbate + TX, milbemectin + TX, milbemycin oxime + TX, momfluorothrin + TX, morzid + TX, moxidectin + TX, muscalure + TX, *Muscodor albus* 620 (NRRL Accession No. 30547) + TX, *Muscodor roseus* A3-5 (NRRL Accession No. 30548) + TX, *Myrothecium verrucaria* composition + TX, nabam + TX, NC-184 + TX, Neem tree based products + TX, Neodiprion sertifer NPV and *N. lecontei* NPV + TX, nickel bis(dimethyldithiocarbamate) + TX, niclosamide + TX, niclosamide-olamine + TX, nicofluprole + TX, nitenpyram + TX, nithiazine + TX, nitrapyrin + TX, octadeca-2,13-dien-1-yl acetate + TX, octadeca-3,13-dien-1-yl acetate + TX, octhilinone + TX, omethoate + TX, orfuralure + TX, *Orius* spp. + TX, oryctalure + TX, ostramone + TX, oxamate + TX, oxamyl + TX, oxazosulfyl + TX, oxolinic acid + TX, oxytetracycline + TX, *Paecilomyces fumosoroseus* + TX, *Paecilomyces lilacinus* + TX, parathion-ethyl + TX, *Pasteuria nishizawae* + TX, *Pasteuria penetrans* + TX, *Pasteuria ramosa* + TX, *Pasteuria thornei* + TX, *Pasteuria usgae* + TX, P-cymene + TX, penfluron + TX, pentachlorophenol + TX, permethrin + TX, phenothrin + TX, phorate + TX, phosphamidon + TX, phosphocarb + TX, *Phytoseiulus persimilis* + TX, picaridin + TX, pioxaniliprole + TX, piperazine + TX, piperonylbutoxide + TX, pirimicarb + TX, pirimiphos-ethyl + TX, pirimiphos-methyl + TX, *Plutella xylostella* Granulosis virus + TX, *Plutella xylostella* Nucleopolyhedrovirus + TX, Polyhedrosis virus + TX, potassium and molybdenum and EDTA-chelated manganese + TX, potassium ethylxanthate + TX, potassium hydroxyquinoline sulfate + TX, prallethrin + TX, probenazole + TX, profenofos + TX, profluthrin + TX, propargite + TX, propetamphos + TX, propoxur + TX, prothiophos + TX, protrifenbute + TX, pyflubumide + TX, pymetrozine + TX, pyraclofos + TX, pyrafluprole + TX, pyrethrum + TX, pyridaben + TX, pyridalyl + TX, pyridin-4-amine + TX, pyrifluquinazon + TX, pyrimidifen + TX, pyriminostrobin + TX, pyriprole [394730-71-3] + TX, pyriprole + TX, pyriproxyfen + TX, QRD 420 (a terpenoid blend) + TX, QRD 452 (a terpenoid blend) + TX, QRD 460 (a terpenoid blend) + TX, *Quillaja saponaria* + TX, quinoclamine + TX, quinonamid + TX, resmethrin + TX, *Rhodococcus globerulus* AQ719 (NRRL Accession No B-21663) + TX, sarolaner + TX, S-bioallethrin + TX, sebufos + TX, selamectin + TX, siglure + TX, silafluofen + TX, simazine + TX, sodium pentachlorophenoxide + TX, sordidin + TX, spidoxamat + TX, spinetoram + TX, spinosad + TX, spirobudifen + TX, spiroidiclofen + TX, spiromesifen + TX, spiropidion + TX, spirotetramat + TX, *Spodoptera exigua* multicapsid nuclear polyhedrosis virus + TX, *Spodoptera frugiperda* Nucleopolyhedrovirus + TX, *Steinernema bibionis* + TX, *Steinernema carpocapsae* + TX, *Steinernema feltiae* + TX, *Steinernema glaseri* + TX, *Steinernema riobrave* + TX, *Steinernema riobravus* + TX, *Steinernema scapterisci* + TX, *Steinernema* spp. + TX, *Streptomyces galbus* (NRRL Accession No. 30232) + TX, *Streptomyces* sp. (NRRL Accession No. B-30145) + TX, streptomycin + TX, streptomycin sesquisulfate + TX, strychnine + TX, sulcatol + TX, sulfiflumin (CAS number: 2377084-09-6) + TX, sulfoxaflor + TX, tazimcarb + TX, tebufenozide + TX, tebufenpyrad + TX, tebupirimiphos + TX, tecloftalam + TX, tefluthrin + TX, temephos + TX, tepa + TX, terbam + TX, terbufos + TX, terpenoid blend + TX, tetrachlorantraniliprole + TX, tetrachlorothiophene + TX, tetradec-11-en-1-yl acetate + TX,

tetradiphon + TX, tetramethrin + TX, tetramethylfluthrin + TX, tetranactin + TX, tetranilprole + TX, theta-cypermethrin + TX, thiacloprid + TX, thiafenox + TX, thiamethoxam + TX, thiocyclam + TX, thiodicarb + TX, thiofanox + TX, thiohempa + TX, thiomersal + TX, thiometon + TX, thionazin + TX, thiophanate + TX, thiosultap + TX, thiotepa + TX, tigolaner + TX, tiorantranilprole + TX, tiozazafen + TX, tolfenpyrad + TX, toxaphene + TX, tralomethrin + TX, transfluthrin + TX, tretamine + TX, triazamate + TX, triazophos + TX, triazuron + TX, tributyltin oxide + TX, trichlorfon + TX, trichloronate + TX, trichlorphon + TX, Trichogramma spp. + TX, trifenmorph + TX, trifluenfurinate + TX, triflumezopyrim + TX, trimedlure + TX, trimedlure A + TX, trimedlure B1 + TX, trimedlure B2 + TX, trimedlure C + TX, trimethacarb + TX, triphenyltin acetate + TX, triphenyltin hydroxide + TX, trunc-call + TX, tyclopyrazoflor + TX, Typhlodromus occidentalis + TX, uredepa + TX, Verticillium lecanii + TX, Verticillium spp. + TX, xylenols + TX, YI-5302 + TX, zeatin + TX, zeta-Cypermethrin + TX;

N-[(1R)-1-benzyl-3-chloro-1-methyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-3-chloro-1-methyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide + TX, N-ethyl-N'-[5-methoxy-2-methyl-4-[(2-trifluoromethyl)tetrahydrofuran-2-yl]phenyl]-N-methyl-formamidine (these compounds may be prepared from the methods described in WO2019/110427) + TX, (3',4',5'-trifluoro-biphenyl-2-yl)-amide + TX, (3-methylisoxazol-5-yl)-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methanone (these compounds may be prepared from the methods described in WO 2017/220485) + TX, (4-phenoxyphenyl)methyl 2-amino-6-methyl-pyridine-3-carboxylate (this compound may be prepared from the methods described in WO 2014/006945) + TX, (5-methyl-2-pyridyl)-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methanone + TX, (7E,9Z)-dodeca-7,9-dien-1-yl acetate + TX, (9Z,11E)-tetradeca-9,11-dien-1-yl acetate + TX, (9Z,12E)-tetradeca-9,12-dien-1-yl acetate + TX, (E)-6-methylhept-2-en-4-ol + TX, (E)-dec-5-en-1-yl acetate with (E)-dec-5-en-1-ol + TX, (E)-tridec-4-en-1-yl acetate + TX, (E,Z)-tetradeca-4,10-dien-1-yl acetate, + TX, (R)-3-(difluoromethyl)-1-methyl-N-[1,1,3-trimethylindan-4-yl]pyrazole-4-carboxamide + TX, (Z)-dodec-7-en-1-yl acetate + TX, (Z)-hexadec-11-en-1-yl acetate + TX, (Z)-hexadec-11-enal + TX, (Z)-hexadec-13-en-11-yn-1-yl acetate + TX, (Z)-icos-13-en-10-one + TX, (Z)-tetradec-7-en-1-yl + TX, (Z)-tetradec-9-en-1-ol + TX, (Z)-tetradec-9-en-1-yl acetate + TX, (Z,2E)-5-[1-(2,4-dichlorophenyl)pyrazol-3-yl]oxy-2-methoxyimino-N,3-dimethyl-pent-3-enamide (this compound may be prepared from the methods described in WO 2018/153707) + TX, (Z,2E)-5-[1-(4-chlorophenyl)pyrazol-3-yl]oxy-2-methoxyimino-N,3-dimethyl-pent-3-enamide + TX, , [2-[3-[2-[1-[2-[3,5-bis(difluoromethyl)pyrazol-1-yl]acetyl]-4-piperidyl]thiazol-4-yl]-4,5-dihydroisoxazol-5-yl]-3-chlorophenyl] methanesulfonate + TX, 1-(4,5-dimethylbenzimidazol-1-yl)-4,4,5-trifluoro-3,3-dimethyl-isoquinoline + TX, 1-(4,5-dimethylbenzimidazol-1-yl)-4,4-difluoro-3,3-dimethyl-isoquinoline + TX, 1-(6,7-dimethylpyrazolo[1,5-a]pyridin-3-yl)-4,4,5-trifluoro-3,3-dimethyl-isoquinoline + TX, 1-(6,7-dimethylpyrazolo[1,5-a]pyridin-3-yl)-4,4,6-trifluoro-3,3-dimethyl-isoquinoline + TX, 1-(6-chloro-7-methylpyrazolo[1,5-a]pyridin-3-yl)-4,4-difluoro-3,3-dimethyl-isoquinoline (these compounds may be prepared from the methods described in WO2017/025510) + TX, 1,1-bis(4-chlorophenyl)-2-ethoxyethanol + TX, 1,1-dichloro-2,2-bis(4-ethylphenyl)ethane + TX, 1,2-dibromo-3-chloropropane + TX, 1,2-dichloropropane with 1,3-dichloropropene + TX, 1,3-dichloropropene + TX, 1,3-dimethoxy-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]urea + TX, 1-[2-[[1-(4-chlorophenyl)pyrazol-3-yl]oxymethyl]-3-methyl-phenyl]-4-methyl-tetrazol-5-one + TX, 10-dien-1-yl acetate + TX, 14-methyloctadec-1-ene + TX, 1-bromo-2-chloroethane + TX, 1-dichloro-1-nitroethane + TX, 1-hydroxy-1H-pyridine-2-thione + TX, 1-methoxy-3-methyl-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-

yl]phenyl)methyl]urea + TX, 1-methyl-4-[3-methyl-2-[[2-methyl-4-(3,4,5-trimethylpyrazol-1-yl)phenoxy]methyl]phenyl]tetrazol-5-one + TX, 2-(difluoromethyl)-N-((3R)-1,1,3-trimethylindan-4-yl)pyridine-3-carboxamide + TX, 2-(difluoromethyl)-N-((3R)-1,1,3-trimethylindan-4-yl)pyridine-3-carboxamide + TX, 2-(1,3-dithiolan-2-yl)phenyl dimethylcarbamate + TX, 2-(2-butoxyethoxy)ethyl piperonylate + TX, 2-(2-butoxyethoxy)ethyl thiocyanate + TX, 2-(4,5-dimethyl-1,3-dioxolan-2-yl)phenyl methylcarbamate + TX, 2-(4-chloro-3,5-xylyloxy)ethanol + TX, 2-(difluoromethyl)-N-(3-ethyl-1,1-dimethyl-indan-4-yl)pyridine-3-carboxamide + TX, 2-(difluoromethyl)-N-[(3R)-3-ethyl-1,1-dimethyl-indan-4-yl]pyridine-3-carboxamide + TX, 2-(difluoromethyl)-N-[(3S)-3-ethyl-1,1-dimethyl-indan-4-yl]pyridine-3-carboxamide (this compound may be prepared from the methods described in WO 2014/095675) + TX, 2-(difluoromethyl)-N-[3-ethyl-1,1-dimethyl-indan-4-yl]pyridine-3-carboxamide + TX, 2-(octylthio)ethanol + TX, 2,2,2-trichloro-1-(3,4-dichlorophenyl)ethyl acetate + TX, 2,2-dichlorovinyl 2-ethylsulfinyethyl methyl phosphate + TX, 2,2-difluoro-N-methyl-2-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]acetamide + TX, 2,4-dichlorophenyl benzenesulfonate + TX, 2,6-Dimethyl-1H,5H-[1,4]dithiino[2,3-c:5,6-c']dipyrrole-1,3,5,7(2H,6H)-tetrone (this compound may be prepared from the methods described in WO 2011/138281) + TX, 2-[2-fluoro-6-[(8-fluoro-2-methyl-3-quinolyl)oxy]phenyl]propan-2-ol + TX, 2-[6-(4-bromophenoxy)-2-(trifluoromethyl)-3-pyridyl]-1-(1,2,4-triazol-1-yl)propan-2-ol (this compound may be prepared from the methods described in WO 2017/029179) + TX, 2-[6-(4-chlorophenoxy)-2-(trifluoromethyl)-3-pyridyl]-1-(1,2,4-triazol-1-yl)propan-2-ol (this compound may be prepared from the methods described in WO 2017/029179) + TX, 2-chlorovinyl diethyl phosphate + TX, 2-fluoro-N-methyl-N-1-naphthylacetamide + TX, 2-imidazolidone + TX, 2-isovalerylindan-1,3-dione + TX, 2-methyl(prop-2-ynyl)aminophenyl methylcarbamate + TX, 2-oxo-N-propyl-2-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]acetamide (this compound may be prepared from the methods described in WO 2018/065414) + TX, 2-thiocyanatoethyl laurate + TX, 3-(4,4-difluoro-3,3-dimethyl-1-isoquinolyl)-7,8-dihydro-6H-cyclopenta[e]benzimidazole (these compounds may be prepared from the methods described in WO2016/156085) + TX, 3-(4,4-difluoro-3,4-dihydro-3,3-dimethylisoquinolin-1-yl)quinolone + TX, 3-(4-chlorophenyl)-5-methylrhodanine + TX, 3-(difluoromethyl)-1-methyl-N-[1,1,3-trimethylindan-4-yl]pyrazole-4-carboxamide + TX, 3,4-dichlorotetrahydrothiophene 1,1-dioxide + TX, 3-[2-(1-chlorocyclopropyl)-3-(2-fluorophenyl)-2-hydroxypropyl]imidazole-4-carbonitrile (this compound may be prepared from the methods described in WO 2016/156290) + TX, 3-[2-(1-chlorocyclopropyl)-3-(3-chloro-2-fluoro-phenyl)-2-hydroxypropyl]imidazole-4-carbonitrile (this compound may be prepared from the methods described in WO 2016/156290) + TX, 3-bromo-1-chloroprop-1-ene + TX, 3-chloro-6-methyl-5-phenyl-4-(2,4,6-trifluorophenyl)pyridazine + TX, 3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid + TX, 3-ethyl-1-methoxy-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]urea + TX, 3-methyl-1-phenylpyrazol-5-yl dimethylcarbamate + TX, 4-(2-bromo-4-fluorophenyl)-N-(2-chloro-6-fluorophenyl)-1,3-dimethyl-1H-pyrazol-5-amine + TX, 4-(2,6-difluorophenyl)-6-methyl-5-phenylpyridazine-3-carbonitrile + TX, 4-(2-bromo-4-fluoro-phenyl)-N-(2-chloro-6-fluoro-phenyl)-2,5-dimethylpyrazol-3-amine + TX, 4-(quinoxalin-2-ylamino)benzenesulfonamide + TX, 4,4-difluoro-1-(5-fluoro-4-methyl-benzimidazol-1-yl)-3,3-dimethyl-isoquinoline + TX, 4,4-difluoro-3,3-dimethyl-1-(6-methylpyrazolo[1,5-a]pyridin-3-yl)isoquinoline + TX, 4,4-dimethyl-2-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]isoxazolidin-3-one + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(1,2,4-

triazol-1-yl)propyl]-3-pyridyl]oxy] benzonitrile + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(5-sulfanyl-1,2,4-triazol-1-yl)propyl]-3-pyridyl]oxy] benzonitrile + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(5-thioxo-4H-1,2,4-triazol-1-yl)propyl]-3-pyridyl]oxy] benzonitrile + TX, 4-chloro-2-(2-chloro-2-methyl-propyl)-5-[(6-iodo-3-pyridyl)methoxy]pyridazin-3-one + TX, 4-chlorophenyl phenyl sulfone + TX, 4-methyl(prop-2-ynyl)amino-3,5-xylyl methylcarbamate + TX, 4-methylnonan-5-ol with 4-methylnonan-5-one + TX, 5-(1,3-benzodioxol-5-yl)-3-hexylcyclohex-2-enone + TX, 5,5-dimethyl-2-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]isoxazolidin-3-one + TX, 5,5-dimethyl-3-oxocyclohex-1-enyl dimethylcarbamate + TX, 5-amino-1,3,4-thiadiazole-2-thiol zinc salt (2:1) + TX, 5-methyl-6-thioxo-1,3,5-thiadiazinan-3-ylacetic acid + TX, 6-chloro-3-(3-cyclopropyl-2-fluoro-phenoxy)-N-[2-(2,4-dimethylphenyl)-2,2-difluoro-ethyl]-5-methyl-pyridazine-4-carboxamide (may be prepared from the methods described in WO 2020/109391) + TX, 6-chloro-3-(3-cyclopropyl-2-fluoro-phenoxy)-N-[2-(3,4-dimethylphenyl)-2,2-difluoro-ethyl]-5-methyl-pyridazine-4-carboxamide (may be prepared from the methods described in WO 2020/109391) + TX, 6-chloro-4,4-difluoro-3,3-dimethyl-1-(4-methylbenzimidazol-1-yl)isoquinoline + TX, 6-chloro-N-[2-(2-chloro-4-methyl-phenyl)-2,2-difluoro-ethyl]-3-(3-cyclopropyl-2-fluoro-phenoxy)-5-methyl-pyridazine-4-carboxamide (may be prepared from the methods described in WO 2020/109391) + TX, 6-ethyl-5,7-dioxo-pyrrolo[4,5][1,4]dithiino[1,2-c]isothiazole-3-carbonitrile + TX, 6-isopentenylaminopurine + TX, 8-fluoro-N-[(1R)-1-[(3-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide + TX, 8-fluoro-N-[(1S)-1-[(3-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide + TX, 8-hydroxyquinoline sulfate + TX, acethion + TX, acetoprole + TX, acibenzolar + TX, acibenzolar-S-methyl + TX, acrylonitrile + TX, Adoxophyes orana GV + TX, Agrobacterium radiobacter + TX, aldoxycarb + TX, aldrin + TX, allosamidin + TX, allyxycarb + TX, alpha-chlorohydrin + TX, alpha-ecdysone + TX, alpha-multistriatin + TX, aluminium phosphide + TX, Amblyseius spp. + TX, amectotractin + TX, ametocradin + TX, amidithion + TX, amidothioate + TX, aminocarb + TX, aminopyrifen + TX, amisulbrom + TX, amiton + TX, amiton hydrogen oxalate + TX, amitraz + TX, anabasine + TX, Anagrapha falcifera NPV + TX, Anagrus atomus + TX, ancymidol + TX, anilazine + TX, anisiflupurin + TX, anthraquinone + TX, antu + TX, Aphelinus abdominalis + TX, Aphidius colemani + TX, Aphidoletes aphidimyza + TX, apholate + TX, aramite + TX, arsenous oxide + TX, athidathion + TX, Autographa californica NPV + TX, azaconazole + TX, azamethiphos + TX, azobenzene + TX, azothoate + TX, azoxystrobin + TX, Bacillus sphaericus Neide + TX, Bacillus thuringiensis delta endotoxins + TX, barium carbonate + TX, barium hexafluorosilicate + TX, barium polysulfide + TX, barthrin + TX, Bayer 22/190 + TX, Bayer 22408 + TX, Beauveria brongniartii + TX, benalaxyl + TX, benclothiaz + TX, benomyl + TX, benoxafos + TX, benthiavalicarb + TX, benzothiofostrobin + TX, benzovindiflupyr + TX, benzyl benzoate + TX, beta-cyfluthrin + TX, beta-cypermethrin + TX, bethoxazin + TX, bioethanomethrin + TX, biopermethrin + TX, bis(2-chloroethyl) ether + TX, bis(tributyltin) oxide + TX, bisazir + TX, bisthiosemi + TX, bitertanol + TX, bixafen + TX, blasticidin-S + TX, borax + TX, bordeaux mixture + TX, boscalid + TX, brevicomin + TX, brodifacoum + TX, brofenvalerate + TX, bromadiolone + TX, bromethalin + TX, bromfeninfos + TX, bromoacetamide + TX, bromocyclen + TX, bromo-DDT + TX, bromophos + TX, bromopropylate + TX, bromuconazole + TX, bronopol + TX, bufencarb + TX, bupirimate + TX, buprofezin + TX, busulfan + TX, but-3-ynyl N-[6-[(Z)-[(1-methyltetrazol-5-yl)-phenyl-methylene]amino]oxymethyl]-2-pyridyl]carbamate + TX, butacarb + TX, butathiofos + TX, butocarboxim + TX, butonate + TX, butopyronoxyl + TX, butoxy(polypropylene glycol) + TX, butoxycarboxim + TX, butylpyridaben + TX, calcium arsenate + TX, calcium cyanide + TX,

calcium polysulfide + TX, camphechlor + TX, captafol + TX, captan + TX, carbanolate + TX, carbendazim + TX, carbon disulfide + TX, carbon tetrachloride + TX, carbophenothion + TX, carboxin + TX, cartap hydrochloride + TX, CAS Number: 2132414-04-9 + TX, CAS Number: 2344721-61-3 + TX, cevadine + TX, chinomethionat + TX, chloralose + TX, chlorbenside + TX, chlorbicyclen + TX, chlordane + TX, chlordecone + TX, chlordimeform + TX, chlordimeform hydrochloride + TX, chlorfenethol + TX, chlorfenson + TX, chlorfensulfide + TX, chlorobenzilate + TX, chloroform + TX, chloroinconazide + TX, chloromebuform + TX, chloromethiuron + TX, chloroneb + TX, chlorophacinone + TX, chloropicrin + TX, chloropropylate + TX, chlorothalonil + TX, chlorphoxim + TX, chlorprazophos + TX, chlorthiophos + TX, chlozolate + TX, cholecalciferol + TX, Chrysoperla carnea + TX, cinerin I + TX, cinerin II + TX, cinerins + TX, cismethrin + TX, cis-resmethrin + TX, clopyralid + TX, closantel + TX, codlelure + TX, codlemone + TX, copper acetoarsenite + TX, copper arsenate + TX, copper dioctanoate + TX, copper hydroxide + TX, copper naphthenate + TX, copper oleate + TX, copper oxide + TX, copper oxychloride + TX, copper sulfate + TX, coumachlor + TX, coumafuryl + TX, coumaphos + TX, coumatetralyl + TX, coumethoxystrobin (jiaxiangjunzhi) + TX, coumithoate + TX, coumoxystrobin + TX, cresol + TX, crimidine + TX, crotamiton + TX, crotoxyphos + TX, cruformate + TX, cryolite + TX, Cryptolaemus montrouzieri + TX, CS 708 + TX, cuclure + TX, cufraneb + TX, cyanofenphos + TX, cyanophos + TX, cyanthoate + TX, cyazofamid + TX, cybutryne + TX, cyclethrin + TX, cyclobutirfluram + TX, Cydia pomonella GV + TX, cyflufenamid + TX, cymiazole + TX, cymoxanil + TX, cyproconazole + TX, cyprodinil + TX, cythioate + TX, cytokinins + TX, Dacnusa sibirica + TX, DAEP + TX, dazomet + TX, DCIP + TX, DCPM + TX, DDT + TX, debacarb + TX, decarbofuran + TX, demephion + TX, demephion-O + TX, demephion-S + TX, demeton-methyl + TX, demeton-O + TX, demeton-O-methyl + TX, demeton-S + TX, demeton-S-methyl + TX, demeton-S-methylsulfon + TX, diamidafos + TX, dibutyl adipate + TX, dibutyl phthalate + TX, dibutyl succinate + TX, dicapthon + TX, dichlobentiazox + TX, dichlofenthion + TX, dichlofluanid + TX, dichlone + TX, dichlorophen + TX, dichlorvos + TX, dichlozoline + TX, dicliphos + TX, diclocymet + TX, diclomezine + TX, dicloran + TX, dicresyl + TX, dicyclanil + TX, dicyclopentadiene + TX, dieldrin + TX, dienochlor + TX, diethofencarb + TX, diethyl 5-methylpyrazol-3-yl phosphate + TX, diethyltoluamide + TX, difenacoum + TX, difenoconazole + TX, difethialone + TX, diflovidazin + TX, Diglyphus isaea + TX, dilor + TX, dimatif + TX, dimefluthrin + TX, dimefox + TX, dimetan + TX, dimethirimol + TX, dimethomorph + TX, dimethrin + TX, dimethyl carbate + TX, dimethyl phthalate + TX, dimethylvinphos + TX, dimetilan + TX, dimoxystrobin + TX, dinex + TX, dinex-diclexine + TX, diniconazole + TX, dinocap-4 + TX, dinocap-6 + TX, dinocron + TX, dinopenton + TX, dinoprop + TX, dinosam + TX, dinoseb + TX, dinosulfon + TX, dinoterbon + TX, diofenolan + TX, dioxabenzofos + TX, dioxathion + TX, diphacinone + TX, diphenyl sulfone + TX, dipymetitrone + TX, dipyrithione + TX, disparlure + TX, disulfiram + TX, dithianon + TX, dithicrofos + TX, DNOC + TX, dodec-8-en-1-yl acetate + TX, dodec-9-en-1-yl acetate + TX, dodeca-8 + TX, dodemorph + TX, dodicin + TX, dodine + TX, dofenapyn + TX, dominicalure + TX, doramectin + TX, DSP + TX, d-tetramethrin + TX, ecdysterone + TX, edifenphos + TX, EI 1642 + TX, EMPC + TX, Encarsia formosa + TX, endothal + TX, endothion + TX, enestroburin + TX, enoxastrobin + TX, EPBP + TX, epoxiconazole + TX, eprinomectin + TX, Eretmocerus eremicus + TX, ergocalciferol + TX, etaphos + TX, ethaboxam + TX, ethiofencarb + TX, ethirimol + TX, ethoate-methyl + TX, ethyl 1-[[4-[(Z)-2-ethoxy-3,3,3-trifluoro-prop-1-en-1-yl]oxy]phenyl]methyl]pyrazole-3-carboxylate (may be prepared from the methods described in WO 2020/056090) + TX, ethyl 1-[[4-[(2-(trifluoromethyl)-1,3-dioxolan-2-yl)methoxy]phenyl]methyl]pyrazole-

3-carboxylate (may be prepared from the methods described in WO 2020/056090) + TX, ethyl 1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]pyrazole-4-carboxylate + TX, ethyl 1-[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-thienyl]methyl]pyrazole-4-carboxylate (this compound may be prepared from the methods described in WO 2018/158365) + TX, ethyl 4-methyloctanoate + TX, ethyl formate + TX, ethyl hexanediol + TX, ethylene dibromide + TX, ethylene dichloride + TX, ethylene oxide + TX, etridiazole + TX, etrimfos + TX, eugenol + TX, EXD + TX, famoxadone + TX, farnesol + TX, farnesol with nerolidol + TX, fenamidone + TX, fenaminosulf + TX, fenaminstrobin + TX, fenanimol + TX, fenazaflor + TX, fenbuconazole + TX, fenbutatin oxide + TX, fenchlorphos + TX, fenethacarb + TX, fenfuram + TX, fenhexamid + TX, fenitrothion + TX, fenothiocarb + TX, fenoxacrim + TX, fenoxanil + TX, fencpiclonil + TX, fencpicoxamid + TX, fencpirithrin + TX, fenpropidin + TX, fenpropimorph + TX, fenpyrad + TX, fenpyrazamine + TX, fenpyroximate + TX, fenson + TX, fensulfothion + TX, fenthion + TX, fenthion-ethyl + TX, fentin + TX, fentrifanil + TX, ferbam + TX, ferimzone + TX, ferric phosphate + TX, flocoumafen + TX, florylpicoxamid + TX, fluazinam + TX, flubeneteram + TX, flubenzimine + TX, flucofuron + TX, flucycloxuron + TX, fludioxonil + TX, fluenetil + TX, flufenoxadiazam + TX, flufenoxystrobin + TX, fluindapyr + TX, flumetylsulforim + TX, flumorph + TX, fluopicolide + TX, fluopimomide + TX, fluopyram + TX, fluorbenside + TX, fluoroacetamide + TX, fluoroimide + TX, fluoxapiprolin + TX, fluoxastrobin + TX, fluoxytioconazole + TX, flupropadine + TX, flupropadine hydrochloride + TX, fluquinconazole + TX, flusilazole + TX, flusulfamide + TX, flutianil + TX, flutolanil + TX, flutriafol + TX, fluxapyroxad + TX, FMC 1137 + TX, folpet + TX, formaldehyde + TX, formetanate + TX, formetanate hydrochloride + TX, formparanate + TX, fosetyl-aluminium + TX, fosmethilan + TX, fospirate + TX, fosthietan + TX, frontaline + TX, fuberidazole + TX, furalaxyl + TX, furametpyr + TX, furathiocarb + TX, furethrin + TX, furfural + TX, gamma-HCH + TX, glyodin + TX, grandlure + TX, grandlure I + TX, grandlure II + TX, grandlure III + TX, grandlure IV + TX, guazatine + TX, guazatine acetates + TX, halfenprox + TX, HCH + TX, hemel + TX, hempa + TX, HEOD + TX, heptachlor + TX, heterophos + TX, Heterorhabditis bacteriophora and H. megidis + TX, hexaconazole + TX, hexadecyl cyclopropanecarboxylate + TX, hexalure + TX, hexamide + TX, HHDN + TX, Hippodamia convergens + TX, hydrargaphen + TX, hydrated lime + TX, hydrogen cyanide + TX, hymexazol + TX, hyquincarb + TX, imanin + TX, imazalil + TX, imibenconazole + TX, iminoctadine + TX, inpyrfluxam + TX, ipconazole + TX, ipfentrifluconazole + TX, ipflufenquin + TX, iprobenphos + TX, iprodione + TX, iprovalicarb + TX, ipsdienol + TX, ipsenol + TX, IPSP + TX, isamidofos + TX, isazofos + TX, isobenzan + TX, isocarbophos + TX, isodrin + TX, isofenphos + TX, isofetamid + TX, isoflucypram + TX, isolane + TX, isoprothiolane + TX, isopyrazam + TX, isotianil + TX, isoxathion + TX, japonilure + TX, jasmolin I + TX, jasmolin II + TX, jodfenphos + TX, juvenile hormone I + TX, juvenile hormone II + TX, juvenile hormone III + TX, kadethrin + TX, kasugamycin + TX, kasugamycin hydrochloride hydrate + TX, kelevan + TX, kinetin + TX, kinoprene + TX, kresoxim-methyl + TX, lead arsenate + TX, Leptomastix dactylopii + TX, leptophos + TX, lindane + TX, lineatin + TX, lirimfos + TX, litlure + TX, looplure + TX, Ivbenmixianan + TX, lythidathion + TX, Macrolophus caliginosus + TX, magnesium phosphide + TX, malonoben + TX, Mamestra brassicae NPV + TX, mancopper + TX, mancozeb + TX, mandestrobin + TX, mandipropamid + TX, maneb + TX, mazidox + TX, m-cumenyl methylcarbamate + TX, mecarbam + TX, mecarphon + TX, medlure + TX, mefentrifluconazole + TX, megatomoic acid + TX, menazon + TX, mepanipyrim + TX, meperfluthrin + TX, mephosfolan + TX, mepronil + TX, mercuric oxide + TX, mercurous chloride + TX, mesulfen + TX, mesulfenfos + TX, metalaxyl + TX, metam + TX, metam-potassium + TX, metam-

sodium + TX, *Metaphycus helvolus* + TX, *Metarhizium anisopliae* var. *acidum* + TX, *Metarhizium anisopliae* var. *anisopliae* + TX, metarylpicoxamid + TX, metconazole + TX, metepa + TX, methacrifos + TX, methanesulfonyl fluoride + TX, methasulfocarb + TX, methiotepa + TX, methocrotophos + TX, methoprene + TX, methoquin-butyl + TX, methothrin + TX, methoxychlor + TX, methyl (Z)-2-(5-cyclohexyl-2-methyl-phenoxy)-3-methoxy-prop-2-enoate + TX, methyl (Z)-2-(5-cyclopentyl-2-methyl-phenoxy)-3-methoxy-prop-2-enoate (these compounds may be prepared from the methods described in WO2020/193387) + TX, methyl (Z)-2-[5-(3-isopropylpyrazol-1-yl)-2-methyl-phenoxy]-3-methoxy-prop-2-enoate + TX, methyl (Z)-3-methoxy-2-[2-methyl-5-(3-propylpyrazol-1-yl)phenoxy]prop-2-enoate + TX, methyl (Z)-3-methoxy-2-[2-methyl-5-(4-propyltriazol-2-yl)phenoxy]prop-2-enoate + TX, methyl (Z)-3-methoxy-2-[2-methyl-5-[3-(trifluoromethyl)pyrazol-1-yl]phenoxy]prop-2-enoate (these compounds may be prepared from the methods described in WO2020/079111) + TX, methyl (Z)-3-methoxy-2-[2-methyl-5-[4-(trifluoromethyl)triazol-2-yl]phenoxy]prop-2-enoate + TX, methyl apholate + TX, methyl bromide + TX, methyl eugenol + TX, methyl isothiocyanate + TX, methyl N-[[4-[1-(2,6-difluoro-4-isopropyl-phenyl)pyrazol-4-yl]-2-methyl-phenyl]methyl]carbamate (may be prepared from the methods described in WO 2020/097012) + TX, methyl N-[[4-[1-(4-cyclopropyl-2,6-difluoro-phenyl)pyrazol-4-yl]-2-methyl-phenyl]methyl]carbamate (may be prepared from the methods described in WO 2020/097012) + TX, methyl N-[[5-[4-(2,4-dimethylphenyl)triazol-2-yl]-2-methyl-phenyl]methyl]carbamate + TX, methylchloroform + TX, methylene chloride + TX, methylneodecanamide + TX, metiram + TX, metolcarb + TX, metominostrobin + TX, metoxadiazone + TX, metrafenone + TX, metyltetraprole + TX, MGK 264 + TX, milbemycin oxime + TX, mipafox + TX, mirex + TX, monocrotophos + TX, morphothion + TX, morzid + TX, moxidectin + TX, muscalure + TX, myclobutanil + TX, myclozoline + TX, *Myrothecium verrucaria* composition + TX, N-((1R)-1-benzyl-3-chloro-1-methyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide (these compounds may be prepared from the methods described in WO2017/153380) + TX, N-((1S)-1-benzyl-3-chloro-1-methyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide (these compounds may be prepared from the methods described in WO2017/153380) + TX, N'-(2,5-dimethyl-4-phenoxy-phenyl)-N-ethyl-N-methyl-formamidine + TX, N'-(2-chloro-5-methyl-4-phenoxy-phenyl)-N-ethyl-N-methyl-formamidine + TX, N,2-dimethoxy-N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]propanamide + TX, N,N-dimethyl-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]-1,2,4-triazol-3-amine (THESE COMPOUNDS may be prepared from the methods described in WO 2017/055473, WO 2017/055469, WO 2017/093348 and WO 2017/118689) + TX, N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-7,8-difluoro-quinoline-3-carboxamide + TX, N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-1,3-dimethyl-butyl]-7,8-difluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(E)-methoxyiminomethyl]-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX, N-[(Z)-methoxyiminomethyl]-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX, N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]propanamide + TX, N-[2-[2,4-dichlorophenoxy]phenyl]-3-(difluoromethyl)-1-methyl-pyrazole-4-carboxamide + TX, N-[2-[2-chloro-4-(trifluoromethyl)phenoxy]phenyl]-3-(difluoromethyl)-1-methyl-pyrazole-4-carboxamide + TX, N'-[2-chloro-4-(2-fluorophenoxy)-5-methyl-phenyl]-N-ethyl-N-methyl-formamidine (this compound may be prepared from the methods described in WO 2016/202742) + TX, N'-[4-(4,5-dichlorothiazol-2-yl)oxy-2,5-

dimethyl-phenyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-bromo-2-methyl-6-(1-methyl-2-propoxy-ethoxy)-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-bromo-2-methyl-6-(1-methyl-2-propoxy-ethoxy)-3-pyridyl]-N-isopropyl-N-methyl-formamidine (these compounds may be prepared from the methods described in WO2015/155075) + TX, N'-[5-bromo-2-methyl-6-(2-propoxypropoxy)-3-pyridyl]-N-ethyl-N-methyl-formamidine (this compound may be prepared from the methods described in IPCOM000249876D) + TX, N'-[5-bromo-2-methyl-6-[(1R)-1-methyl-2-propoxy-ethoxy]-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-bromo-2-methyl-6-[(1S)-1-methyl-2-propoxy-ethoxy]-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-chloro-2-methyl-6-(1-methyl-2-propoxy-ethoxy)-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N-[N-methoxy-C-methyl-carbonimidoyl]-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide (these compounds may be prepared from the methods described in WO 2018/202428) + TX, N'-[4-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxy-ethyl)-5-methoxy-2-methyl-phenyl]-N-isopropyl-N-methyl-formamidine (these compounds may be prepared from the methods described in WO2018/228896) + TX, nabam + TX, naftalofos + TX, naled + TX, naphthalene + TX, NC-170 + TX, Neodiprion sertifer NPV and N. lecontei NPV + TX, nerolidol + TX, N-ethyl-2-methyl-N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]propanamide + TX, N-ethyl-N'-[5-methoxy-2-methyl-4-[(2-trifluoromethyl)oxetan-2-yl]phenyl]-N-methyl-formamidine + TX, nickel bis(dimethyldithiocarbamate) + TX, niclosamide-olamine + TX, nicotine + TX, nicotine sulfate + TX, nifluridide + TX, nikkomycins + TX, N-isopropyl-N'-[5-methoxy-2-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-phenyl-ethyl)phenyl]-N-methyl-formamidine + TX, nithiazine + TX, nitrapyrin + TX, nitrilacarb + TX, nitrilacarb 1:1 zinc chloride complex + TX, nitrothal-isopropyl + TX, N-methoxy-N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]cyclopropanecarboxamide + TX, N-methyl-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX, N-methyl-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzenecarbothioamide + TX, norbormide + TX, nuarimol + TX, O,O,O',O'-tetrapropyl dithiopyrophosphate + TX, octadeca-2,13-dien-1-yl acetate + TX, octadeca-3,13-dien-1-yl acetate + TX, octhilinone + TX, ofurace + TX, oleic acid + TX, omethoate + TX, orfralure + TX, Orius spp. + TX, oryctalure + TX, orysastrobin + TX, ostramone + TX, oxadixyl + TX, oxamate + TX, oxathiapirolin + TX, oxine-copper + TX, oxolinic acid + TX, oxycarboxin + TX, oxydeprofos + TX, oxydisulfoton + TX, oxytetracycline + TX, paclobutrazole + TX, Paecilomyces fumosoroseus + TX, para-dichlorobenzene + TX, parathion + TX, parathion-methyl + TX, pefurazoate + TX, penconazole + TX, pencycuron + TX, penflufen + TX, penfluron + TX, pentachlorophenol + TX, pentachlorophenyl laurate + TX, penthiopyrad + TX, permethrin + TX, PH 60-38 + TX, phenamacril + TX, phenkapton + TX, phosacetim + TX, phosalone + TX, phosdiphen + TX, phosfolan + TX, phosglycin + TX, phosnichlor + TX, phosphamidon + TX, phosphine + TX, phosphorus + TX, phoxim-methyl + TX, phthalide + TX, Phytoseiulus persimilis + TX, picarbutrazox + TX, picaridin + TX, picoxystrobin + TX, pindone + TX, piperazine + TX, piperonyl butoxide + TX, piprotal + TX, pirimetaphos + TX, polychlorodicyclopentadiene isomers + TX, polychloroterpenes + TX, polynactins + TX, polyoxins + TX, potassium arsenite + TX, potassium ethylxanthate + TX, potassium hydroxyquinoline sulfate + TX, potassium thiocyanate + TX, pp'-DDT + TX, precocene I + TX, precocene II + TX, precocene III + TX, primidophos + TX, probenazole + TX, prochloraz + TX, proclonol + TX, procymidone + TX, profluthrin + TX, promacyl + TX, promecarb + TX, propamocarb + TX, propiconazole + TX, propineb + TX, propoxur + TX, propyl isomer + TX, proquinazid + TX, prothidathion + TX, prothioconazole + TX, prothiofos + TX, prothoate + TX, pydiflumetofen + TX, pyraclostrobin + TX, pyrametostrobin + TX, pyraoxystrobin + TX, pyrapropoyne + TX, pyraziflumid + TX,

Aspergillus flavus AF36 (AF36®) + TX, *Aspergillus flavus* NRRL 21882 (Aflaguard®) + TX, *Aspergillus* spp. + TX, *Aureobasidium pullulans* + TX, *Azospirillum* (MicroAZ®, TAZO B®) + TX, *Azotobacter* + TX, *Azotobacter chroococcum* (Azotomeal®) + TX, *Azotobacter* cysts (Bionatural Blooming Blossoms®) + TX, *Bacillus amyloliquefaciens* + TX, *Bacillus cereus* + TX, *Bacillus chitosporus* strain AQ746 + TX, *Bacillus chitosporus* strain CM-1 + TX, *Bacillus circulans* + TX, *Bacillus firmus* (BioSafe®, BioNem-WP®) in particular strain CNMC 1-1582 (e.g. VOTIVO® from BASF SE) + TX, *Bacillus licheniformis* strain 3086 (EcoGuard®, Green Releaf®) + TX, *Bacillus licheniformis* strain HB-2 (Biostart™ formerly RhizoBoost®) + TX, *Bacillus macerans* + TX, *Bacillus marismortui* + TX, *Bacillus megaterium* + TX, *Bacillus mycoides* strain AQ726 + TX, *Bacillus papillae* (Milky Spore Powder®) + TX, *Bacillus pumilus* spp. + TX, *Bacillus pumilus* strain AQ717 + TX, *Bacillus pumilus* strain GB34 (Yield Shield®) + TX, *Bacillus pumilus* strain QST 2808 (Sonata®, Ballad Plus®) + TX, *Bacillus sphaericus* (VectoLex®) + TX, *Bacillus* spp. + TX, *Bacillus* spp. strain AQ175 + TX, *Bacillus* spp. strain AQ177 + TX, *Bacillus* spp. strain AQ178 + TX, *Bacillus subtilis* strain AQ153 + TX, *Bacillus subtilis* strain AQ743 + TX, *Bacillus subtilis* strain QST 713 (CEASE®, Serenade®, Rhapsody®) + TX, *Bacillus subtilis* strain QST 714 (JAZZ®) + TX, *Bacillus subtilis* strain QST3002 + TX, *Bacillus subtilis* strain QST3004 + TX, *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 (Taegro®, Rhizopro®) + TX, *Bacillus thuringiensis* aizawai GC 91 (Agree®) + TX, *Bacillus thuringiensis* Cry 2Ae + TX, *Bacillus thuringiensis* Cry1Ab + TX, *Bacillus thuringiensis israelensis* (BMP123®, Aquabac®, VectoBac®) + TX, *Bacillus thuringiensis kurstaki* (Javelin®, Deliver®, CryMax®, Bonide®, Scutella WP®, Turilav WP®, Astuto®, Dipel WP®, Biobit®, Foray®) + TX, *Bacillus thuringiensis kurstaki* BMP 123 (Baritone®) + TX, *Bacillus thuringiensis kurstaki* HD-1 (Bioprotec-CAF / 3P®) + TX, *Bacillus thuringiensis* strain AQ52 + TX, *Bacillus thuringiensis* strain BD#32 + TX, *Bacillus thuringiensis tenebrionis* (Novodor®, BtBooster) + TX, *Bacillus thuringiensis* var. *aizawai* (XenTari®, DiPel®) + TX, *bacteria* spp. (GROWMEND®, GROWSWEET®, Shootup®) + TX, *bacteriophage* of *Clavipacter michiganensis* (AgriPhage®, Bakflor®) + TX, *Beauveria bassiana* (Beaugenic®, Brocaril WP®) + TX, *Beauveria bassiana* GHA (Mycotrol ES®, Mycotrol O®, BotaniGuard®) + TX, *Beauveria brongniartii* (Engerlingspilz®, Schweizer Beauveria®, Melocont®) + TX, *Beauveria* spp. + TX, *Botrytis cinerea* + TX, *Bradyrhizobium japonicum* (TerraMax®) + TX, *Brevibacillus brevis* + TX, *Burkholderia cepacia* (Deny®, Intercept®, Blue Circle®) + TX, *Burkholderia gladii* + TX, *Burkholderia gladioli* + TX, *Burkholderia* spp. + TX, *Canadian thistle fungus* (CBH Canadian Bioherbicide®) + TX, *Candida butyri* + TX, *Candida famata* + TX, *Candida fructus* + TX, *Candida glabrata* + TX, *Candida guilliermondii* + TX, *Candida melibiosica* + TX, *Candida oleophila* strain O + TX, *Candida parapsilosis* + TX, *Candida pelliculosa* + TX, *Candida pulcherrima* + TX, *Candida reukaufii* + TX, *Candida saitoana* (Bio-Coat®, Biocure®) + TX, *Candida sake* + TX, *Candida* spp. + TX, *Candida tenuis* + TX, *Cedecea davisae* + TX, *Cellulomonas flavigena* + TX, *Chaetomium cochliodes* (Nova-Cide®) + TX, *Chaetomium globosum* (Nova-Cide®) + TX, *Chromobacterium subtsugae* strain PRAA4-1T (Grandevo®) + TX, *Cladosporium chlorocephalum* + TX, *Cladosporium cladosporioides* + TX, *Cladosporium oxysporum* + TX, *Cladosporium* spp. + TX, *Cladosporium tenuissimum* + TX, *Clonostachys rosea* (EndoFine®) + TX, *Colletotrichum acutatum* + TX, *Coniothyrium minitans* (Cotans WG®) + TX, *Coniothyrium* spp. + TX, *Cryptococcus albidus* (YIELDPLUS®) + TX, *Cryptococcus humicola* + TX, *Cryptococcus infirmo-miniatius* + TX, *Cryptococcus laurentii* + TX, *Cryptophlebia leucotreta* granulovirus (Cryptex®) + TX, *Cupriavidus campinensis* + TX, *Cydia pomonella* granulovirus (CYD-X®, Madex®, Madex® Plus, Madex Max, Carpovirusine®) + TX, *Cylindrobasidium laeve*

(Stumpout®) + TX, *Cylindrocladium* + TX, *Debaryomyces hansenii* + TX, *Drechslera hawaiiensis* + TX, *Enterobacter cloacae* + TX, *Enterobacteriaceae* + TX, *Entomophthora virulenta* (Vektor®) + TX, *Epicoccum nigrum* + TX, *Epicoccum purpurascens* + TX, *Epicoccum* spp. + TX, *Filobasidium floriforme* + TX, *Fusarium acuminatum* + TX, *Fusarium chlamydosporum* + TX, *Fusarium oxysporum* (Fusaclean®, Biofox C®) + TX, *Fusarium proliferatum* + TX, *Fusarium* spp. + TX, *Galactomyces geotrichum* + TX, *Gliocladium catenulatum* (Primastop®, Prestop®) + TX, *Gliocladium roseum* + TX, *Gliocladium* spp. (SoilGard®) + TX, *Gliocladium virens* (Soilgard®) + TX, *Granulovirus* (Granupom®) + TX, *Halobacillus halophilus* + TX, *Halobacillus litoralis* + TX, *Halobacillus trueperi* + TX, *Halomonas* spp. + TX, *Halomonas subglaciescola* + TX, *Halovibrio variabilis* + TX, *Hanseniaspora uvarum* + TX, *Helicoverpa armigera* nucleopolyhedrovirus (Helicovex®) + TX, *Helicoverpa zea* nuclear polyhedrosis virus (Gemstar®) + TX, *Isaria fumosorosea* (previously known as *Paecilomyces fumosoroseus* strain, PFR-97®, PreFeRa®) + TX, Isoflavone formononetin (Myconate®) + TX, *Kloeckera apiculata* + TX, *Kloeckera* spp. + TX, *Lagenidium giganteum* (Laginex®) + TX, *Lecanicillium lecanii* (formerly known as *Verticillium lecanii* (Mycotal®) conidia of strain KV01 (e.g. Vertalec® by Koppert/Arysta) + TX, *Lecanicillium longisporum* (Vertiblast®) + TX, *Lecanicillium muscarium* (Vertikil®) + TX, *Lymantria Dispar* nucleopolyhedrosis virus (Disparvirus®) + TX, *Marinococcus halophilus* + TX, *Meira geulakonigii* + TX, *Metarhizium anisopliae* (Destruxin WP®) + TX, *Metarhizium anisopliae* (Met52®) + TX, *Metschnikowia fruticola* (Shemer®) + TX, *Metschnikowia pulcherrima* + TX, *Microdochium dimerum* (Antibot®) + TX, *Micromonospora coerules* + TX, *Microsphaeropsis ochracea* + TX, *Muscodor albus* 620 (Muscudor®) + TX, *Muscodor roseus* in particular strain A3-5 (Accession No. NRRL 30548) + TX, *Mycorrhizae* spp. (AMykor®, Root Maximizer®) + TX, *Myrothecium verrucaria* strain AARC-0255 (DiTera®, BROS PLUS®) + TX, *Ophiostoma piliferum* strain D97 (Sylvanex®) + TX, *Paecilomyces farinosus* + TX, *Paecilomyces lilacinus* strain 251 (MeloCon WG®) + TX, *Paecilomyces linacinus* (Biostat WP®) + TX, *Paenibacillus polymyxa* + TX, *Pantoea agglomerans* (BlightBan C9-1®) + TX, *Pantoea* spp. + TX, *Pasteuria nishizawae* in particular strain Pn1 (CLARIVA from Syngenta/ChemChina); + TX, *Pasteuria* spp. (Econem®) + TX, *Penicillium aurantiogriseum* + TX, *Penicillium billai* (Jumpstart®, TagTeam®) + TX, *Penicillium brevicompactum* + TX, *Penicillium frequentans* + TX, *Penicillium griseofulvum* + TX, *Penicillium purpurogenum* + TX, *Penicillium* spp. + TX, *Penicillium viridicatum* + TX, *Phlebiopsis gigantea* (Rotstop®) + TX, phosphate solubilizing bacteria (Phosphomeal®) + TX, *Phytophthora cryptogea* + TX, *Phytophthora palmivora* (Devine®) + TX, *Pichia anomala* + TX, *Pichia guilliermondii* + TX, *Pichia membranaefaciens* + TX, *Pichia onychis* + TX, *Pichia stipites* + TX, *Pseudomonas aeruginosa* + TX, *Pseudomonas aureofaciens* (Spot-Less Biofungicide®) + TX, *Pseudomonas cepacia* + TX, *Pseudomonas chlororaphis* (AtEze®) + TX, *Pseudomonas corrugate* + TX, *Pseudomonas fluorescens* (Zequanox®) + TX, *Pseudomonas fluorescens* strain A506 (BlightBan A506®) + TX, *Pseudomonas putida* + TX, *Pseudomonas reactans* + TX, *Pseudomonas* spp. + TX, *Pseudomonas syringae* (Bio-Save®) + TX, *Pseudomonas viridiflava* + TX, *Pseudozyma flocculosa* strain PF-A22 UL (Sporodex L®) + TX, *Puccinia canaliculata* + TX, *Puccinia thlaspeos* (Wood Warrior®) + TX, *Pythium paroecandrum* + TX, *Pythium oligandrum* (Polygandron®, Polyversum®) + TX, *Pythium periplocum* + TX, *Rhanella aquatilis* + TX, *Rhanella* spp. + TX, *Rhizobia* (Dormal®, Vault®) + TX, *Rhizoctonia* + TX, *Rhodococcus globerulus* strain AQ719 + TX, *Rhodosporidium diobovatum* + TX, *Rhodosporidium toruloides* + TX, *Rhodotorula glutinis* + TX, *Rhodotorula graminis* + TX, *Rhodotorula mucilagnosa* + TX, *Rhodotorula rubra* + TX, *Rhodotorula* spp.

+ TX, *Saccharomyces cerevisiae* + TX, *Salinococcus roseus* + TX, *Sclerotinia minor* (SARRITOR®) + TX, *Sclerotinia minor* + TX, *Scytalidium* spp. + TX, *Scytalidium uredinicola* + TX, *Serratia marcescens* + TX, *Serratia plymuthica* + TX, *Serratia* spp. + TX, *Sordaria fimicola* + TX, *Spodoptera exigua* nuclear polyhedrosis virus (Spod-X®, Spexit®) + TX, *Spodoptera littoralis* nucleopolyhedrovirus (Littovir®) + TX, *Sporobolomyces roseus* + TX, *Stenotrophomonas maltophilia* + TX, *Streptomyces albaduncus* + TX, *Streptomyces exfoliates* + TX, *Streptomyces galbus* + TX, *Streptomyces griseoplanus* + TX, *Streptomyces griseoviridis* (Mycostop®) + TX, *Streptomyces hygroscopicus* + TX, *Streptomyces lydicus* (Actinovate®) + TX, *Streptomyces lydicus* WYEC-108 (ActinoGrow®) + TX, *Streptomyces violaceus* + TX, *Tilletiopsis minor* + TX, *Tilletiopsis* spp. + TX, *Trichoderma asperellum* (T34 Biocontrol®) + TX, *Trichoderma atroviride* (Plantmate®) + TX, *Trichoderma gamsii* (Tenet®) + TX, *Trichoderma hamatum* TH 382 + TX, *Trichoderma harzianum* rifai (Mycostar®) + TX, *Trichoderma harzianum* T-22 (Trianum-P®, PlantShield HC®, RootShield®, Trianum-G® + TX, *Trichoderma harzianum* T-39 (Trichodex®) + TX, *Trichoderma inhamatum* + TX, *Trichoderma koningii* + TX, *Trichoderma lignorum* + TX, *Trichoderma longibrachiatum* + TX, *Trichoderma polysporum* (Binab T®) + TX, *Trichoderma* spp. LC 52 (Sentinel®) + TX, *Trichoderma taxi* + TX, *Trichoderma virens* (formerly *Gliocladium virens* GL-21) (SoilGuard®) + TX, *Trichoderma virens* + TX, *Trichoderma viride* + TX, *Trichoderma viride* strain ICC 080 (Remedier®) + TX, *Trichosporon pullulans* + TX, *Trichosporon* spp. + TX, *Trichothecium roseum* + TX, *Trichothecium* spp. + TX, *Typhula phacorrhiza* strain 94670 + TX, *Typhula phacorrhiza* strain 94671 + TX, *Ulocladium atrum* + TX, *Ulocladium oudemansii* (Botry-Zen®) + TX, *Ustilago maydis* + TX, various bacteria and supplementary micronutrients (Natural II®) + TX, various fungi (Millennium Microbes®) + TX, *Verticillium chlamydosporium* + TX, Vip3Aa20 (VIPTera®) + TX, *Virgibacillus marismortui* + TX, *Xanthomonas campestris* pv. *Poae* (Camperico®) + TX, *Xenorhabdus bovienii* + TX, *Xenorhabdus nematophilus* + TX;

AGNIQUE® MMF + TX, azadirachtin (Plasma Neem Oil®, AzaGuard®, MeemAza®, Molt-X® e.g. AZATIN XL from Certis, US) + TX, Botanical IGR (Neemazad®, Neemix®) + TX, BugOil® + TX, canola oil (Lilly Miller Vegol®) + TX, *Chenopodium ambrosioides* near *ambrosioides* (Requiem®) + TX, *Chrysanthemum* extract (Crisant®) + TX, essential oils of Labiatae (Botania®) + TX, extract of neem oil (Trilogy®) + TX, extracts of clove rosemary peppermint and thyme oil (Garden insect killer®) + TX, garlic + TX, Glycinebetaine (Greenstim®) + TX, kaolin (Screen®) + TX, lemongrass oil (GreenMatch®) + TX, *Melaleuca alternifolia* extract (also called tea tree oil) (Timorex Gold®) + TX, mixture of clove peppermint garlic oil and mint (Soil Shot®) + TX, mixture of clove rosemary and peppermint extract (EF 400®) + TX, mixture of rosemary sesame peppermint thyme and cinnamon extracts (EF 300®) + TX, neem oil + TX, *Nepeta cataria* (Catnip oil) + TX, *Nepeta catarina* + TX, nicotine + TX, oregano oil (MossBuster®) + TX, Pedaliaceae oil (Nematon®) + TX, pine oil (Retenol®) + TX, pyrethrum + TX, *Quillaja saponaria* (NemaQ®) + TX, *Reynoutria sachalinensis* (Regalia®, Sakalia®) + TX, rotenone (Eco Roten®) + TX, Rutaceae plant extract (Soleo®) + TX, soybean oil (Ortho ecosense®) + TX, storage glucan of brown algae (Laminarin®) + TX, thyme oil + TX;

(E,Z)-7,9-Dodecadien-1-yl acetate + TX, (E,Z,Z)-3,8,11 Tetradecatrienyl acetate + TX, (Z,Z,E)-7,11,13-Hexadecatrienal + TX, 2-Methyl-1-butanol + TX, Biolure® + TX, blackheaded fireworm pheromone (3M Sprayable Blackheaded Fireworm Pheromone®) + TX, Calcium acetate + TX, Check-Mate® + TX, Codling Moth Pheromone (Paramount dispenser-(CM)/ Isomate C-Plus®) + TX, Entostat powder (extract from palm tree) (Exosex CM®) + TX, Grape Berry Moth Pheromone (3M MEC-GBM Sprayable

Pheromone®) + TX, Lavandulyl senecioate + TX, Leafroller pheromone (3M MEC – LR Sprayable Pheromone®) + TX, Muscamone (Snip7 Fly Bait® + TX, Oriental Fruit Moth Pheromone (3M oriental fruit moth sprayable pheromone®) + TX, Peachtree Borer Pheromone (Isomate-P®) + TX, Scenturion® + TX, Starbar Premium Fly Bait®) + TX, Tomato Pinworm Pheromone (3M Sprayable pheromone®) + TX;

Acerophagus papaya + TX, Adalia bipunctata (Adalia-System®) + TX, Adalia bipunctata (Adaline®) + TX, Adalia bipunctata (Aphidalia®) + TX, Ageniaspis citricola + TX, Ageniaspis fuscicollis + TX, Amblyseius andersoni (Anderline®, Andersoni-System®) + TX, Amblyseius californicus (Amblyline®, Spical®) + TX, Amblyseius cucumeris (Thripex®, Bugline cucumeris®) + TX, Amblyseius fallacis (Fallacis®) + TX, Amblyseius swirskii (Bugline swirskii®, Swirskii-Mite®) + TX, Amblyseius womersleyi (WomerMite®) + TX, Amitus hesperidum + TX, Anagrus atomus + TX, Anagrus fusciventris + TX, Anagrus kamali + TX, Anagrus loeckii + TX, Anagrus pseudococchi (Citripar®) + TX, Anicetus benefices + TX, Anisopteromalus calandrae + TX, Anthocoris nemoralis (Anthocoris-System®) + TX, Aphelinus abdominalis (Apheline®, Aphiline®), + TX, Aphelinus asychis + TX, Aphidius colemani (Aphipar®) + TX, Aphidius ervi (Aphelinus-System®) + TX, Aphidius ervi (Ervipar®) + TX, Aphidius gifuensis + TX, Aphidius matricariae (Aphipar-M®) + TX, Aphidoletes aphidimyza (Aphidend®, Aphidoline®) + TX, Aphytis lingnanensis + TX, Aphytis melinus + TX, Aprostocetus hagenowii + TX, Atheta coriaria (Staphyline®) + TX, Bombus spp. + TX, Bombus terrestris (Beeline®, Tripol®) + TX, Bombus terrestris (Natupol Beehive®) + TX, Cephalonomia stephanoderis + TX, Chilocorus nigritus + TX, Chrysoperla carnea (Chrysoline®, Chrysopa®) + TX, Chrysoperla rufilabris + TX, Cirrospilus ingenuus + TX, Cirrospilus quadristriatus + TX, Citrostichus phyllocnistoides + TX, Closterocerus chamaeleon + TX, Closterocerus spp. + TX, Coccidoxenoides perminutus (Planopar®) + TX, Coccophagus cowperi + TX, Coccophagus lycimnia + TX, Cotesia flavipes + TX, Cotesia plutellae + TX, Cryptolaemus montrouzieri (Cryptobug®, Cryptoline®) + TX, Cybocephalus nipponicus + TX, Dacnusa sibirica (Minusa®, DacDigline®, Minex®) + TX, Delphastus catalinae (Delphastus®) + TX, Delphastus pusillus + TX, Diachasmimorpha krausii + TX, Diachasmimorpha longicaudata + TX, Diaparsis jucunda + TX, Diaphorencyrtus aligarhensis + TX, Diglyphus isaea (Diminex®, Miglyphus®, Digline®) + TX, Diversinervus spp. + TX, Encarsia citrina + TX, Encarsia formosa (Encarsia max®, Encarline®, EnStrip®) + TX, Encarsia guadeloupae + TX, Encarsia haitiensis + TX, Episyrphus balteatus (Syrphidend®) + TX, Eretmoceris siphonini + TX, Eretmoceris californicus + TX, Eretmoceris eremicus (Enermix®, Ercal®, Eretline e®, Bemimix®) + TX, Eretmoceris hayati + TX, Eretmoceris mundus (Bemipar®, Eretline m®) + TX, Eretmoceris siphonini + TX, Exochomus quadripustulatus + TX, Feltiella acarisuga (Feltiline®) + TX, Feltiella acarisuga (Spidend®) + TX, Fopius arisanus + TX, Fopius ceratitivorus + TX, Formononetin (Wirless Beehome®) + TX, Franklinothrips vespiformis (Vespop®) + TX, Galendromus occidentalis + TX, Goniozus legneri + TX, Habrobracon hebetor + TX, Harmonia axyridis (HarmoBeetle®) + TX, Heterorhabditis bacteriophora (NemaShield HB®, Nemaseek®, Terranem-Nam®, Terranem®, Larvanem®, B-Green®, NemAttack®, Nematop®) + TX, Heterorhabditis megidis (Nemasys H®, BioNem H®, Exhibitline hm®, Larvanem-M®) + TX, Heterorhabditis spp. (Lawn Patrol®) + TX, Hippodamia convergens + TX, Hypoaspis aculeifer (Aculeifer-System®, Entomite-A®) + TX, Hypoaspis miles (Hypoline m®, Entomite-M®) + TX, Lbalia leucospoides + TX, Lecanoideus floccissimus + TX, Lemophagus errabundus + TX, Leptomastidea abnormis + TX, Leptomastix dactylopii (Leptopar®) + TX, Leptomastix epona + TX, Lindorus lophanthae + TX, Lipolexis oregmae +

TX, *Lucilia caesar* (NatuFly®) + TX, *Lysiphlebus testaceipes* + TX, *Macrolophus caliginosus* (Mirical-N®), *Macroline c*®, *Mirical*®) + TX, *Mesoseiulus longipes* + TX, *Metaphycus flavus* + TX, *Metaphycus lounsburyi* + TX, *Micromus angulatus* (Milacewing®) + TX, *Microterys flavus* + TX, *Muscidifurax raptorellus* and *Spalangia cameroni* (Biopar®) + TX, *Neodryinus typhlocybae* + TX, *Neoseiulus californicus* + TX, *Neoseiulus cucumeris* (THRYPEX®) + TX, *Neoseiulus fallacis* + TX, *Nesideocoris tenuis* (NesidioBug®, Nesibug®) + TX, *Ophyra aenescens* (Biofly®) + TX, *Orius insidiosus* (Thripor-l®, Oriline i®) + TX, *Orius laevigatus* (Thripor-L®, Oriline l®) + TX, *Orius majusculus* (Oriline m®) + TX, *Orius strigicollis* (Thripor-S®) + TX, *Pauesia juniperorum* + TX, *Pediobius foveolatus* + TX, *Phasmarhabditis hermaphrodita* (Nemaslug®) + TX, *Phymastichus coffea* + TX, *Phytoseiulus macropilus* + TX, *Phytoseiulus persimilis* (Spidex®, Phytoline p®) + TX, *Podisus maculiventris* (Podisus®) + TX, *Pseudacteon curvatus* + TX, *Pseudacteon obtusus* + TX, *Pseudacteon tricusps* + TX, *Pseudaphycus maculipennis* + TX, *Pseudleptomastix mexicana* + TX, *Psyllaephagus pilosus* + TX, *Psytalia concolor* (complex) + TX, *Quadrastichus* spp. + TX, *Rhyzobius lophanthae* + TX, *Rodolia cardinalis* + TX, *Rumina decollate* + TX, *Semielacher petiolatus* + TX, *Sitobion avenae* (Ervibank®) + TX, *Steinernema carpocapsae* (Nematac C®, Millenium®, BioNem C®, NemAttack®, Nemastar®, Capsanem®) + TX, *Steinernema feltiae* (NemaShield®, Nemasys F®, BioNem F®, Steinernema-System®, NemAttack®, Nemaplus®, Exhibitline sf®, Scia-rid®, Entonem®) + TX, *Steinernema kraussei* (Nemasys L®, BioNem L®, Exhibitline srb®) + TX, *Steinernema riobrave* (BioVector®, BioVektor®) + TX, *Steinernema scapterisci* (Nematac S®) + TX, *Steinernema* spp. + TX, *Steinernematid* spp. (Guardian Nematodes®) + TX, *Stethorus punctillum* (Stethorus®) + TX, *Tamarixia radiata* + TX, *Tetrastichus setifer* + TX, *Thripobius semiluteus* + TX, *Torymus sinensis* + TX, *Trichogramma brassicae* (Tricholine b®) + TX, *Trichogramma brassicae* (Tricho-Strip®) + TX, *Trichogramma evanescens* + TX, *Trichogramma minutum* + TX, *Trichogramma ostrinae* + TX, *Trichogramma platneri* + TX, *Trichogramma pretiosum* + TX, *Xanthopimpla stemmator* + TX;

abscisic acid + TX, *Aminomite*® + TX, *BioGain*® + TX, *bioSea*® + TX, CAS Number: 2643947-26-4 + TX, *Chondrostereum purpureum* (Chontrol Paste®) + TX, *Colletotrichum gloeosporioides* (Collego®) + TX, *Copper Octanoate* (Cueva®) + TX, *Delta traps* (Trapline d®) + TX, *Erwinia amylovora* (Harpin) (ProAct®, Ni-HIBIT Gold CST®) + TX, fatty acids derived from a natural by-product of extra virgin olive oil (FLIPPER®) + TX, *Ferri-phosphate* (Ferramol®) + TX, *Funnel traps* (Trapline y®) + TX, *Gallex*® + TX, *Grower's Secret*® + TX, *Homo-brassonolide* + TX, *Iron Phosphate* (Lilly Miller Worry Free Ferramol Slug & Snail Bait®) + TX, *MCP hail trap* (Trapline f®) + TX, *Microctonus hyperodae* + TX, *Mycoleptodiscus terrestris* (Des-X®) + TX, *Nosema locustae* (Semaspore Organic Grasshopper Control®) + TX, *Pheromone trap* (Thripline ams®) + TX, *potassium bicarbonate* (MilStop®) + TX, *potassium iodide* + *potassiumthiocyanate* (Enzicur®) + TX, *potassium salts of fatty acids* (Sanova®) + TX, *potassium silicate solution* (Sil-Matrix®) + TX, *Spider venom* + TX, *Sticky traps* (Trapline YF®, Rebell Amarillo®) + TX, *SuffOil-X*® + TX, *Traps* (Takitrapiine y + b®) + TX;

Bacillus mojavenensis strain R3B (Accession No. NCAIM (P) B001389) (WO 2013/034938) from Certis USA LLC + TX, *Bacillus pumilus*, in particular strain BU F-33, having NRRL Accession No. 50185 (CARTISSA® from BASF, EPA Reg. No. 71840-19) + TX, *Bacillus subtilis* CX-9060 from Certis USA LLC, *Bacillus* sp., in particular strain D747 (available as DOUBLE NICKEL® from Kumiai Chemical Industry Co., Ltd.), having Accession No. FERM BP-8234, U.S. Patent No. 7,094,592 + TX, *Bacillus subtilis* strain BU1814, (VELONDIS® PLUS, VELONDIS® FLEX and VELONDIS® EXTRA from BASF

SE) + TX, *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 having Accession No. DSM 10271 (available from Novozymes as TAEGRO® or TAEGRO® ECO (EPA Registration No. 70127-5)) + TX, *Bacillus subtilis*, in particular strain QST713/AQ713 (having NRRL Accession No. B-21661 and described in U.S. Patent No. 6,060,051, available as SERENADE® OPTI or SERENADE® ASO from Bayer CropScience LP, US) + TX, *Paenibacillus polymyxa*, in particular strain AC-1 (e.g. TOPSEED® from Green Biotech Company Ltd.) + TX, *Paenibacillus* sp. strain having Accession No. NRRL B-50972 or Accession No. NRRL B-67129, WO 2016/154297 + TX, *Pantoea agglomerans*, in particular strain E325 (Accession No. NRRL B-21856) (available as BLOOMTIME BIOLOGICAL™ FD BIOPESTICIDE from Northwest Agri Products) + TX, *Pseudomonas proradix* (e.g. PRORADIX® from Sourcon Padena) + TX;

Aureobasidium pullulans, in particular blastospores of strain DSM14940, blastospores of strain DSM 14941 or mixtures of blastospores of strains DSM14940 and DSM14941 (e.g., BOTECTOR® and BLOSSOM PROTECT® from bio-ferm, CH) + TX, *Pseudozyma aphidis* (as disclosed in WO2011/151819 by Yissum Research Development Company of the Hebrew University of Jerusalem) + TX, *Saccharomyces cerevisiae*, in particular strains CNCM No. 1-3936, CNCM No. 1-3937, CNCM No. 1-3938 or CNCM No. 1-3939 (WO 2010/086790) from Lesaffre et Compagnie, FR + TX;

Agrobacterium radiobacter strain K84 (e.g. GALLTROL-A® from AgBioChem, CA) + TX, *Bacillus amyloliquefaciens* isolate B246 (e.g. AVOGREEN™ from University of Pretoria) + TX, *Bacillus amyloliquefaciens* strain F727 (also known as strain MBI110) (NRRL Accession No. B-50768, WO 2014/028521) (STARGUS® from Marrone Bio Innovations) + TX, *Bacillus amyloliquefaciens* strain FZB42, Accession No. DSM 23117 (available as RHIZOVITAL® from ABiTEP, DE) + TX, *Bacillus amyloliquefaciens*, in particular strain D747 (available as Double Nickel™ from Kumiai Chemical Industry Co., Ltd., having accession number FERM BP-8234, US Patent No. 7,094,592) + TX, *Bacillus licheniformis* FMCH001 and *Bacillus subtilis* FMCH002 (QUARTZO® (WG) and PRESENCE® (WP) from FMC Corporation) + TX, *Bacillus licheniformis*, in particular strain SB3086, having Accession No. ATCC 55406, WO 2003/000051 (available as ECOGUARD® Biofungicide and GREEN RELEAF™ from Novozymes) + TX, *Bacillus methylotrophicus* strain BAC-9912 (from Chinese Academy of Sciences' Institute of Applied Ecology) + TX, *Bacillus mycoides*, isolate, having Accession No. B-30890 (available as BMJ TGAi® or WG and LifeGard™ from Certis USA LLC) + TX, *Bacillus pumilus*, in particular strain GB34 (available as Yield Shield® from Bayer AG, DE) + TX, *Bacillus pumilus*, in particular strain QST2808 (available as SONATA® from Bayer CropScience LP, US, having Accession No. NRRL B-30087 and described in U.S. Patent No. 6,245,551) + TX, *Bacillus subtilis* CX-9060 from Certis USA LLC + TX, *Bacillus subtilis* IAB/BS03 (AVIV™ from STK Bio-Ag Technologies, PORTENTO® from Idai Nature) + TX, *Bacillus subtilis* KTSB strain (FOLIACTIVE® from Donaghys) + TX, *Bacillus subtilis* strain BU1814, (available as VELONDIS® PLUS, VELONDIS® FLEX and VELONDIS® EXTRA from BASF SE) + TX, *Bacillus subtilis* strain GB03 (available as Kodiak® from Bayer AG, DE) + TX, *Bacillus subtilis* strain MBI 600 (available as SUBTILEX from BASF SE), having Accession Number NRRL B-50595, U.S. Patent No. 5,061,495 + TX, *Bacillus subtilis* strain Y1336 (available as BIOBAC® WP from Bion-Tech, Taiwan, registered as a biological fungicide in Taiwan under Registration Nos. 4764, 5454, 5096 and 5277) + TX, *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 having Accession No. DSM 10271 (available from Novozymes as TAEGRO® or TAEGRO® ECO (EPA Registration No. 70127-5)) + TX, *Bacillus subtilis* Y1336 (available as BIOBAC® WP from Bion-Tech, Taiwan, registered as a biological

fungicide in Taiwan under Registration Nos. 4764, 5454, 5096 and 5277) + TX, *Paenibacillus epiphyticus* (WO 2016/020371) from BASF SE + TX, *Paenibacillus polymyxa* ssp. *plantarum* (WO 2016/020371) from BASF SE + TX, *Paenibacillus* sp. strain having Accession No. NRRL B-50972 or Accession No. NRRL B-67129, WO 2016/154297 + TX, *Pseudomonas chlororaphis* strain AFS009, having Accession No. NRRL B-50897, WO 2017/019448 (e.g., HOWLER™ and ZIO® from AgBiome Innovations, US) + TX, *Pseudomonas chlororaphis*, in particular strain MA342 (e.g. CEDOMON®, CERALL®, and CEDRESS® by Bioagri and Koppert) + TX, *Pseudomonas fluorescens* strain A506 (e.g. BLIGHTBAN® A506 by NuFarm) + TX, *Pseudomonas proradix* (e.g. PRORADIX® from Sourcon Padena) + TX, *Streptomyces griseoviridis* strain K61 (also known as *Streptomyces galbus* strain K61) (Accession No. DSM 7206) (MYCOSTOP® from Verdera, PREFENCE® from BioWorks, cf. Crop Protection 2006, 25, 468-475) + TX, *Streptomyces lydicus* strain WYEC108 (also known as *Streptomyces lydicus* strain WYCD108US) (ACTINO-IRON® and ACTINOVATE® from Novozymes) + TX;

Trichoderma atroviride strain T11 (IMI352941/ CECT20498) + TX, *Ampelomyces quisqualis* strain AQ10, having Accession No. CNCM 1-807 (e.g., AQ 10® by IntrachemBio Italia) + TX, *Ampelomyces quisqualis*, in particular strain AQ 10 (e.g. AQ 10® by IntrachemBio Italia) + TX, *Aspergillus flavus* strain NRRL 21882 (products known as AFLA-GUARD® from Syngenta/ChemChina) + TX, *Aureobasidium pullulans*, in particular blastospores of strain DSM 14941 + TX, *Aureobasidium pullulans*, in particular blastospores of strain DSM14940 + TX, *Aureobasidium pullulans*, in particular mixtures of blastospores of strains DSM14940 and DSM 14941 (e.g. Botector® by bio-ferm, CH) + TX, *Chaetomium cupreum* (Accession No. CABI 353812) (e.g. BLOKUPRUM™ by AgriLife) + TX, *Chaetomium globosum* (available as RIVADIOM® by Rivale) + TX, *Cladosporium cladosporioides*, strain H39, having Accession No. CBS122244, US 2010/0291039 (by Stichting Dienst Landbouwkundig Onderzoek) + TX, *Coniothyrium minitans*, in particular strain CON/M/91-8 (Accession No. DSM9660, e.g. Contans ® from Bayer CropScience Biologics GmbH) + TX, *Cryptococcus flavescens*, strain 3C (NRRL Y-50378), + TX, *Dactylaria candida*, *Dilophosphora alopecuri* (available as TWIST FUNGUS®), *Fusarium oxysporum*, strain Fo47 (available as FUSACLEAN® by Natural Plant Protection) + TX, *Gliocladium catenulatum* (Synonym: *Clonostachys rosea* f. *catenulate*) strain J1446 (e.g. Prestop ® by Lallemand) + TX, *Gliocladium roseum* (also known as *Clonostachys rosea* f *rosea*) strain IK726 (Jensen DF, et al. Development of a biocontrol agent for plant disease control with special emphasis on the near commercial fungal antagonist *Clonostachys rosea* strain 'IK726', Australasian Plant Pathol. 2007,36(2):95-101) + TX, *Gliocladium roseum* (also known as *Clonostachys rosea* f *rosea*), in particular strain 321U from Adjuvants Plus, strain ACM941 as disclosed in Xue A.G. (Efficacy of *Clonostachys rosea* strain ACM941 and fungicide seed treatments for controlling the root rot complex of field pea, Can Jour Plant Sci 2003, 83(3): 519-524) + TX, *Metschnikowia fructicola*, in particular strain NRRL Y-30752 + TX, *Microsphaeropsis ochracea*, *Penicillium steckii* (DSM 27859, WO 2015/067800) from BASF SE + TX, mixtures of *Trichoderma asperellum* strain ICC 012 (also known as *Trichoderma harzianum* ICC012), having Accession No. CABI CC IMI 392716 and *Trichoderma gamsii* (formerly *T. viride*) strain ICC 080, having Accession No. IMI 392151 (e.g., BIO-TAM™ from Isagro USA, Inc. or BIODERMA® by Agrobiosol de Mexico, S.A. de C.V.) + TX, *Penicillium vermiculatum* + TX, *Phlebiopsis gigantea* strain VRA 1992 (ROTSTOP® C from Danstar Ferment) + TX, *Pseudozyma flocculosa*, strain PF-A22 UL (available as SPORODEX® L by Plant Products Co., CA) + TX, *Saccharomyces cerevisiae* strain

LAS117 cell walls (CEREVISANE® from Lesaffre, ROMEO® from BASF SE) + TX, *Saccharomyces cerevisiae* strains CNCM No. 1-3936, CNCM No. 1-3937, CNCM No. 1-3938, CNCM No. 1-3939 (WO 2010/086790) from Lesaffre et Compagnie, FR + TX, *Saccharomyces cerevisiae*, in particular strain LASO2 (from Agro-Levures et Dérivés) + TX, *Simplicillium lanosoniveum* + TX, strain T34 (e.g. T34 Biocontrol by Biocontrol Technologies S.L., ES) or strain ICC 012 from Isagro + TX, strain WRL-076 (NRRL Y-30842), U.S. Patent No. 7,579,183 + TX, *Talaromyces flavus*, strain V117b + TX, *Trichoderma asperelloides* JM41R (Accession No. NRRL B-50759) (TRICHO PLUS® from BASF SE) + TX, *Trichoderma asperellum*, in particular strain SKT-1, having Accession No. FERM P-16510 (e.g. ECO-HOPE® from Kumiai Chemical Industry) + TX, *Trichoderma asperellum*, in particular, strain kd (e.g. T-Gro from Andermatt Biocontrol) + TX, *Trichoderma atroviride* strain 77B (T77 from Andermatt Biocontrol) + TX, *Trichoderma atroviride* strain ATCC 20476 (IMI 206040) + TX, *Trichoderma atroviride* strain LC52 (e.g. Tenet by Agrimm Technologies Limited) + TX, *Trichoderma atroviride* strain LU132 (e.g. Sentinel from Agrimm Technologies Limited) + TX, *Trichoderma atroviride* strain NMI no. V08/002388 + TX, *Trichoderma atroviride* strain NMI no. V08/002389 + TX, *Trichoderma atroviride* strain NMI no. V08/002390 + TX, *Trichoderma atroviride* strain no. V08/002387 + TX, *Trichoderma atroviride* strain SKT-1 (FERM P-16510), JP Patent Publication (Kokai) 11-253151 A + TX, *Trichoderma atroviride* strain SKT-2 (FERM P-16511), JP Patent Publication (Kokai) 11-253151 A + TX, *Trichoderma atroviride* strain SKT-3 (FERM P-17021), JP Patent Publication (Kokai) 11-253151 A + TX, *Trichoderma atroviride*, in particular strain SC1 (Accession No. CBS 122089, WO 2009/116106 and U.S. Patent No. 8,431,120 (from Bi-PA)) + TX, *Trichoderma atroviride*, strain CNCM 1-1237 (e.g. Esquive® WP from Agrauxine, FR) + TX, *Trichoderma fertile* (e.g. product TrichoPlus from BASF) + TX, *Trichoderma gamsii* (formerly *T. viride*) + TX, *Trichoderma gamsii* (formerly *T. viride*) strain ICC 080 (IMI CC 392151 CABI) (available as BIODERMA® by AGROBIOSOL DE MEXICO, S.A. DE C.V.), + TX, *Trichoderma gamsii* strain ICC080 (IMI CC 392151 CABI, e.g. BioDerma by AGROBIOSOL DE MEXICO, S.A. DE C.V.), + TX, *Trichoderma harmatum* + TX, *Trichoderma harmatum*, having Accession No. ATCC 28012 + TX, *Trichoderma harzianum* + TX, *Trichoderma harzianum* rifai T39 (e.g. Trichodex® from Makhteshim, US) + TX, *Trichoderma harzianum* strain Cepa SimbT5 (from Simbiose Agro), + TX, *Trichoderma harzianum* strain DB 103 (available as T-GRO® 7456 by Dagutat Biolab) + TX, *Trichoderma harzianum* strain ITEM 908 (e.g. Trianum-P from Koppert) + TX, *Trichoderma harzianum* strain T-22 (e.g. Trianum-P from Andermatt Biocontrol or Koppert) + TX, *Trichoderma harzianum* strain TH35 (e.g. Root-Pro by Mycontrol) + TX, *Trichoderma polysporum* strain IMI 206039 (e.g. Binab TF WP by BINAB Bio-Innovation AB, Sweden) + TX, *Trichoderma stromaticum* having Accession No. Ts3550 (e.g. Tricovab by CEPLAC, Brazil) + TX, *Trichoderma virens* (also known as *Gliocladium virens*) in particular strain GL-21 (e.g. SoilGard by Certis, US) + TX, *Trichoderma virens* strain G-41, formerly known as *Gliocladium virens* (Accession No. ATCC 20906) (e.g., ROOTSHIELD® PLUS WP and TURFSHIELD® PLUS WP from BioWorks, US) + TX, *Trichoderma viride* in particular strain B35 (Pietr et al., 1993, Zesz. Nauk. A R w Szczecinie 161: 125-137) + TX, *Trichoderma viride* strain TV1 (e.g. Trianum-P by Koppert) + TX, *Ulocladium oudemansii* strain U3, having Accession No. NM 99/06216 (e.g., BOTRY-ZEN® by Botry-Zen Ltd, New Zealand and BOTRYSTOP® from BioWorks, Inc.) + TX, *Verticillium albo-atrum* (formerly *V. dahliae*) strain WCS850 having Accession No. WCS850, deposited at the Central Bureau for Fungi Cultures (e.g., DUTCH TRIG® by Tree Care Innovations) + TX, *Verticillium chlamydosporium* + TX;

a mixture of *Azotobacter vinelandii* and *Clostridium pasteurianum* (available as INVIGORATE® from Agrinos) + TX, a mixture of *Bacillus licheniformis* FMCH001 and *Bacillus subtilis* FMCH002 (available as QUARTZO® (WG), PRESENCE® (WP) from FMC Corporation) + TX, *Azorhizobium caulinodans*, in particular strain ZB-SK-5 + TX, *Azospirillum brasilense* (e.g., VIGOR® from KALO, Inc.) + TX, *Azospirillum lipoferum* (e.g., VERTEX-IF™ from TerraMax, Inc.) + TX, *Azotobacter chroococcum*, in particular strain H23 + TX, *Azotobacter vinelandii*, in particular strain ATCC 12837 + TX, *Bacillus amyloliquefaciens* BS27 (Accession No. NRRL B-5015) + TX, *Bacillus amyloliquefaciens* in particular strain FZB42 (e.g. RHIZOVITAL® from ABiTEP, DE) + TX, *Bacillus amyloliquefaciens* in particular strain IN937a + TX, *Bacillus amyloliquefaciens* pm414 (LOLI-PEPTA® from Biofilm Crop Protection) + TX, *Bacillus amyloliquefaciens* SB3281 (ATCC # PTA-7542, WO 2017/205258) + TX, *Bacillus amyloliquefaciens* TJ1000 (available as QUIKROOTS® from Novozymes) + TX, *Bacillus cereus* family member EE128 (NRRL No. B-50917) + TX, *Bacillus cereus* family member EE349 (NRRL No. B-50928) + TX, *Bacillus cereus* in particular strain BP01 (ATCC 55675, e.g. MEPICHLOR® from Arysta Lifescience, US) + TX, *Bacillus mycoides* BT155 (NRRL No. B-50921) + TX, *Bacillus mycoides* BT46-3 (NRRL No. B-50922) + TX, *Bacillus mycoides* EE118 (NRRL No. B-50918) + TX, *Bacillus mycoides* EE141 (NRRL No. B-50916) + TX, *Bacillus pumilus* in particular strain GB34 (e.g. YIELD SHIELD® from Bayer Crop Science, DE), + TX, *Bacillus pumilus* in particular strain QST2808 (Accession No. NRRL No. B-30087) + TX, *Bacillus siamensis* in particular strain KCTC 13613T + TX, *Bacillus subtilis* in particular strain AQ30002 (Accession No. NRRL No. B-50421 and described in U.S. Patent Application No. 13/330,576) + TX, *Bacillus subtilis* in particular strain AQ30004 (NRRL No. B-50455 and described in U.S. Patent Application No. 13/330,576) + TX, *Bacillus subtilis* in particular strain MBI 600 (e.g. SUBTILEX® from BASF SE) + TX, *Bacillus subtilis* rm303 (RHIZOMAX® from Biofilm Crop Protection) + TX, *Bacillus subtilis* strain BU1814 (available as TEQUALIS® from BASF SE) + TX, *Bacillus tequilensis* in particular strain NII-0943 + TX, *Bacillus thuringiensis* BT013A (NRRL No. B-50924) also known as *Bacillus thuringiensis* 4Q7 + TX, *Bradyrhizobium japonicum* (e.g. OPTIMIZE® from Novozymes) + TX, *Delftia acidovorans* in particular strain RAY209 (e.g. BIOBOOST® from Brett Young Seeds) + TX, *Lactobacillus* sp. (e.g. LACTOPLANT® from LactoPAFI) + TX, *Mesorhizobium cicer* (e.g., NODULATOR from BASF SE) + TX, *Paenibacillus polymyxa* in particular strain AC-1 (e.g. TOPSEED® from Green Biotech Company Ltd.) + TX, *Pseudomonas aeruginosa* in particular strain PN1 + TX, *Pseudomonas proradix* (e.g. PRORADIX® from Sourcon Padena) + TX, *Rhizobium leguminosarium* biovar *viciae* (e.g., NODULATOR from BASF SE) + TX, *Rhizobium leguminosarum* in particular bv. *viceae* strain Z25 (Accession No. CECT 4585) + TX, *Serratia marcescens* in particular strain SRM (Accession No. MTCC 8708), + TX, *Sinorhizobium meliloti* strain NRG-185-1 (NITRAGIN® GOLD from Bayer CropScience) + TX, *Thiobacillus* sp. (e.g. CROPAID® from Cropaid Ltd UK) + TX; *Myrothecium verrucaria* strain AARC-0255 (e.g. DiTera™ from Valent Biosciences) + TX, *Penicillium bilaii* strain ATCC 22348 (e.g. JumpStart® from Acceleron BioAg) + TX, *Penicillium bilaii* strain ATCC ATCC20851 + TX, *Purpureocillium lilacinum* (previously known as *Paecilomyces lilacinus*) strain 251 (AGAL 89/030550, e.g. BioAct from Bayer CropScience Biologics GmbH) + TX, *Pythium oligandrum* strain DV74 + TX, *Pythium oligandrum* strain M1 (ATCC 38472 e.g. Polyversum from Bioprepaty, CZ) + TX, *Rhizopogon amylopogon* (Myco-Sol from Agri-Enterprise, LLC, formerly Helena Chemical Company) + TX, *Rhizopogon fulvigleba* (e.g. Myco-Sol from Agri-Enterprise, LLC, formerly Helena Chemical Company) + TX, *Talaromyces flavus* strain V117b + TX, *Trichoderma asperellum* strain (Eco-

T from Plant Health Products, ZA) + TX, *Trichoderma asperellum* strain kd (e.g. T-Gro from Andermatt Biocontrol) + TX, *Trichoderma atroviride* in particular strain no. V08/002387 + TX, *Trichoderma atroviride* strain CNCM 1-1237 (e.g. Esquive® WP from Agrauxine, FR) + TX, *Trichoderma atroviride* strain LC52 (also known as *Trichoderma atroviride* strain LU132, e.g. Sentinel from Agrimm Technologies Limited) + TX, *Trichoderma atroviride* strain no. NMI No. V08/002388 + TX, *Trichoderma atroviride* strain no. NMI No. V08/002389 + TX, *Trichoderma atroviride* strain no. NMI No. V08/002390 + TX, *Trichoderma atroviride* strain SC1 (described in WO2009/116106) + TX, *Trichoderma harzianum* strain 1295-22 + TX, *Trichoderma harzianum* strain ITEM 908 + TX, *Trichoderma harzianum* strain T-22 (e.g. Trianum-P from Andermatt Biocontrol or Koppert) + TX, *Trichoderma harzianum* strain TSTh20, + TX, *Trichoderma virens* strain GI-3 + TX, *Trichoderma virens* strain GL-21 (e.g. SoilGard® from Certis, USA) + TX, *Trichoderma viride* strain B35 (Pietr et al., 1993, Zesz. Nauk. A R w Szczecinie 161: 125-137) + TX, *Verticillium albo-atrum* (formerly *V. dahliae*) strain WCS850 (CBS 276.92, e.g. Dutch Trig from Tree Care Innovations) + TX;

Agrobacterium radiobacter strain K84 (Galltrol from AgBiochem Inc.), + TX, *Bacillus amyloliquefaciens* in particular strain PTS-4838 (e.g. AVEO from Valent Biosciences, US), + TX, *Bacillus mycoides*, isolate J. (e.g. BmJ from Certis USA LLC), + TX, *Bacillus sphaericus* in particular Serotype H5a5b strain 2362 (strain ABTS-1743) (e.g. VECTOLEX® from Valent BioSciences, US), + TX, *Bacillus thuringiensis israelensis* strain BMP 144 (e.g. AQUABAC® by Becker Microbial Products IL) + TX, *Bacillus thuringiensis* subsp. *aizawai* strain GC-91 + TX, *Bacillus thuringiensis* subsp. *aizawai*, in particular serotype H-7 (e.g. FLORBAC® WG from Valent BioSciences, US) + TX, *Bacillus thuringiensis* subsp. *aizawai*, in particular strain ABTS-1857 (SD-1372, e.g. XENTARI® from Valent BioSciences) + TX, *Bacillus thuringiensis* subsp. *israelensis* (serotype H-14) strain AM65-52 (Accession No. ATCC 1276) (e.g. VECTOBAC® by Valent BioSciences, US) + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain ABTS 351 + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain BMP 123 (from Becker Microbial Products, IL, BARITONE from Bayer CropScience) + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain EG 2348 (LEPINOX from Certis, US) + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain EG 7841 (CRYMAX from Certis, US) + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain HD-1 (e.g. DIPEL® ES from Valent BioSciences, US) + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain PB 54 + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain SA 11 (JAVELIN from Certis, US) + TX, *Bacillus thuringiensis* subsp. *kurstaki* strain SA 12 (THURICIDE from Certis, US) + TX, *Bacillus thuringiensis* subsp. *tenebrionis* strain NB 176 (SD-5428, e.g. NOVODOR® FC from BioFa DE) + TX, *Bacillus thuringiensis* var. *Colmeri* (e.g. TIANBAOBTC by Changzhou Jianghai Chemical Factory) + TX, *Bacillus thuringiensis* var. *japonensis* strain Buibui + TX, *Bacillus thuringiensis* var. *kurstaki* strain EVB-113-19 (e.g., BIOPROTEC® from AEF Global) + TX, *Brevibacillus laterosporus* + TX, *Burkholderia* spp. in particular *Burkholderia rinojensis* strain A396 (also known as *Burkholderia rinojensis* strain MBI 305) (Accession No. NRRL B-50319, WO 2011/106491 and WO 2013/032693, e.g. MBI206 TGA1 and ZELTO® from Marrone Bio Innovations), + TX, *Chromobacterium subtsugae* in particular strain PRAA4-1T (e.g. MBI-203, e.g. GRANDEVO® from Marrone Bio Innovations) + TX, *Lecanicillium muscarium* Ve6 (MYCOTAL from Koppert) + TX, *Paenibacillus popilliae* (formerly *Bacillus popilliae*, e.g. MILKY SPORE POWDER™ or MILKY SPORE GRANULAR™ from St. Gabriel Laboratories) + TX, *Serratia entomophila* (e.g. INVADE® by Wrightson Seeds) + TX, *Serratia marcescens* in particular strain SRM (Accession No. MTCC 8708) + TX,

Trichoderma asperellum (TRICHODERMAX from Novozymes) + TX, *Wolbachia pipientis* ZAP strain (e.g., ZAP MALES® from MosquitoMate) + TX;

Beauveria bassiana strain ATCC 74040 (e.g. NATURALIS® from Intrachem Bio Italia) + TX, *Beauveria bassiana* strain ATP02 (Accession No. DSM 24665), *Apopka 97* (PREFERAL from SePRO) + TX, *Beauveria bassiana* strain GHA (Accession No. ATCC74250, e.g. BOTANIGUARD® ES and MYCONTROL-O® from Laverlam International Corporation) + TX, *Metarhizium anisopliae* 3213-1 (deposited under NRRL accession number 67074 disclosed in WO 2017/066094, Pioneer Hi-Bred International) + TX, *Metarhizium robertsii* 15013-1 (deposited under NRRL accession number 67073) + TX, *Metarhizium robertsii* 23013-3 (deposited under NRRL accession number 67075) + TX, *Paecilomyces lilacinus* strain 251 (MELOCON from Certis, US) + TX;

Cydia pomonella (codling moth) granulosis virus (GV) + TX, *Helicoverpa armigera* (cotton bollworm) nuclear polyhedrosis virus (NPV) + TX, of *Adoxophyes orana* (summer fruit tortrix) granulosis virus (GV) + TX, *Spodoptera exigua* (beet armyworm) mNPV + TX, *Spodoptera frugiperda* (fall armyworm) mNPV + TX;

Burkholderia spp. in particular *Burkholderia cepacia* (formerly known as *Pseudomonas cepacia*) + TX, *Gigaspora* spp. + TX, *Glomus* spp. + TX, *Laccaria* spp. + TX, *LactoBacillus buchneri* + TX, *Paraglomus* spp. + TX, *Pisolithus tinctorius* + TX, *Pseudomonas* spp. + TX, *Rhizobium* spp. in particular *Rhizobium trifolii* + TX, *Rhizopogon* spp. + TX, *Scleroderma* spp. + TX, *Streptomyces* spp. + TX, *Suillus* spp. + TX, *Agrobacterium* spp. + TX, *Azorhizobium caulinodans* + TX, *Azospirillum* spp. + TX, *Azotobacter* spp. + TX, *Bradyrhizobium* spp. + TX, *Gigaspora monosporum* + TX;

Allium sativum (NEMGUARD from Eco-Spray, BRALIC from ADAMA) + TX, *Armour-Zen* + TX, *Artemisia absinthium* + TX, *Biokeeper WP* + TX, *Brassicaceae* extract in particular oilseed rape powder or mustard powder + TX, *Cassia nigricans* + TX, *Celastrus angulatus* + TX, *Chenopodium anthelminticum* + TX, *Chenopodium quinoa* saponin extract from quinoa seeds (e.g. Heads Up® (Saponins of Quinoa) from Heads Up plant Protectants, CA) + TX, *Chitin* + TX, *Dryopteris filix-mas* + TX, *Equisetum arvense* + TX, *Fortune Aza* + TX, *Fungastop* + TX, *Melaleuca alternifolia* extract (TIMOREX GOLD from STK) + TX, naturally occurring *Blad* polypeptide extracted from *Lupin* seeds (FRACTURE® from FMC) + TX, naturally occurring *Blad* polypeptide extracted from *Lupin* seeds (PROBLAD® from Certis EU) + TX, *Pyrethrins* + TX, *Quassia amara* + TX, *Quercus* + TX, *Quillaja* extract (QL AGRI 35 from BASF) + TX, *REGALIA MAXX* from Marrone Bio) + TX, *Requiem™* Insecticide + TX, *Reynoutria sachalinensis* extract (REGALLIA + TX, *ryania/ryanodine* + TX, *Symphytum officinale* + TX, *Tanacetum vulgare* + TX, *Thymol* + TX, *Thymol* mixed with *Geraniol* (CEDROZ from Eden Research) + TX, *Thymol* mixed with *Geraniol* and *Eugenol* (MEVALONE from Eden Research) + TX, *Triact 70* + TX, *TriCon* + TX, *Tropaeolum majus* + TX, *Urtica dioica* + TX, *Veratrin* + TX, *Viscum album* + TX;

mercuric oxide + TX, octhilinone + TX, thiophanate-methyl + TX;

MGK 264 + TX, 2-(2-butoxyethoxy)ethyl piperonylate + TX, 2-isovalerylindan-1,3-dione + TX, 4-(quinoxalin-2-ylamino)benzenesulfonamide + TX, 5-(1,3-benzodioxol-5-yl)-3-hexylcyclohex-2-enone + TX, acibenzolar + TX, acibenzolar-S-methyl + TX, alpha-bromadiolone + TX, alpha-chlorohydrin + TX, aluminium phosphide + TX, anthraquinone + TX, antu + TX, arsenous oxide + TX, barium carbonate + TX, benoxacor + TX, bisthiosemi + TX, brodifacoum + TX, bromadiolone + TX, bromethalin + TX, calcium cyanide + TX, chloralose + TX, chlorophacinone + TX, cholecalciferol + TX, cloquintocet (including cloquintocet-mexyl) + TX, copper naphthenate + TX, copper oxychloride + TX, coumachlor +

TX, coumafuryl + TX, coumatetralyl + TX, crimidine + TX, cyprosulfamide + TX, diazinon + TX, dichlormid + TX, dicyclopentadiene + TX, difenacoum + TX, difethialone + TX, diphacinone + TX, ergocalciferol + TX, farnesol + TX, farnesol with nerolidol + TX, fenchlorazole (including fenchlorazole-ethyl) + TX, fencloirim + TX, flocoumafen + TX, fluoroacetamide + TX, flupropadine + TX, flupropadine hydrochloride + TX, fluxofenim + TX, furilazole + TX, gamma-HCH + TX, guazatine + TX, guazatine acetates + TX, HCH + TX, hydrogen cyanide + TX, imanin + TX, iodomethane + TX, isoxadifen (including isoxadifen-ethyl) + TX, lindane + TX, magnesium phosphide + TX, MB-599 + TX, mefenpyr (including mefenpyr-diethyl) + TX, metcamifen + TX, methiocarb + TX, methyl bromide + TX, nerolidol + TX, norbormide + TX, petroleum oils + TX, phosacetim + TX, phosphine + TX, phosphorus + TX, pindone + TX, piperonyl butoxide + TX, piprotal + TX, potassium arsenite + TX, probenazole + TX, propyl isomer + TX, pyridin-4-amine + TX, pyrinuron + TX, Reynoutria sachalinensis extract + TX, ribavirin + TX, S421 + TX, scilliroside + TX, sesamex + TX, sesasmolin + TX, sodium arsenite + TX, sodium cyanide + TX, sodium fluoroacetate + TX, strychnine + TX, sulfoxide + TX, thallium sulfate + TX, thiram + TX, trimethacarb + TX, warfarin + TX, zinc naphthenate + TX, zinc phosphide + TX, ziram + TX.

In addition, the compositions of the invention may also be applied with one or more systemically acquired resistance inducers ("SAR" inducer). SAR inducers are known and described in, for example, United States Patent No. US 6,919,298 and include, for example, salicylates and the commercial SAR inducer
5 acibenzolar-S-methyl.

The compounds of formula (I) as defined in the present invention are normally used in the form of compositions and can be applied to the crop area or plant to be treated, simultaneously or in succession with further compounds. These further compounds can be e.g. fertilizers or micronutrient donors or other
10 preparations, which influence the growth of plants. They can also be selective herbicides or non-selective herbicides as well as insecticides, fungicides, bactericides, nematocides, molluscicides or mixtures of several of these preparations, if desired together with further carriers, surfactants or application promoting adjuvants customarily employed in the art of formulation.

15 The compounds of formula (I) as defined in the present invention may be used in the form of (fungicidal) compositions for controlling or protecting against phytopathogenic microorganisms, comprising as active ingredient at least one compound of formula (I) as defined in the present invention or of at least one preferred individual compound as above-defined, in free form or in agrochemically usable salt form, and at least one of the above-mentioned adjuvants.

20

The invention therefore provides a composition, preferably a fungicidal composition, comprising at least one compound of formula (I) as defined in the present invention, an agriculturally acceptable carrier and optionally an adjuvant. An agricultural acceptable carrier is for example a carrier that is suitable for agricultural use. Agricultural carriers are well known in the art. Preferably said composition may
25 comprise at least one or more pesticidally active compounds, for example an additional fungicidal active ingredient in addition to the compound of formula (I) as defined in the present invention.

A further aspect of invention is related to a method of controlling or preventing an infestation of plants, e.g. useful plants such as crop plants, propagation material thereof, e.g. seeds, harvested crops, e.g. harvested food crops, or of non-living materials by phytopathogenic or spoilage microorganisms or organisms potentially harmful to man, especially fungal organisms, which comprises the application of
5 a compound of formula (I) as defined in the present invention or of a preferred individual compound as above-defined as active ingredient to the plants, to parts of the plants or to the locus thereof, to the propagation material thereof, or to any part of the non-living materials.

Controlling or preventing means reducing infestation by insects or by phytopathogenic or spoilage
10 microorganisms or organisms potentially harmful to man, especially fungal organisms, to such a level that an improvement is demonstrated.

A preferred method of controlling or preventing an infestation of crop plants by phytopathogenic microorganisms, especially fungal organisms, which comprises the application of a compound of formula
15 (I) as defined in the present invention, or an agrochemical composition which contains at least one of said compounds, is foliar application. The frequency of application and the rate of application will depend on the risk of infestation by the corresponding pathogen or insect. However, the compounds of formula (I) as defined in the present invention can also penetrate the plant through the roots via the soil (systemic action) by drenching the locus of the plant with a liquid formulation, or by applying the compounds in
20 solid form to the soil, e.g. in granular form (soil application). In crops of water rice such granulates can be applied to the flooded rice field. The compounds of formula (I) as defined in any the present invention may also be applied to seeds (coating) by impregnating the seeds or tubers either with a liquid formulation of the fungicide or coating them with a solid formulation.

25 A formulation, e.g. a composition containing the compound of formula (I) as defined in the present invention, and, if desired, a solid or liquid adjuvant or monomers for encapsulating the compound of formula (I) as defined in the present invention, may be prepared in a known manner, typically by intimately mixing and/or grinding the compound with extenders, for example solvents, solid carriers and, optionally, surface active compounds (surfactants).

30

The application methods for the compositions, that is the methods of controlling pathogens of the abovementioned type, such as spraying, atomizing, dusting, brushing on, dressing, scattering or pouring - which are to be selected to suit the intended aims of the prevailing circumstances - and the use of the compositions for controlling pathogens of the abovementioned type are other subjects of the invention.

35 Typical rates of concentration are between 0.1 and 1000 ppm, preferably between 0.1 and 500 ppm, of active ingredient. The rate of application per hectare is preferably 1g to 2000 g of active ingredient per hectare, more preferably 10 to 1000 g/ha, most preferably 10 to 600 g/ha. When used as seed drenching agent, convenient dosages are from 10mg to 1g of active substance per kg of seeds.

40 When the combinations of the present invention are used for treating seed, rates of 0.001 to 50 g of a compound of formula (I) per kg of seed, preferably from 0.01 to 10g per kg of seed are generally sufficient.

Suitably, a composition comprising a compound of formula (I) as defined in the present invention according to the present invention is applied either preventative, meaning prior to disease development or curative, meaning after disease development.

5

The compositions of the invention may be employed in any conventional form, for example in the form of a twin pack, a powder for dry seed treatment (DS), an emulsion for seed treatment (ES), a flowable concentrate for seed treatment (FS), a solution for seed treatment (LS), a water dispersible powder for seed treatment (WS), a capsule suspension for seed treatment (CF), a gel for seed treatment (GF), an
10 emulsion concentrate (EC), a suspension concentrate (SC), a suspo-emulsion (SE), a capsule suspension (CS), a water dispersible granule (WG), an emulsifiable granule (EG), an emulsion, water in oil (EO), an emulsion, oil in water (EW), a micro-emulsion (ME), an oil dispersion (OD), an oil miscible flowable (OF), an oil miscible liquid (OL), a soluble concentrate (SL), an ultra-low volume suspension (SU), an ultra-low volume liquid (UL), a technical concentrate (TK), a dispersible concentrate (DC), a
15 wettable powder (WP) or any technically feasible formulation in combination with agriculturally acceptable adjuvants.

Such compositions may be produced in conventional manner, e.g. by mixing the active ingredients with appropriate formulation inerts (diluent, solvents, fillers and optionally other formulating ingredients such
20 as surfactants, biocides, anti-freeze, stickers, thickeners and compounds that provide adjuvancy effects). Also conventional slow release formulations may be employed where long lasting efficacy is intended. Particularly formulations to be applied in spraying forms, such as water dispersible concentrates (e.g. EC, SC, DC, OD, SE, EW, EO and the like), wettable powders and granules, may contain surfactants such as wetting and dispersing agents and other compounds that provide adjuvancy
25 effects, e.g. the condensation product of formaldehyde with naphthalene sulphonate, an alkylarylsulphonate, a lignin sulphonate, a fatty alkyl sulphate, and ethoxylated alkylphenol and an ethoxylated fatty alcohol.

A seed dressing formulation is applied in a manner known per se to the seeds employing the
30 combination of the invention and a diluent in suitable seed dressing formulation form, e.g. as an aqueous suspension or in a dry powder form having good adherence to the seeds. Such seed dressing formulations are known in the art. Seed dressing formulations may contain the single active ingredients or the combination of active ingredients in encapsulated form, e.g. as slow release capsules or microcapsules.

35

In general, the formulations include from 0.01 to 90% by weight of active agent, from 0 to 20% agriculturally acceptable surfactant and 10 to 99.99% solid or liquid formulation inerts and adjuvant(s), the active agent consisting of at least the compound of formula (I) as defined in the present invention together with component (B) and (C), and optionally other active agents, particularly microbiocides or
40 conservatives or the like. Concentrated forms of compositions generally contain in between about 2 and 80%, preferably between about 5 and 70% by weight of active agent. Application forms of formulation may for example contain from 0.01 to 20% by weight, preferably from 0.01 to 5% by weight of active

agent. Whereas commercial products will preferably be formulated as concentrates, the end user will normally employ diluted formulations.

Whereas it is preferred to formulate commercial products as concentrates, the end user will normally
5 use dilute formulations.

EXAMPLES

10 The Examples which follow serve to illustrate the invention. Certain compounds of the invention can be distinguished from known compounds by virtue of greater efficacy at low application rates, which can be verified by the person skilled in the art using the experimental procedures outlined in the Examples.

Formulation Examples

15

Wettable powders

	a)	b)	c)
active ingredient [compound of formula (I)]	25 %	50 %	75 %
sodium lignosulfonate	5 %	5 %	-
sodium lauryl sulfate	3 %	-	5 %
sodium diisobutylphthalenesulfonate	-	6 %	10 %
phenol polyethylene glycol ether (7-8 mol of ethylene oxide)	-	2 %	-
highly dispersed silicic acid	5 %	10 %	10 %
Kaolin	62 %	27 %	-

The active ingredient is thoroughly mixed with the adjuvants and the mixture is thoroughly ground in a suitable mill, affording wettable powders that can be diluted with water to give suspensions of the desired concentration.

20

Powders for dry seed treatment

	a)	b)	c)
active ingredient [compound of formula (I)]	25 %	50 %	75 %
light mineral oil	5 %	5 %	5 %
highly dispersed silicic acid	5 %	5 %	-
Kaolin	65 %	40 %	-
Talcum	-		20%

The active ingredient is thoroughly mixed with the adjuvants and the mixture is thoroughly ground in a suitable mill, affording powders that can be used directly for seed treatment.

Emulsifiable concentrate

active ingredient [compound of formula (I)]	10 %
octylphenol polyethylene glycol ether	3 %

(4-5 mol of ethylene oxide)

calcium dodecylbenzenesulfonate	3 %
castor oil polyglycol ether (35 mol of ethylene oxide)	4 %
Cyclohexanone	30 %
xylene mixture	50 %

Emulsions of any required dilution, which can be used in plant protection, can be obtained from this concentrate by dilution with water.

<u>Dusts</u>	a)	b)	c)
Active ingredient [compound of formula (I)]	5 %	6 %	4 %
talcum	95 %	-	-
Kaolin	-	94 %	-
mineral filler	-	-	96 %

5

Ready-for-use dusts are obtained by mixing the active ingredient with the carrier and grinding the mixture in a suitable mill. Such powders can also be used for dry dressings for seed.

Extruder granules

Active ingredient [compound of formula (I)]	15 %
sodium lignosulfonate	2 %
carboxymethylcellulose	1 %
Kaolin	82 %

- 10 The active ingredient is mixed and ground with the adjuvants, and the mixture is moistened with water. The mixture is extruded and then dried in a stream of air.

Coated granules

Active ingredient [compound of formula (I)]	8 %
polyethylene glycol (mol. wt. 200)	3 %
Kaolin	89 %

- The finely ground active ingredient is uniformly applied, in a mixer, to the kaolin moistened with polyethylene glycol. Non-dusty coated granules are obtained in this manner.
- 15

Suspension concentrate

active ingredient [compound of formula (I)]	40 %
propylene glycol	10 %
nonylphenol polyethylene glycol ether (15 mol of ethylene oxide)	6 %
Sodium lignosulfonate	10 %
carboxymethylcellulose	1 %
silicone oil (in the form of a 75 % emulsion in water)	1 %

Water

32 %

The finely ground active ingredient is intimately mixed with the adjuvants, giving a suspension concentrate from which suspensions of any desired dilution can be obtained by dilution with water. Using such dilutions, living plants as well as plant propagation material can be treated and protected against infestation by microorganisms, by spraying, pouring or immersion.

Flowable concentrate for seed treatment

active ingredient [compound of formula (I)]	40 %
propylene glycol	5 %
copolymer butanol PO/EO	2 %
tristyrenephenol with 10-20 moles EO	2 %
1,2-benzisothiazolin-3-one (in the form of a 20% solution in water)	0.5 %
monoazo-pigment calcium salt	5 %
Silicone oil (in the form of a 75 % emulsion in water)	0.2 %
Water	45.3 %

The finely ground active ingredient is intimately mixed with the adjuvants, giving a suspension concentrate from which suspensions of any desired dilution can be obtained by dilution with water. Using such dilutions, living plants as well as plant propagation material can be treated and protected against infestation by microorganisms, by spraying, pouring or immersion.

Slow Release Capsule Suspension

28 parts of a combination of the compound of formula (I) are mixed with 2 parts of an aromatic solvent and 7 parts of toluene diisocyanate/polymethylene-polyphenylisocyanate-mixture (8:1). This mixture is emulsified in a mixture of 1.2 parts of polyvinylalcohol, 0.05 parts of a defoamer and 51.6 parts of water until the desired particle size is achieved. To this emulsion a mixture of 2.8 parts 1,6-diaminohexane in 5.3 parts of water is added. The mixture is agitated until the polymerization reaction is completed.

The obtained capsule suspension is stabilized by adding 0.25 parts of a thickener and 3 parts of a dispersing agent. The capsule suspension formulation contains 28% of the active ingredients. The medium capsule diameter is 8-15 microns.

The resulting formulation is applied to seeds as an aqueous suspension in an apparatus suitable for that purpose.

Analytical Methods:

Throughout this description, temperatures are given in degrees Celsius (°C) and "mp." means melting point. LC/MS means Liquid Chromatography Mass Spectrometry and the description of the apparatus and the method is as follows:

Method A:

Equipment: Shimadzu LCMS 2020 Mass Spectrometer; Column: HALO C₁₈ 2.7 µm, 3.0 mm × 30 mm; Mobile Phase: MeCN (with either 0.05% HCOOH or 0.05% TFA) - Water (with either 0.05% HCOOH or 0.05% TFA); Gradient: MeCN from 5% to 95% over 1.4 min, hold 0.6 min, total run time is 2.5 min; Flow rate: 1.8 mL/min; Column temperature: 50 °C; Wavelength: 214 and 254 nm PDA.

5

Method B:

Spectra were recorded on a Mass Spectrometer from Waters (Acquity QDa Mass Spectrometer) equipped with an electrospray source (Polarity: Positive and Negative Polarity Switch), Capillary: 0.8 kV, Cone range: 25 V, Extractor: V (No extractor voltage for QDa detector) Source Temperature: 120°C, Desolvation Temperature: 600°C, Cone Gas Flow: 50 L/h, Desolvation Gas Flow: 1000 L/h, Mass range: 110 to 850 Da) and an Acquity UPLC from Waters: Quaternary solvent manager, heated column compartment, diode-array detector. Column: Acquity UPLC HSS T3 C18, 1.8 µm, 30 x 2.1 mm, Temp: 40 °C, DAD Wavelength range (nm): 200 to 400, Solvent Gradient: A = water + 5% Acetonitrile + 0.1 % HCOOH, B= Acetonitrile + 0.05 % HCOOH: gradient: 0 min 10% B; 0.-0.2 min 10-50% B; 0.2-0.6 min 50-100% B; 0.6-1.3 min 100% B; 1.3-1.4 min 100-10% B; 1.4-1.6 min 10% B; Flow (mL/min) 0.6.

Method C:

Spectra were recorded on a ACQUITY Mass Spectrometer from Waters Corporations (SQD or SQDII Single quadrupole mass spectrometer) equipped with an electrospray source (Polarity: positive or negative ions, Capillary: 3.0 kV, Cone: 30V, Extractor: 3.00 V, Source Temperature: 150°C, Desolvation Temperature: 400°C, Cone Gas Flow: 60 L/hr, Desolvation Gas Flow: 700 L/hr, Mass range: 140 to 800 Da) and an ACQUITY UPLC from Waters Corporations with solvent degasser, binary pump, heated column compartment and diode-array detector. Column: Waters UPLC HSS T3, 1.8 µm, 30 x 2.1 mm, Temp: 60 °C, DAD Wavelength range (nm): 210 to 400, Solvent Gradient: A = Water/Methanol 9:1 + 0.1% formic acid, B= Acetonitrile + 0.1% formic acid, gradient: 0-100% B in 2.5 min; Flow (mL/min) 0.75.

Method D:

Spectra were recorded on a Mass Spectrometer from Agilent (Single quad mass spectrometer) equipped with a Multimode- Electron Spray and APCI (Polarity: positive and negative ions), Capillary: 4.00 kV, Corona Current 4.0 µA, Charging Voltage, 2.00 kV, Nitrogen Gas Flow: 12.0 L/min, Nebulizer Pressure: 40 psig, Mass range: 100 to 1000 m/z, dry gas temperature 250 °C, Vaporizer temperature 200 °C and an UPLC from Waters: quaternary pump, heated column compartment, Variable wave length detector. Column: X-Bridge BEH C18, 2.5 µm (2.1 * 50 mm), column Temp: Ambient, Wavelength (nm): 215 nm, Gradient: A = 0.05% TFA in water, B = 0.05% TFA in Acetonitrile. Gradient: time/%B: 0/5, 1/5, 5/70, 7/95, 8.5/95, 8.6/5, 10/5; Flow rate: 0.6 mL/min.

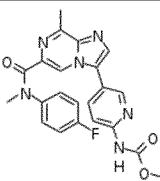
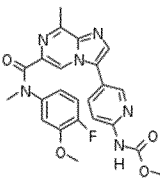
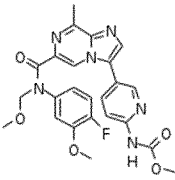
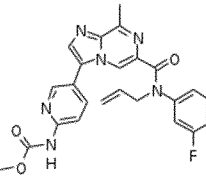
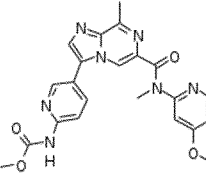
The below Table A gathers for compounds of formula (I):

- LC-MS data, such as retention time (RT), [M+H]⁺,
- the type of method, and/or

40 - melting point (mp).

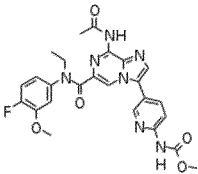
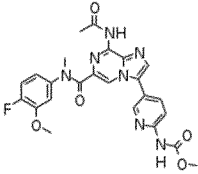
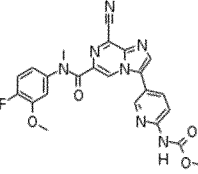
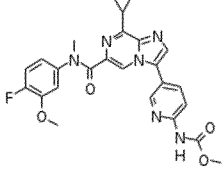
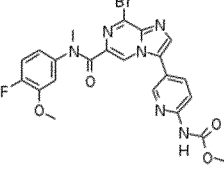
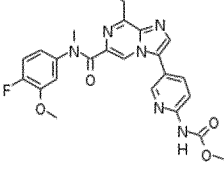
Table A:

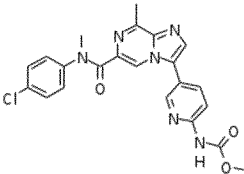
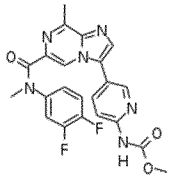
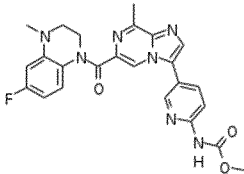
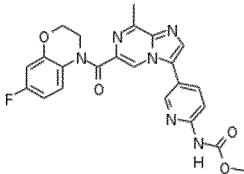
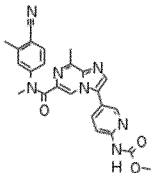
	Compound Name	STRUCTURE	RT (min)	[M+H] (measured)	Method	mp (°C)
1	methyl <i>N</i> -[5-[6-[2-cyanoethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.06	504	B	
2	methyl <i>N</i> -[5-[6-[cyanomethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.02	490	B	208 - 210
3	methyl <i>N</i> -[5-[6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.03	479	B	204 - 206
4	methyl <i>N</i> -[5-[6-(6-fluoro-3,4-dihydro-2 <i>H</i> -quinoline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.03	461	B	220 - 222
5	methyl <i>N</i> -[5-[6-[(4-fluoro-3-methyl-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-		1.00	449	B	209 - 211

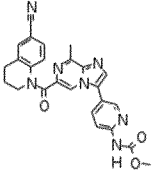
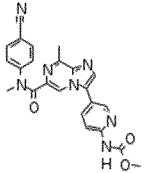
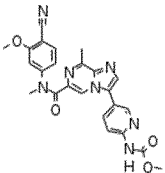
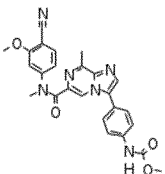
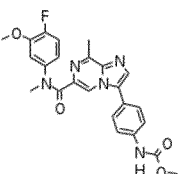
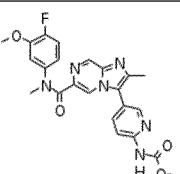
	a]pyrazin-3-yl]-2-pyridyl]carbamate					
6	methyl <i>N</i> -[5-[6-[(4-fluorophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		0.98	435	B	200 - 202
7	methyl <i>N</i> -[5-[6-[(4-fluoro-3-methoxyphenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		3.20	465	D	170 - 175
8	methyl <i>N</i> -[5-[6-[(4-fluoro-3-methoxyphenyl)-(methoxymethyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		3.30	495	D	217 - 222
9	methyl <i>N</i> -[5-[6-[allyl-(3-fluorophenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.32	461	C	
10	methyl <i>N</i> -[5-[6-[(4-methoxy-2-pyridyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		0.96	448	C	

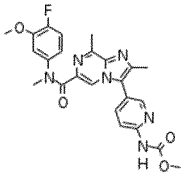
11	methyl <i>N</i> -[5-[8-methyl-6-[methyl-(3-methylsulfonylphenyl)carbamoyl]imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		0.95	495	C	
12	3-[6-(cyclopropanecarboxylamino)-3-pyridyl]- <i>N</i> -(3,4-difluorophenyl)- <i>N</i> ,8-dimethylimidazo[1,2- <i>a</i>]pyrazine-6-carboxamide		1.02	463	B	190 - 192
13	3-[6-(ethylcarbamoylamino)-3-pyridyl]- <i>N</i> -(4-fluoro-3-methoxyphenyl)- <i>N</i> ,8-dimethylimidazo[1,2- <i>a</i>]pyrazine-6-carboxamide		1.15	478	C	
14	<i>N</i> -(4-fluoro-3-methoxyphenyl)-3-[4-[(2-methoxyacetyl)amino]phenyl]- <i>N</i> ,8-dimethylimidazo[1,2- <i>a</i>]pyrazine-6-carboxamide		1.16	478	C	
15	3-[4-(cyclopropanecarboxylamino)phenyl]- <i>N</i> -(4-fluoro-3-methoxyphenyl)- <i>N</i> ,8-dimethylimidazo[1,2-		1.25	474	C	

	a]pyrazine-6-carboxamide					
16	3-[4-(ethylcarbamoylamino)phenyl]- <i>N</i> -(4-fluoro-3-methoxyphenyl)- <i>N</i> ,8-dimethylimidazo[1,2-a]pyrazine-6-carboxamide		1.15	477	C	
17	3-(4-acetamidophenyl)- <i>N</i> -(4-fluoro-3-methoxyphenyl)- <i>N</i> ,8-dimethylimidazo[1,2-a]pyrazine-6-carboxamide		1.09	448	C	
18	3-(6-acetamido-3-pyridyl)- <i>N</i> -(4-fluoro-3-methoxyphenyl)- <i>N</i> ,8-dimethylimidazo[1,2-a]pyrazine-6-carboxamide		1.05	449	C	230 - 232
19	3-[6-(cyclopropanecarbonylamino)-3-pyridyl]- <i>N</i> -(4-fluoro-3-methoxyphenyl)- <i>N</i> ,8-dimethylimidazo[1,2-a]pyrazine-6-carboxamide		1.21	475	C	124 - 126
20	3-(6-acetamido-3-pyridyl)- <i>N</i> -(3,4-difluorophenyl)- <i>N</i> ,8-dimethylimidazo[1,2-		0.95	436	B	120 - 122

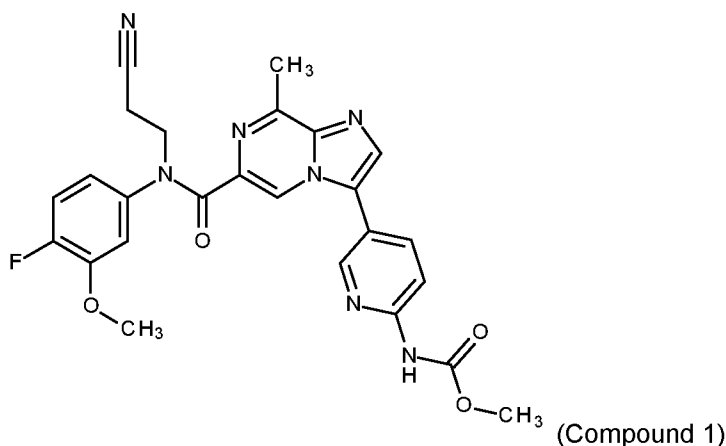
	a]pyrazine-6-carboxamide					
21	methyl <i>N</i> -[5-[8-acetamido-6-[(4-fluoro-3-methoxy-phenyl)carbamoyl]imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.43	522	A	241 - 244
22	methyl <i>N</i> -[5-[8-acetamido-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.79	508	A	147 - 149
23	methyl <i>N</i> -[5-[8-cyano-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.16	476	A	214 - 216
24	methyl <i>N</i> -[5-[8-cyclopropyl-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.23	491	A	121 - 123
25	methyl <i>N</i> -[5-[8-bromo-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.21	529	A	201 - 204
26	methyl <i>N</i> -[5-[8-ethyl-6-[(4-fluoro-3-methoxy-phenyl)-methyl-		1.16	479	A	178 - 181

	carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate					
27	methyl <i>N</i> -[5-[6-[(4-chlorophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.04	450	B	200 - 202
28	methyl <i>N</i> -[5-[6-[(3,4-difluorophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.00	453	B	222 - 224
29	methyl <i>N</i> -[5-[6-(6-fluoro-4-methyl-2,3-dihydroquinoxaline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.19	476	A	215 - 217
30	methyl <i>N</i> -[5-[6-(7-fluoro-2,3-dihydro-1,4-benzoxazine-4-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.19	463	A	230 - 232
31	methyl <i>N</i> -[5-[6-[(4-cyano-3-methylphenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.09	456	A	213 - 215

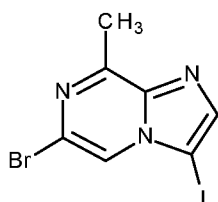
32	methyl <i>N</i> -[5-[6-(6-cyano-3,4-dihydro-2 <i>H</i> -quinoline-1-carbonyl)-8-methyl-imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.15	468	A	224 - 227
33	methyl <i>N</i> -[5-[6-[(4-cyanophenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.06	442	A	214 - 216
34	methyl <i>N</i> -[5-[6-[(4-cyano-3-methoxyphenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2- <i>a</i>]pyrazin-3-yl]-2-pyridyl]carbamate		1.07	472	A	234 - 236
35	methyl <i>N</i> -[4-[6-[(4-cyano-3-methoxyphenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2- <i>a</i>]pyrazin-3-yl]phenyl]carbamate		1.10	471	A	137 - 139
36	methyl <i>N</i> -[4-[6-[(4-fluoro-3-methoxyphenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2- <i>a</i>]pyrazin-3-yl]phenyl]carbamate		1.14	464	A	109 - 111
37	methyl <i>N</i> -[5-[6-[(4-fluoro-3-methoxyphenyl)-methyl-carbamoyl]-2-methyl-imidazo[1,2-		1.08	465	A	206 - 208

	a]pyrazin-3-yl]-2-pyridyl]carbamate					
38	methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2,8-dimethyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate		1.09	479	A	205-207

Example 1: Preparation of methyl N-[5-[6-[2-cyanoethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 1)



5 Step A: Preparation of 6-bromo-3-iodo-8-methyl-imidazo[1,2-a]pyrazine

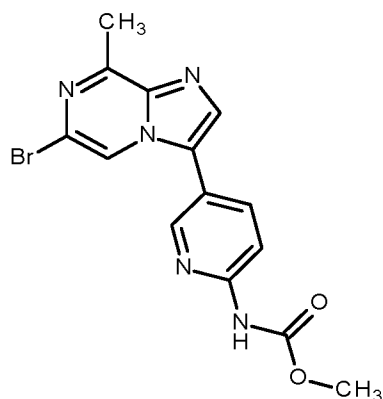


To a solution of 6-bromo-8-methyl-imidazo[1,2-a]pyrazine (CAS: 1073372-02-7) (1 g, 4.71 mmol, 1.00 equiv.) in acetonitrile (18.9 mL) was added N-iodosuccinimide (1.19 g, 5.18 mmol, 1.10 equiv.). The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduce pressure and the residue was quenched with 10% NaOH, followed with a saturated solution of Na₂S₂O₃ and extracted with chloroform. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford 6-bromo-3-iodo-8-methyl-imidazo[1,2-a]pyrazine.

LC-MS (method B): Rt 1.01 min, m/z = 338/340 (M+H)⁺

15

Step B: Preparation of methyl N-[5-(6-bromo-8-methyl-imidazo[1,2-a]pyrazin-3-yl)-2-pyridyl]carbamate



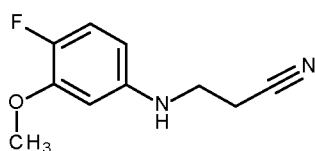
To a mixture of methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.36 g, 1.30 mmol, 1.10 equiv.), 6-bromo-3-iodo-8-methyl-imidazo[1,2-a]pyrazine (400 mg, 1.18 mmol, 1.10 equiv) and potassium carbonate (0.25 g, 1.77 mmol, 1.5 equiv.) in 2-methyltetrahydrofuran (12 mL) 5 was added tetrakis(triphenylphosphine)palladium(0) (0.069 g, 0.059 mmol, 0.05 equiv.). The reaction mixture was degassed with argon and then stirred in the microwave at 80 °C for 2 hours. After cooling down to room temperature, the reaction mixture was filtered through a Celite pad and washed with methanol. The filtrate was washed with water, then brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl 10 acetate) to afford methyl N-[5-(6-bromo-8-methyl-imidazo[1,2-a]pyrazin-3-yl)-2-pyridyl]carbamate.

LC-MS (method B): Rt 1.02 min, m/z = 361 (M-H)⁻

¹H-NMR (400 MHz, CDCl₃, ppm) δ = 1.22-1.37 (m, 4 H), 2.05 (s, 1 H), 2.95 (s, 3 H), 3.82 (s, 1 H), 3.88 (s, 3 H), 4.12 (d, J = 7.09 Hz, 1 H), 7.84 (s, 1 H), 7.89 8dd, J = 8.68, 2.32 Hz, 1 H), 8.21 (s, 1 H), 8.26 (d, J = 8.68 Hz, 1 H), 8.50-8.54 (m, 1 H), 9.02 (s, 1 H)

15

Step C: Preparation of 3-(4-fluoro-3-methoxy-anilino)propanenitrile



To a solution of 4-fluoro-3-methoxy-aniline (CAS: 64465-53-8) (0.750 g, 4.78 mmol, 1.00 equiv.) in acetonitrile (4.78 mL) were added sodium iodide (0.755 g, 4.78 mmol, 1.00 equiv.), potassium carbonate 20 (0.696 g, 4.78 mmol, 1.00 equiv.) and 3-bromopropanenitrile (CAS: 2417-90-5) (1.48 g, 10.5 mmol, 2.2 equiv.). The reaction mixture was stirred at 60 °C for 16 hours. The reaction mixture was cooled down to room temperature and then dissolved with water and extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford 3-(4-fluoro-3- 25 methoxy-anilino)propanenitrile.

LC-MS (method B): Rt 1.08 min, m/z = 195 (M+H)⁺

¹H-NMR (400 MHz, CDCl₃, ppm) δ = 2.63 (t, 2 H), 3.45 (t, 2 H), 3.87 (m, 3 H), 3.93 (s, 1 H), 6.08 (dt, J = 3.04, 8.71 Hz, 1 H), 6.26 (dd, J = 2.69, 7.21 Hz, 1 H), 6.91 (dd, J = 8.68, 11.25 Hz, 1 H)

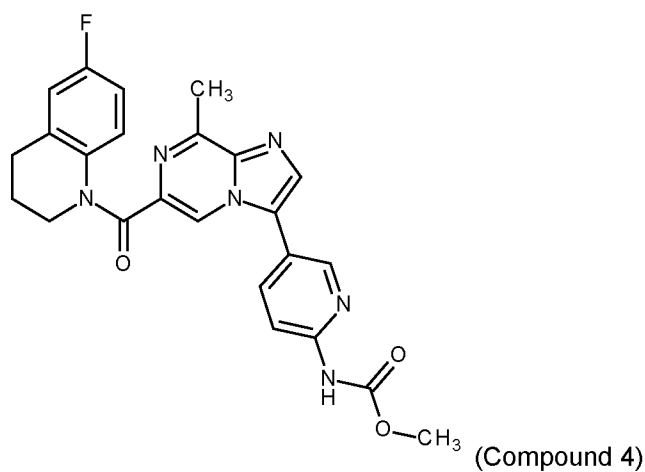
Step D: Preparation of methyl N-[5-[6-[2-cyanoethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 1)

A mixture of methyl N-[5-(6-bromo-8-methyl-imidazo[1,2-a]pyrazin-3-yl)-2-pyridyl]carbamate (200 mg, 0.55 mmol, 1.00 equiv.), 3-(4-fluoro-3-methoxy-anilino)propanenitrile (CAS: 1073372-02-7) (0.118 g, 0.60 mmol, 1.1 equiv.), bis(benzonitrile)palladium chloride (0.022 g, 0.055 mmol, 0.10 equiv.) and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (0.032 g, 0.055 mmol, 0.10 equiv.) and triethylamine (0.116 mL, 0.82 mmol, 1.50 equiv.) in toluene (1.38 mL), in a high pressure vessel, was flushed with nitrogen. The vial was pressurised with nitrogen and then with CO gas. The reaction mixture was stirred at 110 °C for 6 hours. The reaction mixture was filtered through celite and the filtrate was concentrated under reduce pressure. The residue was purified by reverse phase chromatography (C18 column, eluting with 5% to 90% MeCN/H₂O) to afford methyl N-[5-[6-[2-cyanoethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate.

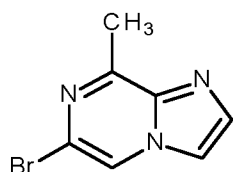
LC-MS (method B): Rt 1.07 min, m/z = 504 (M+H)⁺

¹H-NMR (400 MHz, CDCl₃, ppm) δ = 2.54 (m, 3 H), 2.86 (t, J = 6.69 Hz, 2 H), 3.74 (m, 6 H), 4.10 (t, J = 6.63 Hz, 2 H), 6.74 (br s, 1 H), 7.07 (br s, 1 H), 7.25 - 7.32 (m, 1 H), 7.98 - 8.05 (m, 3 H), 8.51 (br s, 2 H), 10.54 (s, 1 H).

Example 2: Preparation of methyl N-[5-[6-(6-fluoro-3,4-dihydro-2H-quinoline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 4)



Step A: Preparation of 6-bromo-8-methyl-imidazo[1,2-a]pyrazine

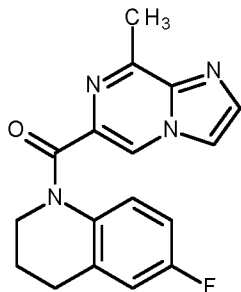


To a solution of 5-bromo-3-methyl-pyrazin-2-amine (10.00 g, 53.19 mmol 1.00 equiv.) in ethanol (212 mL) was added a chloroacetaldehyde solution 50% in water (20.27 mL, 159.6 mmol, 3.00 equiv.). The reaction mixture was stirred at 78 °C for 16 hours. The reaction mixture was quenched with a saturated NaHCO₃ solution, extracted with ethyl acetate and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford 6-bromo-8-methyl-imidazo[1,2-a]pyrazine.

LC-MS (method B): Rt 0.36 min, m/z = 212/214 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.74 (s, 3 H), 7.79 (d, *J* = 0.88 Hz, 1 H), 8.08 (d, *J* = 0.88 Hz, 1 H), 8.83 (s, 1 H).

5 Step B: Preparation of (6-fluoro-3,4-dihydro-2H-quinolin-1-yl)-(8-methylimidazo[1,2-a]pyrazin-6-yl)methanone

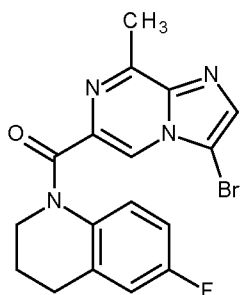


A mixture of 6-bromo-8-methyl-imidazo[1,2-a]pyrazine (1.00 g, 4.72 mmol, 1.00 equiv.), 6-fluoro-1,2,3,4-tetrahydroquinoline (0.720 g, 4.763 mmol, 1.01 equiv.), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (0.278 g, 0.471 mmol, 0.10 equiv.), bis(benzonitrile)palladium chloride (0.190 g, 0.471 mmol, 0.10 equiv.) and triethylamine (0.991 mL, 7.07 mmol, 1.50 equiv.) in toluene (10 mL) in a high pressure reactor, filled with 10 bar CO gas, was stirred at 110 °C for 6 hours. The mixture was filtered off and the filtrate was concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford (6-fluoro-3,4-dihydro-2H-quinolin-1-yl)-(8-methylimidazo[1,2-a]pyrazin-6-yl)methanone as a white solid.

15 LC-MS (method B): Rt 1.07 min, *m/z* = 311 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 1.88 - 1.97 (m, 2 H), 2.63 (s, 3 H), 2.76 - 2.86 (m, 2 H), 3.80 (t, *J* = 6.11 Hz, 2 H), 6.85 (br s, 1 H), 7.03 - 7.33 (m, 2 H), 7.76 - 7.83 (m, 1 H), 8.17 (d, *J* = 0.98 Hz, 1 H), 8.86 (s, 1 H).

20 Step C: Preparation of (3-bromo-8-methyl-imidazo[1,2-a]pyrazin-6-yl)-(6-fluoro-3,4-dihydro-2H-quinolin-1-yl)methanone



To a stirred solution of (6-fluoro-3,4-dihydro-2H-quinolin-1-yl)-(8-methylimidazo[1,2-a]pyrazin-6-yl)methanone (0.300 g, 0.966 mmol, 1.00 equiv.) in acetonitrile (3.86 mL) was added N-bromosuccinimide (0.172 g, 0.966 mmol, 1.00 equiv.) at room temperature and the reaction mixture was stirred for 1 hour. The reaction mixture was quenched with a saturated aqueous solution of Na₂S₂O₃ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to afford (3-bromo-8-methyl-imidazo[1,2-a]pyrazin-6-yl)-(6-fluoro-3,4-dihydro-2H-quinolin-1-yl)methanone.

LC-MS (method B): Rt 1.10 min, m/z = 389/391 (M+H)⁺

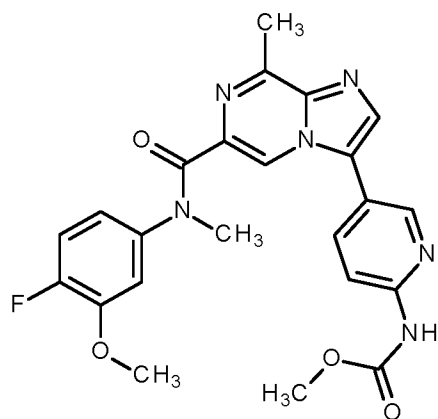
Step D: Preparation of methyl N-[5-[6-(6-fluoro-3,4-dihydro-2H-quinoline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 4)

- 5 To a solution of (3-bromo-8-methyl-imidazo[1,2-a]pyrazin-6-yl)-(6-fluoro-3,4-dihydro-2H-quinolin-1-yl)methanone (0.300 g, 0.770 mmol, 1.00 equiv.) and methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.271 g, 0.924 mmol, 1.20 equiv.) in acetonitrile (3 mL) and water (0.024 mL) was added sodium carbonate (0.257 g, 2.312 mmol, 3.00 equiv.). The mixture was purged with argon for 5 minutes. Then chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (0.063 g, 0.077 mmol, 10 equiv.) was added and the mixture was irradiated in the microwave oven at 100 °C for 1.25 hour. After cooling down to room temperature, the reaction mixture was filtered through a Celite pad and washed with methanol. The filtrate was concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford methyl N-[5-[6-(6-fluoro-3,4-dihydro-2H-quinoline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method B): Rt 1.03 min, m/z = 461 (M+H)⁺

- ¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 1.89 - 1.97 (m, 2 H), 2.63 - 2.72 (m, 3 H), 2.81 (t, J = 6.60 Hz, 2 H), 3.65 - 3.81 (m, 5 H), 6.78 - 6.90 (m, 1 H), 7.08 (dd, J = 9.23, 3.00 Hz, 1 H), 7.10 - 7.39 (m, 1 H), 8.02 - 8.05 (m, 1 H), 8.08 (s, 1 H), 8.09 - 8.13 (m, 1 H), 8.60 (d, J=2.08Hz, 1 H), 8.64 (s, 1 H), 10.53 (s, 1 H).

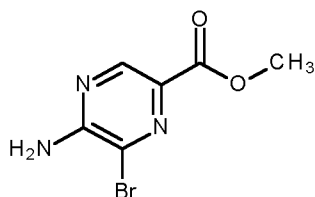
Example 3: preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (compound 7)



(Compound 7)

25

Step A: Preparation of methyl 5-amino-6-bromo-pyrazine-2-carboxylate



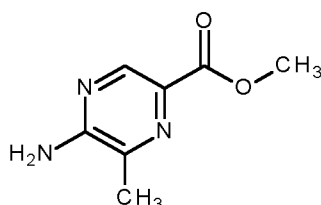
To an ice-cooled solution of methyl 5-aminopyrazine-2-carboxylate (10.0 g, 62.0 mmol, 1.00 equiv.) in acetonitrile (100 mL) was added N-bromosuccinimide (12.1 g, 68.2 mmol, 1.10 equiv.). The reaction

mixture was stirred at room temperature for 16 hours. The reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford methyl 5-amino-6-bromo-pyrazine-2-carboxylate as

5 brown solid.

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 3.81 (s, 3 H), 7.68 (brs, 2 H), 8.53 (s, 1 H).

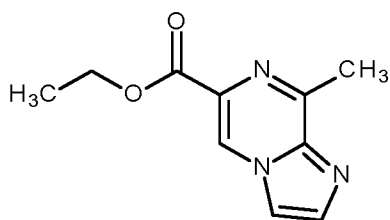
Step B: Preparation of methyl 5-amino-6-methyl-pyrazine-2-carboxylate



- 10 To a solution of methyl 5-amino-6-bromo-pyrazine-2-carboxylate (15.0 g, 61.4 mmol, 1.00 equiv.) and 2,4,6-trimethyl-1,3,5,2,4,6-trioxatriborinane (15.4 g, 123 mmol, 2.00 equiv.) in dioxane (150 mL) was added potassium carbonate (21.22 g, 153.5 mmol, 2.50 equiv.) and the mixture was purged with argon for 5 minutes. Then [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (2.246 g, 3.070 mmol, 0.05 equiv.) was added and the mixture was irradiated in the microwave oven at 110 °C for 1 hour. The
- 15 reaction mixture was concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (dichloromethane/methanol) to afford methyl 5-amino-6-methyl-pyrazine-2-carboxylate as a white solid.

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.31 (s, 3 H), 3.78 (s, 3 H), 7.13 (brs, 2 H), 8.44 (s, 1 H).

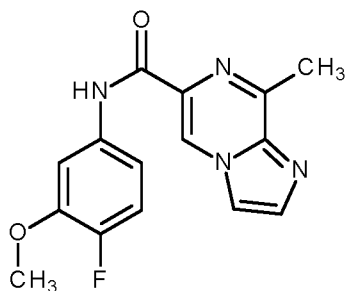
20 Step C: Preparation of ethyl 8-methylimidazo[1,2-a]pyrazine-6-carboxylate (Compound X-1)



- To a stirred solution of methyl 5-amino-6-methyl-pyrazine-2-carboxylate (1.10 g, 5.92 mmol, 1.00 equiv.) in ethanol (25.0 mL) was added 2-chloroacetaldehyde (2.32 g, 11.8 mmol, 2.00 equiv.). The reaction mixture was stirred at 100 °C for 16 hours. The reaction mixture was concentrated under reduced
- 25 pressure, then diluted with ethyl acetate and washed with a saturated solution of NaHCO₃. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford a mixture (1:1) of ethyl 8-methylimidazo[1,2-a]pyrazine-6-carboxylate and methyl 8-methylimidazo[1,2-a]pyrazine-6-carboxylate as brown solid.

- 30 ¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.77 (s, 3 H), 3.89 (s, 3 H), 7.84 (s, 1 H), 8.22 (s, 1 H), 9.30 (s, 1 H).

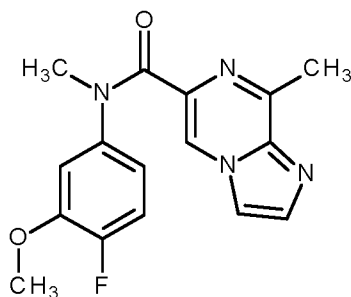
Step D: Preparation of N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



To a stirred solution of ethyl 8-methylimidazo[1,2-a]pyrazine-6-carboxylate (Compound X-1) (2.20 g, 9.65 mmol, 1.00 equiv.), 4-fluoro-3-methoxy-aniline (1.63 g, 11.6 mmol, 1.20 equiv.) in dry toluene (50.0 mL) was added trimethylaluminium (9.65 mL, 19.3 mmol, 2.00 equiv.) in toluene. The resulting reaction mixture was stirred at 80 °C for 4 hours under nitrogen atmosphere. The reaction mixture was cooled to 0 °C, quenched with aqueous Rochelle's salt and diluted with ethyl acetate. The reaction mixture was filtered through a celite pad and washed with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a brown solid.

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.88 (s, 3 H), 3.86 (s, 3 H), 7.19-7.24 (m, 1 H), 7.56-7.59 (m, 1 H), 7.74-7.76 (dd, J = 2.4, 8.0 Hz, 1 H), 7.86 (d, J = 0.8 Hz, 1 H), 8.29 (d, J = 0.8 Hz, 1 H), 9.26 (s, 1 H), 10.40 (s, 1 H).

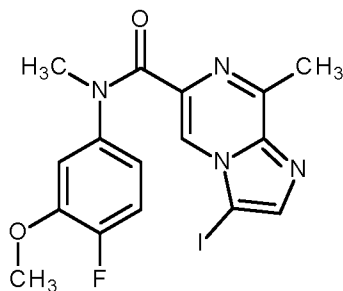
15 Step E: Preparation of N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide



To an ice-cooled solution of N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (1.00 g, 3.16 mmol, 1.00 equiv.) in dry THF (20.0 mL) was added sodium hydride 60% in oil (0.380 g, 9.49 mmol, 3.00 equiv.). After 30 minutes of stirring, iodomethane (0.591 mL, 9.49 mmol, 3.00 equiv.) was added dropwise and the reaction mixture was stirred at room temperature for 6 hours. The reaction mixture was cooled to 0 °C, quenched with NH₄Cl solution and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge (dichloromethane/methanol) to afford N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as an off white solid.

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.46 (s, 3 H), 3.40 (s, 3 H), 3.74 (s, 3 H), 6.68-6.70 (d, J = 7.6 Hz, 1 H), 7.03- 7.08 (m, 1 H), 7.13 - 7.15 (dd, J = 2.4, 7.6 Hz, 1 H), 7.75 (d, J = 0.8 Hz, 1 H), 8.13 (d, J = 1.2 Hz, 1 H), 8.80 (s, 1 H).

Step F: Preparation of N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide

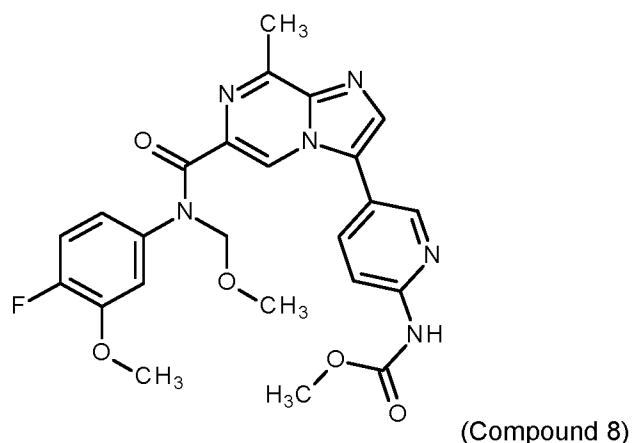


- 5 To a stirred solution of N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (30.0 mg, 0.0859 mmol, 1.00 equiv.) in DMF (2 mL) was added N-iodosuccinimide (21.3 mg, 0.0945 mmol, 1.10 equiv.) at room temperature and stirred for 16 hours. The reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was
- 10 purified over a silica gel cartridge (cyclohexane/ethyl acetate) to afford N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide as an off-white solid.
- ¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.45 (s, 3 H), 3.41 (s, 3 H), 3.75 (s, 3 H), 6.74 (s, 1H), 7.03-7.08 (m, 1 H), 7.23- 7.26 (dd, J = 2.4, 8.0 Hz, 1 H), 7.90 (s, 1 H), 8.37 (s, 1H).

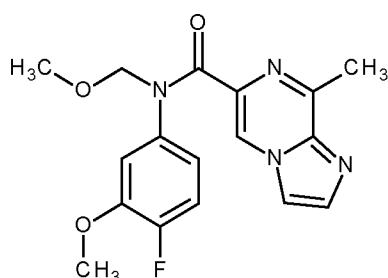
15 Step G: Preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 7)

- To a stirred solution of N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (400 mg, 0.818 mmol, 1.00 equiv.), methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.273 g, 0.981 mmol, 1.20 equiv.) in 1,4-dioxane/ water (3:1) (16.0 mL) was
- 20 added cesium carbonate (0.533 g, 1.64 mmol, 2.00 equiv.), the mixture was purged with a stream of argon for 2 minutes. cataCXium® A Pd G3 (29.8 mg, 0.0409 mmol, 0.05 equiv.) was added to the reaction mixture under N₂ atmosphere. The resulting reaction mixture was irradiated in the microwaves at 100 °C for 1 hour. After cooling down to room temperature, the reaction mixture was filtered through a Celite pad and washed with ethyl acetate. The filtrate was washed with water, then brine, dried over
- 25 Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over silica gel cartridge (dichloromethane/ methanol) to afford methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as an off white solid.
- ¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.56 (s, 3 H), 3.38 (s, 3 H), 3.71 (s, 3 H), 3.73 (s, 3 H), 6.75 (s, 1 H), 7.03-7.08 (t, J = 9.2 Hz, 1 H), 7.20- 7.23 (dd, J = 2.4, 8.0 Hz, 1 H), 7.98-8.05 (m, 3 H), 8.52 (s, 2
- 30 H), 10.50 (s, 1 H).

Example 4: preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-(methoxymethyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (compound 8)



Step A: Preparation of N-(4-fluoro-3-methoxy-phenyl)-N-(methoxymethyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



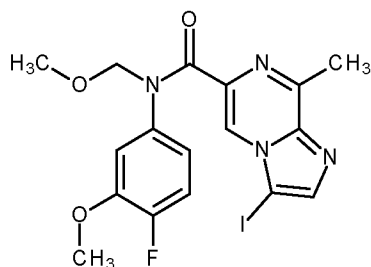
5

To an ice-cooled solution of N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (1.20 g, 3.80 mmol, 1.00 equiv.) in DMF (50.0 mL) was added sodium hydride 60 % in oil (497 mg, 11.4 mmol, 3.00 equiv.). After 30 minutes of stirring, chloro(methoxy)methane (611 mg, 7.59 mmol, 2.00 equiv.) was added dropwise and the reaction mixture was stirred at room temperature for 2

10 hours. The reaction mixture was cooled to 0 °C, quenched with NH₄Cl solution and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge C-18 (acetonitrile/water) to afford N-(4-fluoro-3-methoxy-phenyl)-N-(methoxymethyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a solid.

15 ¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 2.63 (s, 3 H), 3.48 (s, 3 H), 3.84 (s, 3 H), 5.28 (s, 2 H), 6.68 (s, 1H), 6.91-6.96 (m, 2 H), 7.68 (s, 1 H), 7.76 (s, 1 H), 8.54 (s, 1H).

Step B: Preparation of N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N-(methoxymethyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



20

To a stirred solution of N-(4-fluoro-3-methoxy-phenyl)-N-(methoxymethyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.500 g, 1.31 mmol, 1.00 equiv.) in DMF (10 mL) was added N-

iodosuccinimide (0.676 g, 3.01 mmol, 2.30 equiv.) at room temperature and stirred for 16 hours. The reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over a silica gel cartridge C-18 (acetonitrile/water) to afford N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N-(methoxymethyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as solid.

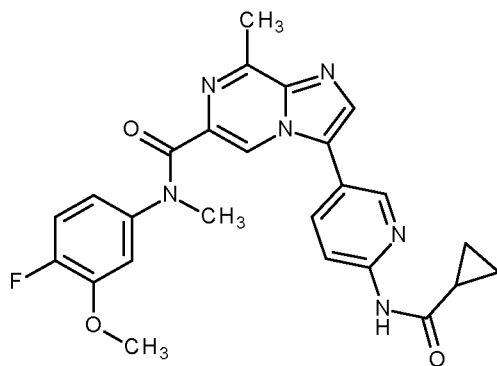
¹H-NMR (400 MHz, CDCl₃, ppm) δ = 2.64 (s, 3 H), 3.50 (s, 3 H), 3.85 (s, 3 H), 5.28 (s, 2 H), 6.68 (brs, 1H), 6.91-6.98 (m, 2 H), 7.81 (s, 1 H), 8.47 (s, 1H).

10 Step C: Preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-(methoxymethyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 8)

To a stirred solution of N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N-(methoxymethyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.400 g, 0.766 mmol, 1.00 equiv.), methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (255 mg, 0.919 mmol, 1.20 equiv.) in DMF (5.0 mL) was added cesium carbonate (499 mg, 1.53 mmol, 2.00 equiv.), the mixture was purged with a stream of argon for 2 minutes. cataCXium® A Pd G3 (27.9 mg, 0.0383 mmol, 0.05 equiv.) was added to the reaction mixture under N₂ atmosphere. The resulting reaction mixture was irradiated in the microwave at 100 °C for 1 hour. After cooling down to room temperature, the reaction mixture was filtered through a Celite pad and washed with ethyl acetate. The filtrate was washed with water, then brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified over silica gel cartridge (dichloromethane/ methanol) to afford methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-(methoxymethyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as an off white solid.

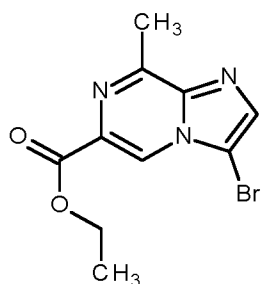
¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.50 (s, 1 H), 8.62 (s, 1 H), 8.51 (s, 1 H), 8.07-7.99 (m, 3 H), 7.23-7.19 (dd, J = 8.0, 2.4 Hz, 1 H), 7.11-7.03 (t, J = 9.2 Hz, 1H), 6.78 (br. s, 1H), 5.20 (s, 2 H), 3.72 (s, 3H), 3.33 (s, 3H), 2.50 (s, 3H).

Example 5: Preparation of 3-[6-(cyclopropanecarbonylamino)-3-pyridyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound 19)



(Compound 19)

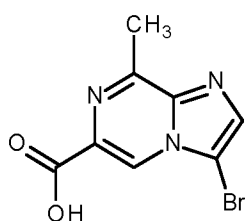
Step A: Preparation of ethyl 3-bromo-8-methyl-imidazo[1,2-a]pyrazine-6-carboxylate



To a solution of ethyl 8-methylimidazo[1,2-a]pyrazine-6-carboxylate (Compound X-1) (5.40 g, 26.3 mmol) in dimethylformamide (60.0 mL) was added N-bromosuccinimide (5.62 g, 31.6 mmol) in portions at room temperature. The mixture was stirred at room temperature for 2 hours. After full consumption of the starting material, the reaction was diluted with water. The precipitate was collected by filtration, washed with water and concentrated under reduced pressure to afford ethyl 3-bromo-8-methylimidazo[1,2-a]pyrazine-6-carboxylate as a brown solid.

LC-MS (method A): Rt 1.04 min, m/z = 284 (M+H)⁺

10 Step B: Preparation of 3-bromo-8-methyl-imidazo[1,2-a]pyrazine-6-carboxylic acid (Compound X-2)

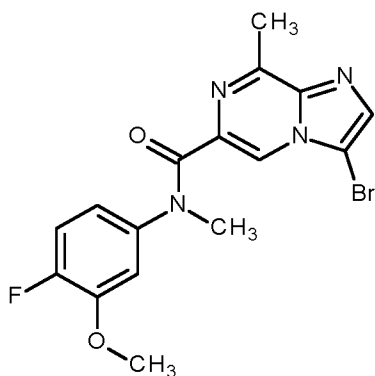


(Compound X-2)

To a solution of ethyl 3-bromo-8-methyl-imidazo[1,2-a]pyrazine-6-carboxylate (6.50 g, 22.9 mmol) in tetrahydrofuran/H₂O (1:1, 70.0 mL) was added lithium hydroxide (1.10 g, 45.8 mmol). The mixture was stirred at room temperature for 3 hours. Then, the organic solvent was removed under reduced pressure. The aqueous solution was adjusted to pH 2-3 with aqueous HCl (2N). The precipitate was collected by filtration, washed with water to afford 3-bromo-8-methyl-imidazo[1,2-a]pyrazine-6-carboxylic acid as a white solid.

LC-MS (method A): Rt 0.83 min, m/z = 256 (M+H)⁺

20 Step C: Preparation of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-3)

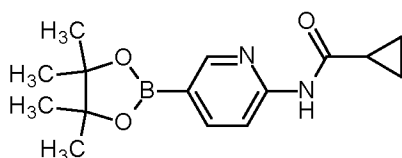


(Compound X-3)

To a mixture of 3-bromo-8-methyl-imidazo[1,2-a] pyrazine-6-carboxylic acid (Compound X-2) (0.800 g, 3.12 mmol) in dimethylformamide (10.0 mL) was added 1-methylimidazole (0.770 g, 9.37 mmol) and [chloro(dimethylamine)methylene]-dimethyl-ammonium hexafluorophosphate (CAS 94790-35-9, 1.32 g, 4.68 mmol) at room temperature. The solution was stirred at room temperature for 5 min. Then, 4-fluoro-3-methoxy-N-methyl-aniline (0.0145 g, 0.0937 mmol) was added by portions. The resulting solution was stirred for 2 hours. The reaction mixture was diluted with ethyl acetate washed with water and saturated aqueous NaCl, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using a dichloromethane/methanol gradient to afford 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a] pyrazine-6-carboxamide as a brown solid.

LC-MS (method A): Rt 1.10 min, m/z = 393 (M+H)⁺

Step D: Preparation of N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]cyclopropanecarboxamide



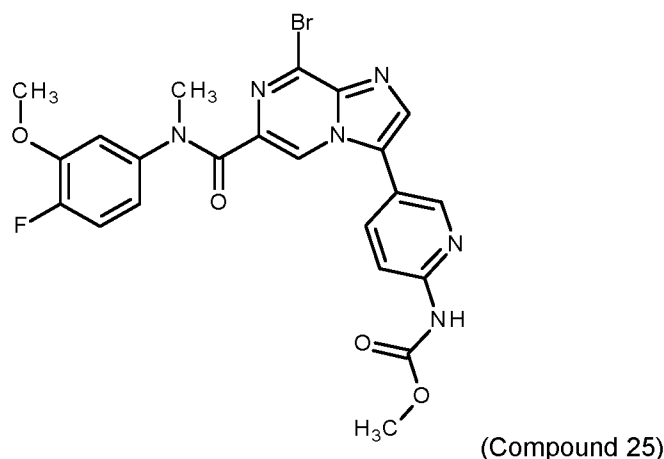
Under a nitrogen atmosphere, 2-aminopyridine-5-boronic acid pinacolester, CAS 827614-64-2, (1.00 g, 4.31 mmol) was dissolved in ethyl acetate (50 mL). Then pyridine (1.39 g, 17.3 mmol, 1.42 mL) was added. The reaction mixture was cooled to 0 °C. Then cyclopropanecarbonyl chloride, CAS 4023-34-1, (1.84 g, 17.26 mmol, 1.60 mL) was added. The resulting mixture was stirred at room temperature for 1 hour. Cold water and ethyl acetate were added to the mixture. Then the layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude material was used as such in the following step, without further purification.

Step E: Preparation of 3-[6-(cyclopropanecarbonylamino)-3-pyridyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound 19)

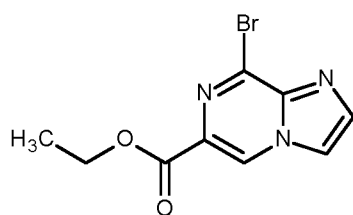
Under an argon atmosphere, N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]cyclopropanecarboxamide (0.052 mmol), XPhos Pd G3, CAS 1445085-55-1, (3.455 mg, 0.004 mmol) were placed in a vial. Then, a solution of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-3) (0.040 mmol) in 1,4-dioxane (0.4 mL, degassed with argon) was added, followed by a solution of sodium carbonate (12.85 mg, 0.12 mmol) in water (0.1 mL, degassed with argon). The reaction mixture was stirred under argon, at 100 °C for 16 hours. Then, the solvent was evaporated. The residue was dissolved in dimethylacetamide (0.4 mL) and methanol (0.4 mL). The resulting suspension was filtered and filtrate was purified by reverse phase chromatography to afford the desired compound.

LC-MS (method C): Rt 1.24 min, m/z = 474 (M+H)⁺

Example 6: Preparation of methyl N-[5-[8-bromo-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 25)



Step A: Preparation of ethyl 8-bromoimidazo[1,2-a]pyrazine-6-carboxylate

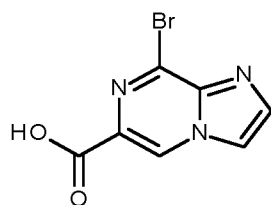


- 5 To a solution of ethyl 5-amino-6-bromo-pyrazine-2-carboxylate (preparation described in patent US9242996, 2016, B2) (4.00 g, 16.3 mmol) in acetonitrile (60.0 mL) was added 2-bromo-1,1-dimethoxyethane (2.75 g, 16.3 mmol) successively. The mixture was heated at 140 °C in a microwave reactor for 2 hours. After completion of the reaction, the resulting mixture was concentrated under vacuum. The crude product was purified by flash chromatography using a dichloromethane/methanol gradient to
- 10 obtain ethyl 8-bromoimidazo[1,2-a]pyrazine-6-carboxylate as a yellow solid.

LC-MS (method A): Rt 0.92 min, m/z = 270 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 9.46 (s, 1H), 8.40 (d, J = 1.0 Hz, 1H), 7.96 (d, J = 1.0 Hz, 1H), 4.38 (q, J = 7.0 Hz, 2H), 1.36 (t, J = 7.0 Hz, 3H).

- 15 Step B: Preparation of 8-bromoimidazo[1,2-a]pyrazine-6-carboxylic acid (Compound X-4)

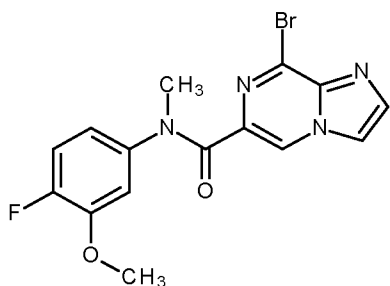


(Compound X-4)

- To a solution of ethyl 8-bromoimidazo[1,2-a]pyrazine-6-carboxylate (1.00 g, 3.70 mmol) in tetrahydrofuran (10.0 mL) and water (2.50 mL) was added lithium hydroxide (0.177 g, 7.41 mmol). The mixture was stirred at room temperature for 3 hours. The mixture was diluted with water and extracted
- 20 with ethyl acetate. The pH of the water layer was adjusted to pH 4-5 with aqueous HCl (1N) and lyophilized to afford 8-bromoimidazo[1,2-a]pyrazine-6-carboxylic acid which was used in next step without further purification.

LC-MS (method A): Rt 0.71 min, m/z = 244 (M+H)⁺

Step C: Preparation of 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-5)



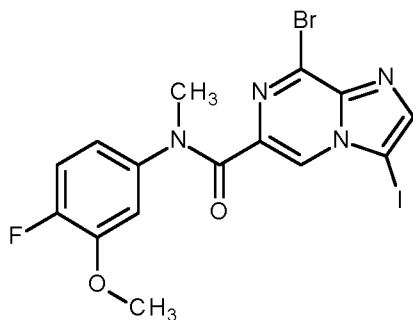
(Compound X-5)

To a solution of 8-bromoimidazo[1,2-a]pyrazine-6-carboxylic acid (Compound X-4) (0.130 g, 0.537 mmol) and 4-fluoro-3-methoxy-N-methyl-aniline (0.0917 g, 0.591 mmol) in pyridine (2.0 mL) was added propylphosphonic anhydride (50.0 wt. % solution in ethyl acetate, 1.03 g, 1.61 mmol) dropwise at 65 °C under nitrogen atmosphere. The mixture was heated at 65 °C for 2 hours. The final mixture was diluted with saturated aqueous NaHCO₃ and extracted with ethyl acetate. The combined organic layers were washed with water, dried with sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to give 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a yellow oil.

LC-MS (method A): Rt 1.07 min, m/z = 380 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 9.03 (s, 1H), 8.32 (s, 1H), 7.87 (s, 1H), 7.18 (dd, J = 7.8, 2.2 Hz, 1H), 7.07 (dd, J = 11.0, 9.0 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 3.76 (s, 3H), 3.40 (d, J = 6.6 Hz, 3H).

Step D: Preparation of 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



To a solution of 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-5) (0.200 g, 0.527 mmol) in acetonitrile (2.0 mL) was added N-iodosuccinimide (0.119 g, 0.527 mmol) dropwise at 0 °C. The reaction was stirred at 65 °C for 16 hours. Then, the resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to give 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a yellow solid.

LC-MS (method A): Rt 2.46 min, m/z = 505 (M+H)⁺

¹H-NMR (400 MHz, CDCl₃, ppm) δ = 8.59 (s, 1H), 7.90 (s, 1H), 6.95 (d, J = 8.2 Hz, 2H), 6.58 (s, 1H), 3.89 (d, J = 4.4 Hz, 3H), 3.51 (s, 3H).

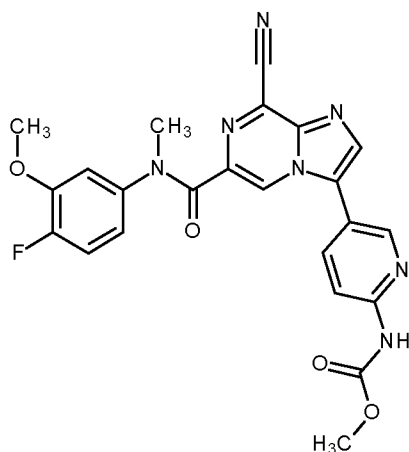
Step F: Preparation of methyl N-[5-[8-bromo-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 25)

To a solution of 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-3-iodo-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.120 g, 0.238 mmol) in dioxane (10.0 mL) and water (2.00 mL) was added methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.0991 g, 0.356 mmol), bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.0172 g, 0.0238 mmol) and K₂CO₃ (0.0662 g, 0.475 mmol). The mixture was stirred at room temperature under an atmosphere of N₂ for 2 hours. The mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by silica gel column chromatography (eluting with methanol/dichloromethane) to afford methyl N-[5-[8-bromo-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method A): Rt 2.41 min, *m/z* = 529 (M+H)⁺

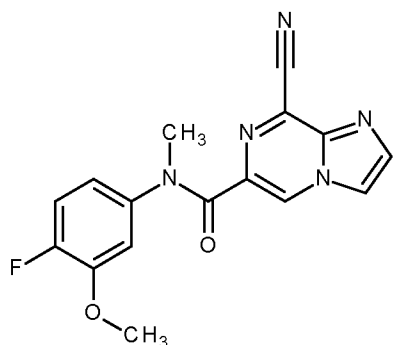
¹H-NMR (400 MHz, CDCl₃, ppm) δ = 8.59 (s, 1H), 8.41 (s, 1H), 8.29 – 8.17 (m, 2H), 7.90 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 2H), 6.58 (s, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.48 (s, 3H).

Example 7: Preparation of methyl N-[5-[8-cyano-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 23)



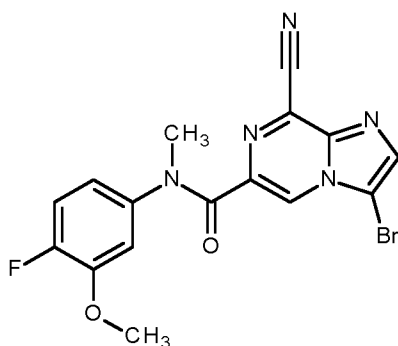
(Compound 23)

Step A: Preparation of 8-cyano-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



- To a solution of 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-5) (0.200 g, 0.527 mmol) in dimethylformamide (4.00 mL) was added zinc dicyanide (0.124 g, 1.05 mmol), (5-diphenylphosphanyl-9,9-dimethyl-xanthen-4-yl)-diphenyl-phosphane (0.0610 g, 0.105 mmol) and Pd₂(dba)₃ (CAS 51364-51-3, 0.0483 g, 0.0527 mmol) successively. The mixture was heated at 100 °C in a microwave reactor for 1 hour under an atmosphere of N₂. Then the resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to afford 8-cyano-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a yellow solid.
- LC-MS (method A): Rt 1.06 min, *m/z* = 326 (M+H)⁺

Step B: Preparation of 3-bromo-8-cyano-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



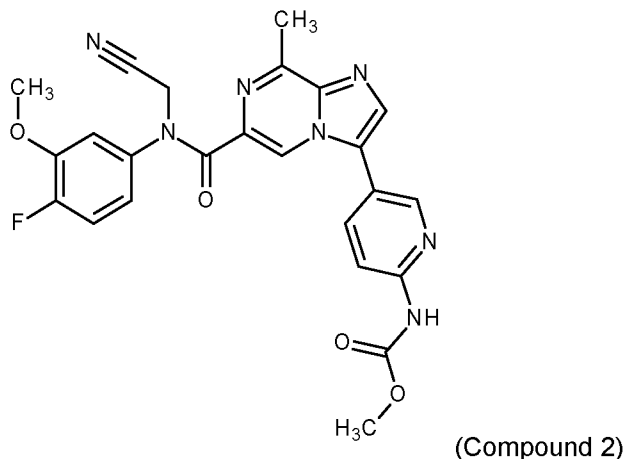
- To a solution of 8-cyano-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.150 g, 0.461 mmol) in acetonitrile (3.0 mL) was added 1-bromopyrrolidine-2,5-dione (0.0821 g, 0.461 mmol) dropwise at 0 °C. The reaction was stirred at room temperature for 5 hours. Then the resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to afford 3-bromo-8-cyano-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a yellow solid.
- LC-MS (method A): Rt 1.21 min, *m/z* = 406 (M+H)⁺

Step C: Preparation of methyl N-[5-[8-cyano-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 23)

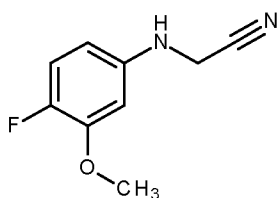
- To a solution of 3-bromo-8-cyano-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.0700 g, 0.173 mmol) in dioxane/H₂O (4:1, 2.5 mL) was added methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.0722 g, 0.260 mmol), K₂CO₃ (0.0598 g, 0.433 mmol) and bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.0127 g, 0.0173 mmol). The mixture was stirred at 50 °C for 1.5 hours under N₂ atmosphere. Then the resulting mixture was concentrated under reduced pressure. The crude product was purified by flash chromatography using a dichloromethane/methanol gradient to afford methyl N-[5-[8-cyano-6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a yellow solid.
- LC-MS (method A): Rt 1.16 min, *m/z* = 476 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.57 (s, 1H), 8.98 (s, 1H), 8.59 (s, 1H), 8.32 (s, 1H), 8.07 (s, 2H), 7.25 (d, J = 5.8 Hz, 1H), 7.08 (s, 1H), 6.78 (s, 1H), 3.74 (s, 6H), 3.41 (s, 3H).

Example 8: Preparation of methyl N-[5-[6-[cyanomethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 2)



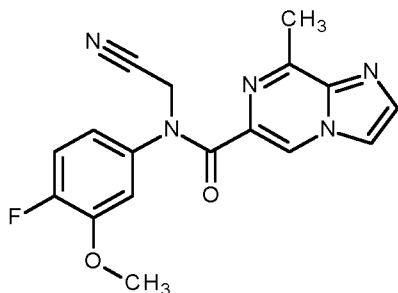
Step A: Preparation of 2-(4-fluoro-3-methoxy-anilino)acetonitrile



To a solution of 4-fluoro-3-methoxy-aniline (0.500 g, 3.188 mmol) in acetonitrile (3.18 mL) was added sodium iodide (0.503 g, 3.188 mmol) and 2-chloroacetonitrile (0.225 mL, 3.379 mmol). The mixture was stirred at 70 °C for 3 hours. Then, the reaction was cooled to room temperature and water was added. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was used as such without further purification in the following step.

LC-MS (method B): Rt 1.01 min, m/z = 181 (M+H)⁺

Step B: N-(cyanomethyl)-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide



A vial was charged with 6-bromo-8-methyl-imidazo[1,2-a]pyrazine, CAS 1159815-50-5 (0.300 g, 1.414 mmol), 2-(4-fluoro-3-methoxy-anilino)acetonitrile (0.267 g, 1.49 mmol), bis(benzonitrile)palladium chloride (0.057 g, 0.14 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (0.083 g, 0.14 mmol),

toluene (3.5 mL) and triethylamine (0.297 mL). The vial was flushed with nitrogen, then the vial was pressurized with nitrogen, then flushed with carbon monoxide twice and finally pressurized with 10 bar of carbon monoxide. The pressurized vial was heated at 110 °C for 7 hours. Then, the mixture was filtered through celite pad, concentrated under reduced pressure. The crude material was purified by

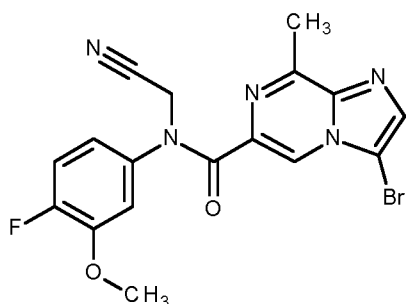
5 flash chromatography using a cyclohexane/ethyl acetate gradient to afford *N*-(cyanomethyl)-*N*-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-*a*]pyrazine-6-carboxamide.

LC-MS (method B): Rt 0.97 min, m/z = 340 (M+H)⁺

¹H-NMR (400 MHz, CDCl₃, ppm) δ = 8.62 (br s, 1 H), 7.66 - 7.75 (m, 2 H), 6.84 – 6.97 (m, 2 H), 6.60-6.73 (m, 1 H), 4.68 (br s, 2 H), 3.79 (s, 3 H), 2.47 (s, 3 H)

10

Step C: Preparation of 3-bromo-N-(cyanomethyl)-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-*a*]pyrazine-6-carboxamide



To a solution of *N*-(cyanomethyl)-*N*-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-*a*]pyrazine-6-carboxamide (0.037 g, 0.11 mmol) in acetonitrile (0.43 mL) was added 1-bromopyrrolidine-2,5-dione (0.0213 g, 0.120 mmol) dropwise. The reaction was stirred at room temperature for 3 hours. Then the resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a cyclohexane/ethyl acetate gradient to afford 3-bromo-N-

15 (cyanomethyl)-*N*-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-*a*]pyrazine-6-carboxamide

20

LC-MS (method B): Rt 1.03 min, m/z = 418 (M+H)⁺

¹H-NMR (400 MHz, CDCl₃, ppm) δ = 8.62 (br s, 1 H), 7.76 (s, 1 H), 6.90 – 7.08 (m, 2 H), 6.74 (br s, 1 H), 4.76 (br s, 2 H), 3.87 (s, 3 H), 2.54 (s, 3 H)

25 Step D: Preparation of methyl N-[5-[6-[cyanomethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-*a*]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 2)

To a solution of 3-bromo-N-(cyanomethyl)-*N*-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-*a*]pyrazine-6-carboxamide (0.23 g, 0.55 mmol), methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.211 g, 0.715 mmol) in acetonitrile (4.40 mL) was added sodium carbonate (0.175 g, 1.65 mmol) in water (2.19 mL). The resulting solution was degassed with nitrogen for 15 minutes. Then, chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (CAS: 1310584-14-5) (0.044 g, 0.055 mmol) was added and the vial was heated at 100 °C in a microwave reactor for 2.5 hours. Then, the reaction was diluted with methanol, filtered through celite pad and the filtrate was evaporated under reduced pressure. The crude material was

30 purified by flash chromatography using a ethyl acetate/methanol gradient to afford methyl N-[5-[6-

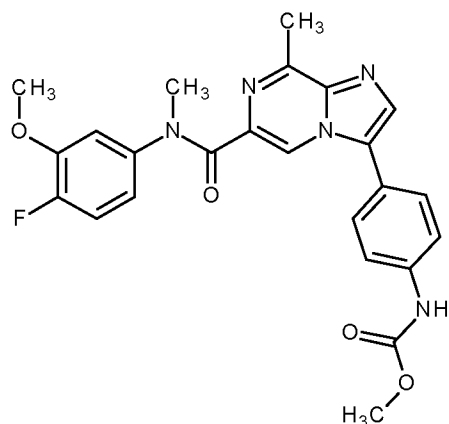
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[cyanomethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method B): Rt 1.02 min, m/z = 490 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.52 (s, 1 H), 8.66 (s, 1 H), 8.55 (s, 1 H), 8.03 (d, 3 H), 7.30-7.32 (dd, 1 H), 7.09 - 7.14 (m, 1 H), 6.76 - 6.79 (m, 1 H), 4.97 (s, 2 H), 3.76 (s, 3 H), 3.73 (s, 3 H), 2.52 (s, 3 H).

Example 9: Preparation of methyl N-[4-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]phenyl]carbamate (Compound 36)



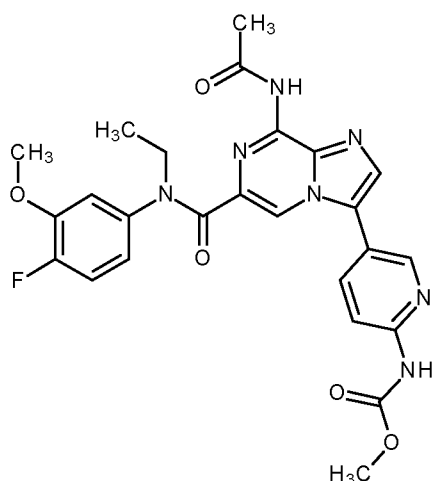
(Compound 36)

To a mixture of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-3) (0.200 g, 0.509 mmol) and methyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]carbamate, CAS 844500-75-0 (0.169 g, 0.610 mmol) in mixture of dioxane/H₂O (4:1, 5.0 mL) was added 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (0.0415 g, 0.0509 mmol) and potassium carbonate (0.211 g, 1.53 mmol). The mixture was stirred at 55 °C for 2 hours under a N₂ atmosphere. The mixture was concentrated under reduced pressure, the residue was purified by flash chromatography using a dichloromethane/methanol gradient to afford the desired compound, which was triturated with acetonitrile/ petroleum ether (2:1) to afford methyl N-[4-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]phenyl]carbamate as a white solid.

LC-MS (method A): Rt 1.14 min, m/z = 464 (M+H)⁺

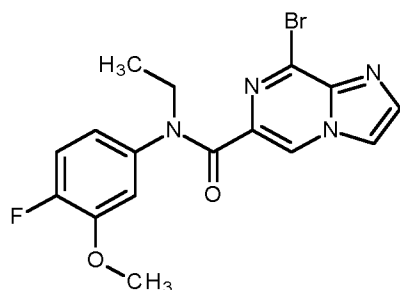
¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 9.94 (s, 1H), 8.47 (s, 1H), 7.91 (s, 1H), 7.67 (d, J = 8.6 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 7.24 (dd, J = 7.8, 2.4 Hz, 1H), 7.08-7.03 (m, 1H), 6.74 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.39 (s, 3H), 2.55 (s, 3H).

Example 10: Preparation of methyl N-[5-[8-acetamido-6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 21)



(Compound 21)

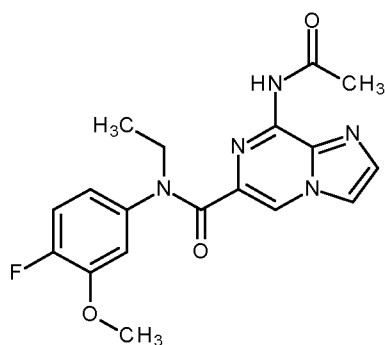
Step A: Preparation of 8-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide



- 5 To a solution of 8-bromoimidazo[1,2-a]pyrazine-6-carboxylic acid (Compound X-4) (0.440 g, 1.818 mmol) and N-ethyl-4-fluoro-3-methoxy-aniline (0.369 g, 2.18 mmol) in pyridine (5.0 mL) was added propylphosphonic anhydride (50.0 wt. % solution in ethyl acetate, 5.78 g, 9.09 mmol) dropwise at 70 °C under nitrogen atmosphere. The mixture was heated at 70 °C for 2 hours. The final mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried
- 10 with sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to give 8-bromo-N-(4-fluoro-3-methoxy-phenyl)-N-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a yellow solid.

LC-MS (method A): Rt 1.12 min, m/z = 393 (M+H)⁺

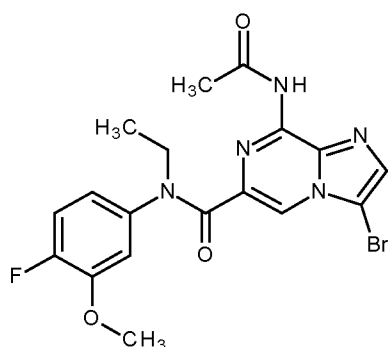
- 15 Step B: Preparation of 8-acetamido-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide



To a solution of 8-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide (0.400 g, 1.02 mmol) in dioxane (5.00 mL) was added acetamide (0.120 g, 2.03 mmol), Xantphos-Pd-G2 (CAS 1375325-77-1, 0.0904 g, 0.102 mmol) and cesium carbonate (0.497 g, 1.53 mmol). The mixture was stirred at 70 °C under an atmosphere of N₂ for 2 hours. The mixture was diluted with water and extracted with ethyl acetate. The organic layer was concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to give 8-acetamido-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide as a white solid.

LC-MS (method A): Rt 0.97 min, m/z = 372 (M+H)⁺

10 Step C: 8-acetamido-3-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide



To a solution of 8-acetamido-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide (0.400 g, 1.077 mmol) in dichloromethane (10.0 mL) was added 1-bromopyrrolidine-2,5-dione (0.192 g, 1.077 mmol, 1.0 eq.) portionwise at 0 °C. The reaction was stirred at room temperature for 4 hours. Then the resulting mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient to afford 8-acetamido-3-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide as a white solid.

LC-MS (method A): Rt 2.43 min, m/z = 452 (M+H)⁺

Step D: Preparation of methyl N-[5-[8-acetamido-6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 21)

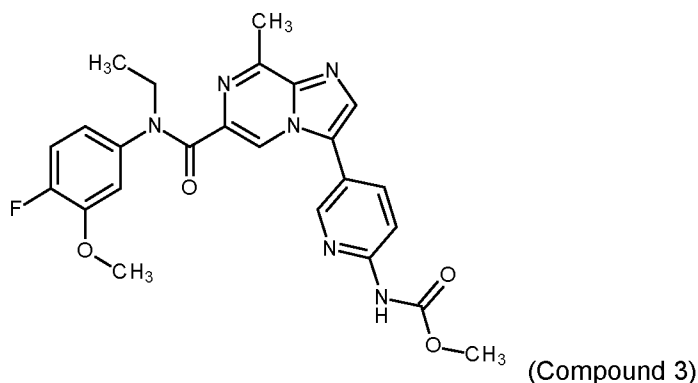
To a solution of 8-acetamido-3-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)imidazo[1,2-a]pyrazine-6-carboxamide (0.180 g, 0.400 mmol) in dioxane (5.0 mL) and water (1.00 mL) was added methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.222 g, 0.800 mmol), bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.0293 g, 0.0400 mmol) and K₂CO₃ (0.167 g, 1.20 mmol). The mixture was stirred at 50 °C under an atmosphere of N₂ for 2 hours. The mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by silica gel column chromatography (eluting with methanol/dichloromethane) to afford methyl N-[5-[8-acetamido-6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method A): Rt 1.46 min, m/z = 522 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.10 (s, 1H), 9.75 (s, 1H), 8.49 (d, *J* = 2.3 Hz, 1H), 8.33 (s, 1H), 7.98 (dt, *J* = 8.6, 5.5 Hz, 2H), 7.91 (s, 1H), 7.10 (dd, *J* = 7.8, 2.5 Hz, 1H), 7.01 (dd, *J* = 11.3, 8.5 Hz, 1H), 6.77 – 6.69 (m, 1H), 3.88 (d, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 2.19 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H).

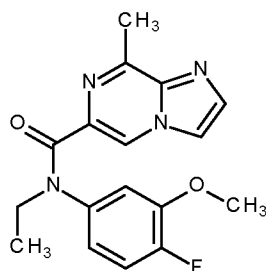
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Example 11: Preparation of methyl N-[5-[6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 3)



Step A: Preparation of N-ethyl-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide

10



A vial was charged with 6-bromo-8-methyl-imidazo[1,2-a]pyrazine (CAS 1159815-50-5) (0.600 g, 2.83 mmol), N-ethyl-4-fluoro-3-methoxy-aniline (0.484 g, 2.86 mmol), bis(benzonitrile)palladium chloride (0.114 g, 0.283 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (0.167 g, 0.283 mmol),
 15 toluene (6.0 mL) and triethylamine (0.60 mL, 4.24 mmol). The vial was flushed with nitrogen, then the vial was pressurized with nitrogen, then flushed with carbon monoxide twice and finally pressurized with 10 bar of carbon monoxide. The pressurized vial was heated at 110 °C for 6 hours. Then, the mixture was filtered through celite pad, concentrated under reduced pressure. The crude material was purified by flash chromatography using a cyclohexane/ethyl acetate gradient to afford N-ethyl-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a brown solid.

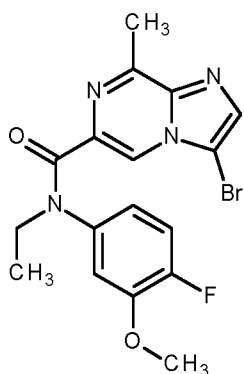
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LC-MS (method B): Rt 0.84 min, *m/z* = 329 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 8.38 (s, 1 H), 8.12 (s, 1 H), 7.75 (s, 1 H), 7.00 – 7.15 (m, 2 H), 6.65 (br s, 1 H), 3.88 (q, *J* = 6.92 Hz, 2 H), 3.76 (s, 3 H), 2.44 – 2.49 (m, 3 H), 1.10 – 1.24 (m, 3 H)

Step B: Preparation of 3-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide

25



To a solution of N-ethyl-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.600 g, 1.83 mmol) in acetonitrile (7.3 mL) was added 1-bromopyrrolidine-2,5-dione (0.325 g, 1.83 mmol) dropwise at 0 °C. The reaction was stirred at room temperature for 1 hour. Then the resulting mixture was diluted with saturated aqueous thiosulfate and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a cyclohexane/ethyl acetate gradient to afford 3-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide as a white solid.

LC-MS (method B): Rt 1.07 min, m/z = 407 (M+H)⁺

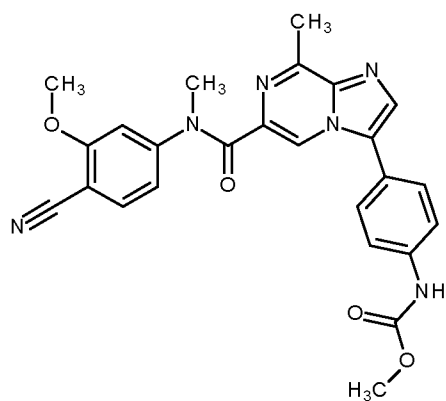
Step C: Preparation of methyl N-[5-[6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 3)

To a solution of 3-bromo-N-ethyl-N-(4-fluoro-3-methoxy-phenyl)-8-methyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.412 g, 1.01 mmol), methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.355 g, 1.21 mmol) in acetonitrile (4.12 mL) was added sodium carbonate (0.324 g, 3.04 mmol) in water (0.033 mL). The resulting solution was degassed with nitrogen for 15 minutes. Then, chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (CAS: 1310584-14-5) (0.084 g, 0.101 mmol) was added and the vial was heated at 100 °C in a microwave reactor for 1.5 hours. Then, the reaction was filtered through celite pad and the filtrate was evaporated under reduced pressure. The crude material was purified by flash chromatography using a ethyl acetate/methanol gradient to afford methyl N-[5-[6-[ethyl-(4-fluoro-3-methoxy-phenyl)carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method B): Rt 1.03 min, m/z = 479 (M+H)⁺

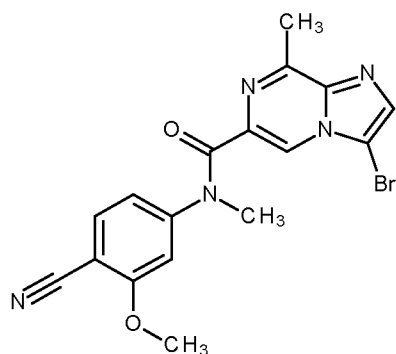
¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.47 (s, 1H), 8.45 (br s, 2 H), 7.95 - 8.00 (m, 1 H), 7.93 (s, 2 H), 7.13 (s, 1 H), 6.91 - 7.06 (m, 1 H), 6.63 (br s, 1 H), 3.71 - 3.89 (m, 2 H), 3.66 (s, 6 H), 2.46 - 2.51 (m, 3 H), 1.06 (t, J = 7.07 Hz, 3 H)

Example 12: Preparation of methyl N-[4-[6-[4-cyano-3-methoxy-phenyl]-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]phenyl]carbamate (Compound 35)



(Compound 35)

Step A: Preparation of 3-bromo-N-(4-cyano-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-6)



(Compound X-6)

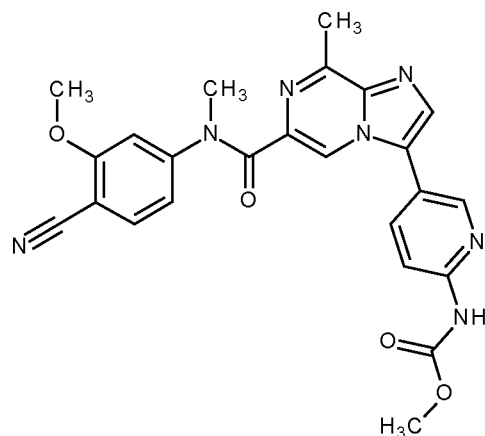
- 5 To a mixture of 3-bromo-8-methyl-imidazo[1,2-a] pyrazine-6-carboxylic acid (Compound X-2) (0.700 g, 3.12 mmol) in pyridine (10.0 mL) and 4-fluoro-3-methoxy-N-methyl-aniline (0.532 g, 3.28 mmol) was added 1-propanephosphonic acid cyclic anhydride (50% in ethyl acetate, 2.61 g, 8.20 mmol). The resulting solution was stirred at 65 °C for 2 hours. The reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous
- 10 sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using a dichloromethane/methanol gradient to afford 3-bromo-N-(4-cyano-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide as a yellow solid.
- LC-MS (method A): Rt 1.09 min, m/z = 401 (M+H)⁺

- 15 Step B: Preparation of methyl N-[4-{6-[4-(4-cyano-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl}phenyl]carbamate (Compound 35)

- To a solution of 3-bromo-N-(4-cyano-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-6) (0.300 g, 0.750 mmol) in dioxane (8.0 mL) and water (2.0 mL) was added methyl N-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]carbamate (0.249 g, 0.899 mmol),
- 20 bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.0612 g, 0.0750 mmol) and K₂CO₃ (0.104 g, 0.750 mmol). The mixture was stirred at 55 °C under an atmosphere of N₂ for 2 hours. The mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluting with methanol/dichloromethane), and the obtained product was further purified by trituration with acetonitrile/petroleum ether (2:1) to afford methyl N-[4-{6-[4-(4-cyano-3-methoxy-phenyl)-methyl-
- 25 carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl}phenyl]carbamate as a white solid.
- LC-MS (method A): Rt 1.10 min, m/z = 471 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 9.95 (s, 1H), 8.59 (s, 1H), 7.94 (s, 1H), 7.69 (d, J = 8.6 Hz, 2H), 7.57 (dd, J = 13.9, 8.4 Hz, 3H), 7.26 (d, J = 1.5 Hz, 1H), 6.90 (dd, J = 8.3, 1.6 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.46 (s, 3H), 2.51 (s, 3H).

5 **Example 13: Preparation of methyl N-[5-[6-[(4-cyano-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 34)**



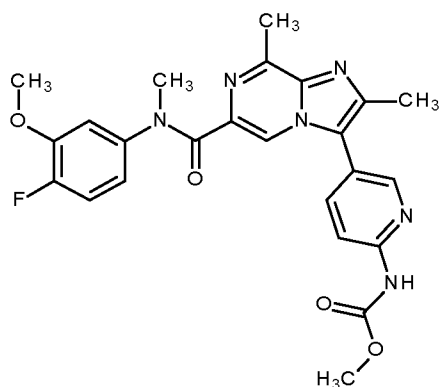
(Compound 34)

To a solution of 3-bromo-N-(4-cyano-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-6) (0.400 g, 0.999 mmol) in dioxane (4.0 mL) and water (1.0 mL) was added
10 methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.278 g, 0.999 mmol), bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.0816 g, 0.0999 mmol) and K₂CO₃ (0.414 g, 3.00 mmol). The mixture was stirred at 55 °C under an atmosphere of N₂ for 2 hours. The mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluting with methanol/dichloromethane), and the obtained product was further purified by trituration with
15 acetonitrile/petroleum ether (2:1) to afford methyl N-[5-[6-[(4-cyano-3-methoxy-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

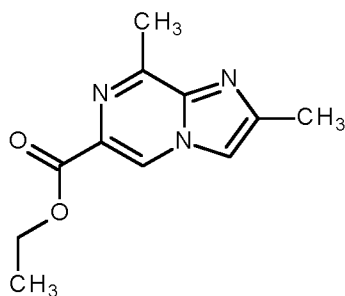
LC-MS (method A): Rt 1.065 min, m/z = 472 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.52 (s, 1H), 8.63 (s, 1H), 8.56 (s, 1H), 8.04 (d, J = 5.0 Hz, 3H), 7.58 (d, J = 8.3 Hz, 1H), 7.25 (s, 1H), 6.91 (d, J = 8.3 Hz, 1H), 3.78 (s, 3H), 3.73 (s, 3H), 3.46 (s,
20 3H), 2.51 (s, 3H).

Example 14: Preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2,8-dimethyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 38)

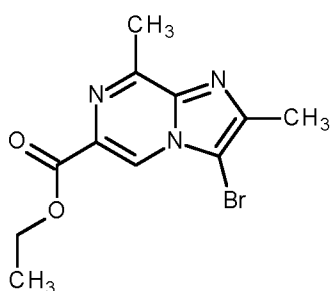


(Compound 38)

Step A: Preparation of ethyl 2,8-dimethylimidazo[1,2-a]pyrazine-6-carboxylate

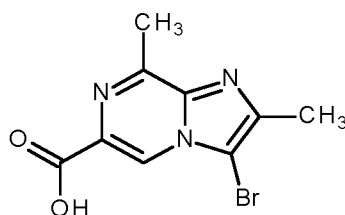
A reaction mixture of 6-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine, preparation described in patent WO2015/197503, 2015, A1 (0.800 g, 3.54 mmol), EtOH (10.0 mL), 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (CAS 95464-05-4, 0.289 g, 0.354 mmol), and N,N-diethylethanamine (1.07 g, 10.62 mmol) was flushed with carbon monoxide. The vial was sealed and pressurized to 2.5 MPa with carbon monoxide. The reaction mixture was stirred at 100 °C for 8 hours. Then the vessel was cooled to room temperature and pressure was released. The reaction mixture was concentrated and the residue was purified by flash chromatography using a methanol/dichloromethane gradient to afford ethyl 2,8-dimethylimidazo[1,2-a]pyrazine-6-carboxylate as a brown solid.

LC-MS (method A): Rt 0.877 min, m/z = 220 (M+H)⁺

Step B: Preparation of ethyl 3-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxylate

To a solution of ethyl 2,8-dimethylimidazo[1,2-a]pyrazine-6-carboxylate (0.800 g, 3.65 mmol) in acetonitrile (10.0 mL) was added 1-bromopyrrolidine-2,5-dione (0.779 g, 4.38 mmol) dropwise at room temperature. The reaction was stirred at room temperature for 2 hours. Then the resulting mixture was diluted with water. The precipitate was collected by filtration, washed with water and dried under reduced pressure to afford ethyl 3-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxylate as a brown solid.

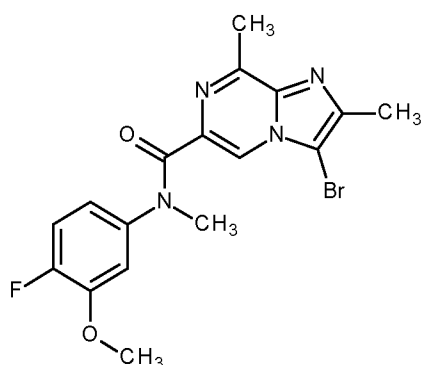
LC-MS (method A): Rt 1.218 min, m/z = 298 (M+H)⁺

Step C: Preparation of 3-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxylic acid

To a solution of ethyl 3-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxylate (0.400 g, 1.34 mmol) in tetrahydrofuran/H₂O (1:1, 10.0 mL) was added lithium hydroxide (0.064 g, 2.7 mmol). The mixture was stirred at room temperature for 3 hours. Then, the organic solvent was removed under reduced pressure. The aqueous solution was adjusted to pH 2-3 with aqueous HCl (2N). The precipitate was collected by filtration, washed with water and dried under reduced pressure to afford 3-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxylic acid as a white solid.

LC-MS (method A): Rt 0.998 min, m/z = 270 (M+H)⁺

Step D: Preparation of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,2,8-trimethyl-imidazo[1,2-a]pyrazine-6-carboxamide



To a mixture of 3-bromo-2,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxylic acid (0.260 g, 0.963 mmol) in dimethylformamide (5.0 mL) was added 1-methylimidazole (0.237 g, 2.89 mmol) and [chloro(dimethylamine)methylene]-dimethyl-ammonium hexafluorophosphate (CAS 94790-35-9, 0.405 g, 1.44 mmol) at room temperature. The solution was stirred at room temperature for 5 min. Then, 4-fluoro-3-methoxy-N-methyl-aniline (0.179 g, 1.16 mmol) was added by portions. The resulting solution was stirred for 2 hours. The reaction mixture was diluted with ethyl acetate washed with water and saturated aqueous NaCl, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using a dichloromethane/methanol gradient to afford 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,2,8-trimethyl-imidazo[1,2-a]pyrazine-6-carboxamide as a brown solid.

LC-MS (method A): Rt 1.170 min, m/z = 409 (M+H)⁺

Step E: Preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2,8-dimethyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 38)

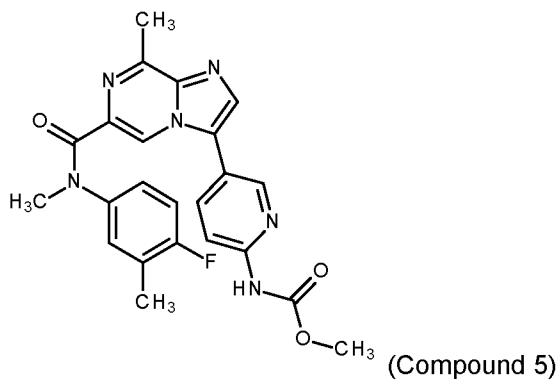
To a solution of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,2,8-trimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.240 g, 0.589 mmol) in dioxane (4.0 mL) and water (1.00 mL) was added methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.246 g, 0.884 mmol), bis(diphenylphosphino)ferrocene-palladium(II)dichloride (0.0431 g, 0.0589 mmol) and K₂CO₃ (0.2447 g, 1.77 mmol). The mixture was stirred at 55 °C under an atmosphere of N₂ for 2 hours. The mixture was concentrated under vacuum. The residue was purified by silica gel column chromatography (eluting with methanol/dichloromethane) and further triturated with acetonitrile/petroleum ether (2:1) to afford methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2,8-dimethyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method A): Rt 1.09 min, m/z = 479 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.51 (s, 1H), 8.39 (s, 1H), 8.23 (s, 1H), 8.05 (d, J = 8.6 Hz, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.18 (dd, J = 7.8, 2.3 Hz, 1H), 7.04 (m, 1H), 6.70 (s, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.36 (s, 3H), 3.32 (s, 3H), 2.40 (s, 3H).

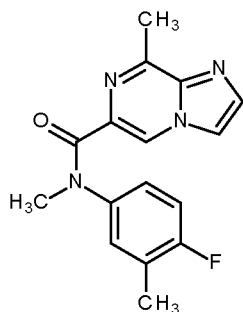
5

Example 15: Preparation of methyl N-[5-[6-[(4-fluoro-3-methyl-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 5)



Step A: Preparation of N-(4-fluoro-3-methyl-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide

10



A vial was charged with 6-bromo-8-methyl-imidazo[1,2-a]pyrazine (CAS 1159815-50-5) (0.700 g, 3.30 mmol), 4-fluoro-N,3-dimethylaniline (0.464 g, 3.33 mmol), bis(benzonitrile)palladium chloride (0.133 g, 0.330 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (0.194 g, 0.330 mmol), toluene (7.0 mL) and triethylamine (0.694 mL). The vial was flushed with nitrogen, then the vial was pressurized with nitrogen, then flushed with carbon monoxide twice and finally pressurized with 10 bar of carbon monoxide. The pressurized vial was heated at 110 °C for 6 hours. Then, the mixture was filtered through celite pad, concentrated under reduced pressure. The crude material was purified by flash chromatography using a cyclohexane/ethyl acetate gradient to afford N-(4-fluoro-3-methyl-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide.

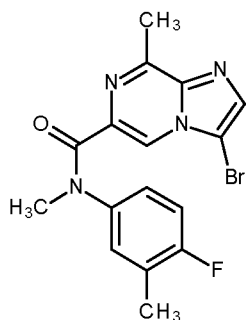
20

LC-MS (method B): Rt 0.96 min, m/z = 299 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 7.96 (s, 1 H), 7.28 (d, J = 0.98 Hz, 1 H), 6.90 (s, 1 H), 6.38 (br d, J = 7.21 Hz, 1 H), 6.15 (br d, J = 6.72 Hz, 2 H), 2.52 (s, 3 H), 1.57 - 1.63 (br s, 3 H), 1.27-1.34 (m, 3 H)

25

Step B: Preparation of 3-bromo-N-(4-fluoro-3-methyl-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide



To a solution of N-(4-fluoro-3-methyl-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.680 g, 2.28 mmol) in acetonitrile (9.1 mL) was added 1-bromopyrrolidine-2,5-dione (0.406 g, 2.28 mmol) dropwise at room temperature. The reaction was stirred at room temperature for 1 hour. Then
 5 the resulting mixture was diluted with a saturated aqueous thiosulfate solution and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated under vacuum. The residue was used in the next step without further purification.

LC-MS (method B): Rt 1.05 min, m/z = 379 (M+H)⁺

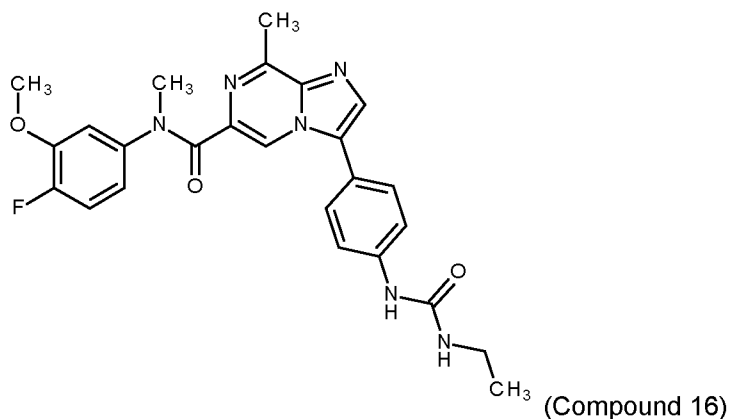
10 Step C: Preparation of methyl N-[5-[6-[(4-fluoro-3-methyl-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 5)

To a solution of 3-bromo-N-(4-fluoro-3-methyl-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.700 g, 1.86 mmol), methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.652 g, 2.23 mmol) in acetonitrile (7.00 mL) was added sodium carbonate (0.621 g,
 15 5.57 mmol) in water (0.060 mL). The resulting solution was degassed with nitrogen for 15 minutes. Then, chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (CAS: 1310584-14-5) (0.154 g, 0.186 mmol) was added and the vial was heated at 100 °C in a microwave reactor for 1.5 hours. Then, the reaction was diluted with methanol, filtered through celite pad and the filtrate was evaporated under reduced pressure. The crude material was
 20 purified by flash chromatography to afford methyl N-[5-[6-[(4-fluoro-3-methyl-phenyl)-methyl-carbamoyl]-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method B): Rt 1.00 min, m/z = 449 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 9.69 (s, 1 H), 7.64 - 7.72 (m, 2 H), 7.13 - 7.27 (m, 3 H), 6.44 - 6.50 (m, 1 H), 6.18 (br d, J = 8.88 Hz, 2 H), 2.90 (s, 3 H), 2.52 (s, 3 H), 1.70 - 1.74 (m, 3 H), 1.33 (s, 3
 25 H)

Example 16: Preparation of 3-[4-(ethylcarbamoylamino)phenyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound 16)

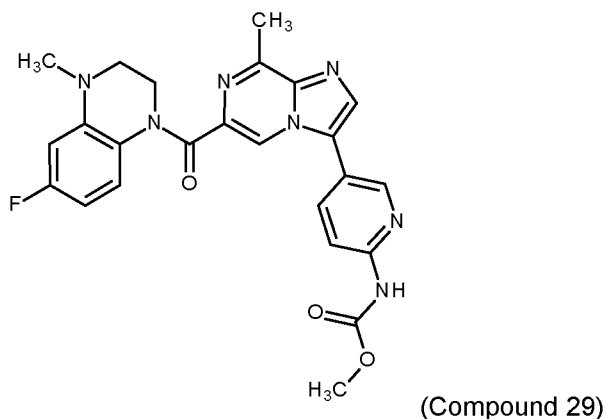


Under an argon atmosphere, 1-ethyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)urea (0.052 mmol) and XPhos Pd G3 (CAS 1445085-55-1) (3.455 mg, 0.004 mmol) were placed in a vial. Then, a solution of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (Compound X-3) (0.040 mmol) in 1,4-dioxane (0.4 mL, degassed with argon) was added, followed by a solution of sodium carbonate (12.85 mg, 0.12 mmol) in water (0.1 mL, degassed with argon). The reaction mixture was stirred under argon, at 100 °C for 16 hours. Then, the solvent was evaporated. The residue was dissolved in dimethylacetamide (0.4 mL) and methanol (0.4 mL). The resulting suspension was filtered and filtrate was purified by reverse phase chromatography to afford 3-

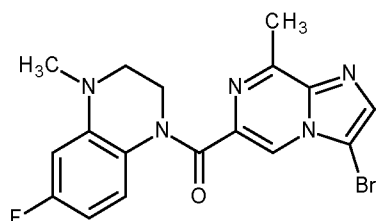
5 [4-(ethylcarbamoylamino)phenyl]-N-(4-fluoro-3-methoxy-phenyl)-N,8-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide.

LC-MS (method C): Rt 1.15 min, $m/z = 477$ (M+H)⁺

Example 17: Preparation of methyl N-[5-[6-(6-fluoro-4-methyl-2,3-dihydroquinoxaline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 29)



Step A: Preparation of (3-bromo-8-methyl-imidazo[1,2-a]pyrazin-6-yl)-(6-fluoro-4-methyl-2,3-dihydroquinoxalin-1-yl)methanone



To a solution of 8-bromoimidazo[1,2-a]pyrazine-6-carboxylic acid (Compound X-4) (0.140 g, 0.547 mmol) and 6-fluoro-4-methyl-2,3-dihydro-1H-quinoxaline (0.109 g, 0.656 mmol) in pyridine (5.0 mL) was added propylphosphonic anhydride (50.0 wt. % solution in ethyl acetate, 0.522 g, 1.64 mmol) dropwise at 70 °C under nitrogen atmosphere. The mixture was heated at 70 °C for 2 hours. The final mixture was diluted with water and extracted with ethyl acetate. The combined organic layers were washed with water, dried with sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography using a dichloromethane/methanol gradient, then further purified by trituration with acetonitrile/petroleum ether (1:10) to give (3-bromo-8-methyl-imidazo[1,2-a]pyrazin-6-yl)-(6-fluoro-4-methyl-2,3-dihydroquinoxalin-1-yl)methanone as a yellow oil.

LC-MS (method A): Rt 1.22 min, m/z = 406 ($M+2H$)²⁺

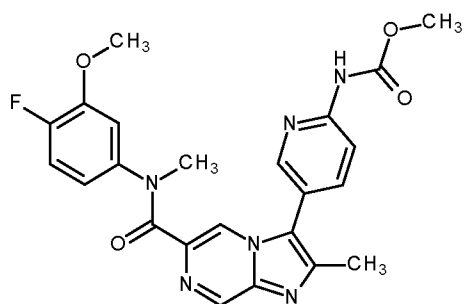
Step B: Preparation of methyl N-[5-[6-(6-fluoro-4-methyl-2,3-dihydroquinoxaline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 29)

A solution of (3-bromo-8-methyl-imidazo[1,2-a]pyrazin-6-yl)-(6-fluoro-4-methyl-2,3-dihydroquinoxalin-1-yl)methanone (0.130 g, 0.322 mmol) and methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (0.0894 g, 0.322 mmol) in acetonitrile/water (4.0 mL) was degassed with nitrogen for 15 minutes. Then potassium carbonate (0.133 g, 0.965 mmol) and 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (0.026 g, 0.032 mmol) was added and the reaction mixture was heated at 50 °C for 2.0 hours. Then, the reaction was concentrated under reduced pressure. The crude material was purified by flash chromatography using a dichloromethane/methanol gradient to afford methyl N-[5-[6-(6-fluoro-4-methyl-2,3-dihydroquinoxaline-1-carbonyl)-8-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a pink solid.

LC-MS (method A): Rt 1.19 min, m/z = 476 ($M+H$)⁺

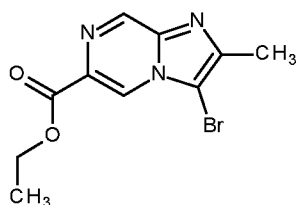
¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.08 (s, 1 H), 8.53 (d, J = 3.8 Hz, 2 H), 8.03-7.96 (m, 3 H), 7.15 (s, 1 H), 6.49 (dd, J = 12.0, 2.7 Hz, 1 H), 6.21 (td, J = 8.5, 2.6 Hz, 1 H), 3.88 (t, J = 5.3 Hz, 2 H), 3.73 (s, 3 H), 3.41 (t, J = 5.3 Hz, 2 H), 2.92 (s, 3 H), 2.73 (s, 3 H).

Example 18: Preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 37)



(Compound 37)

Step A: Preparation of ethyl 3-bromo-2-methyl-imidazo[1,2-a]pyrazine-6-carboxylate

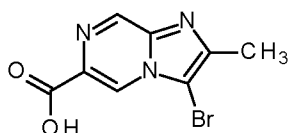


To a solution of ethyl 2-methylimidazo[1,2-a]pyrazine-6-carboxylate (CAS 1610666-95-9) (0.800 g, 3.90 mmol) in acetonitrile (10.0 mL) was added 1-bromopyrrolidine-2,5-dione (0.833 g, 4.68 mmol) portionwise at room temperature. The reaction was stirred at room temperature for 2 hours. Then the

5 resulting mixture was concentrated under vacuum. The residue was purified by flash chromatography using a petroleum ether/ethyl acetate gradient to afford ethyl 3-bromo-2-methyl-imidazo[1,2-a]pyrazine-6-carboxylate as a yellow solid.

LC-MS (method A): Rt 1.04 min, m/z = 284 (M+H)⁺

10 Step B: Preparation of 3-bromo-2-methyl-imidazo[1,2-a]pyrazine-6-carboxylic acid

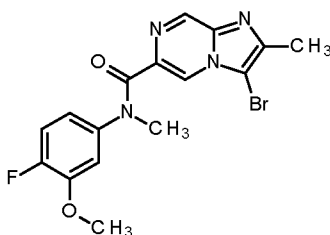


To a solution of ethyl 3-bromo-2-methyl-imidazo[1,2-a]pyrazine-6-carboxylate (0.600 g, 2.11 mmol) in tetrahydrofuran/H₂O (1:1, 10.0 mL) was added lithium hydroxide (0.101 g, 4.22 mmol). The mixture was stirred at room temperature for 3 hours. Then, the organic solvent was removed under reduced pressure.

15 The aqueous solution was adjusted to pH 2-3 with aqueous HCl (2N). The precipitate was collected by filtration, washed with water to afford 3-bromo-2-methyl-imidazo[1,2-a]pyrazine-6-carboxylic acid as a white solid.

LC-MS (method A): Rt 0.19 min, m/z = 254 (M-H)⁺

20 Step C: Preparation of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,2-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide



To a mixture of 3-bromo-2-methyl-imidazo[1,2-a]pyrazine-6-carboxylic acid (0.020 g, 0.078 mmol) in acetonitrile (3.0 mL) was added 1-methylimidazole (0.019 g, 0.23 mmol) and

25 [chloro(dimethylamine)methylene]-dimethyl-ammonium hexafluorophosphate (CAS 94790-35-9, 0.0329 g, 0.117 mmol) at room temperature. The solution was stirred at room temperature for 5 min. Then, 4-fluoro-3-methoxy-N-methyl-aniline (0.0145 g, 0.0937 mmol) was added by portions. The resulting solution was stirred for 2 hours. The reaction mixture was diluted with ethyl acetate washed with water and saturated aqueous NaCl, dried over anhydrous sodium sulfate, filtered, and concentrated

30 under reduced pressure. The residue was purified by silica gel column chromatography using a

dichloromethane/methanol gradient to afford 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,2-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide.

LC-MS (method A): Rt 1.43 min, m/z = 394 (M+H)⁺

5 Step D: Preparation of methyl N-[5-[6-[(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate (Compound 37)

To a mixture of 3-bromo-N-(4-fluoro-3-methoxy-phenyl)-N,2-dimethyl-imidazo[1,2-a]pyrazine-6-carboxamide (0.400 g, 1.02 mmol) and methyl N-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]carbamate (CAS 844500-75-0) (0.424 g, 1.53 mmol) in mixture of dioxane/H₂O (4:1, 10.0 mL)

10 was added 1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (0.0831 g, 0.102 mmol) and potassium carbonate (0.422 g, 3.05 mmol). The mixture was stirred at 60 °C for 2 hours under a N₂ atmosphere. The mixture was concentrated under reduced pressure, the residue was purified by flash chromatography using a dichloromethane/methanol gradient to afford the desired compound, which was triturated with acetonitrile/ petroleum ether (2:1) to afford methyl N-[5-[6-
15 [(4-fluoro-3-methoxy-phenyl)-methyl-carbamoyl]-2-methyl-imidazo[1,2-a]pyrazin-3-yl]-2-pyridyl]carbamate as a white solid.

LC-MS (method A): Rt 1.08 min, m/z = 465 (M+H)⁺

¹H-NMR (400 MHz, DMSO-d₆, ppm) δ = 10.52 (s, 1 H), 8.75 (br s, 1 H), 8.40 - 8.46 (m, 2 H), 8.06 (d, J = 8.8 Hz, 1 H), 7.81 - 8.03 (m, 1 H), 7.18 (dd, J = 7.9, 2.4 Hz, 1 H), 6.93 - 7.15 (m, 1 H), 6.72 (br s, 1 H),

20 3.69 - 3.76 (m, 6 H), 3.38 (s, 3 H), 2.42 (s, 3 H)

Biological examples:

The fungicidal activity of the compounds of the invention have been tested as follows:

25

***Phytophthora infestans* / tomato / leaf disc preventative (late blight)**

Tomato leaf disks are placed on water agar in multiwell plates (24-well format) and sprayed with the formulated test compound diluted in water. The leaf disks are inoculated with a spore suspension of the fungus 1 day after application. The inoculated leaf disks are incubated at 16 °C and 75% rh under a light regime of 24 h darkness followed by 12 h light / 12 h darkness in a climate cabinet and the activity of a compound is assessed as percent disease control compared to untreated when an appropriate level of disease damage appears in untreated check leaf disks (5 - 7 days after application).

The following compounds gave at least 80% control of *Phytophthora infestans* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

1, 2, 3, 4, 5, 7, 8, 12, 15, 16, 17, 18, 19, 21, 23, 24, 25, 26, 29, 31, 33, 34, 35, 36

***Plasmopara viticola* / grape / leaf disc preventative (late blight)**

Grape vine leaf disks are placed on water agar in multiwell plates (24-well format) and sprayed with the formulated test compound diluted in water. The leaf disks are inoculated with a spore suspension of the fungus 1 day after application. The inoculated leaf disks are incubated at 19 °C and 80% rh under a light regime of 12 h light / 12 h darkness in a climate cabinet and the activity of a compound is assessed as percent disease

control compared to untreated when an appropriate level of disease damage appears in untreated check leaf disks (6 - 8 days after application).

The following compounds gave at least 80% control of *Plasmopara viticola* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

1, 2, 3, 4, 6, 7, 8, 15, 16, 19, 23, 24, 25, 29, 30, 31, 34, 35, 36

Pythium ultimum / liquid culture (seedling damping off)

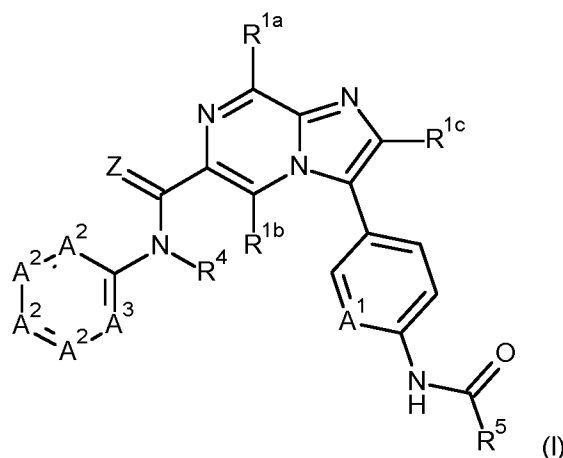
Mycelia fragments and oospores of a newly grown liquid culture of the fungus are directly mixed into nutrient broth (PDB potato dextrose broth). After placing a (DMSO) solution of test compound into a microtiter plate (96-well format), the nutrient broth containing the fungal mycelia/spore mixture is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 2-3 days after application.

The following compounds gave at least 80% control of *Pythium ultimum* at 20 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

1, 2, 3, 6, 7, 8, 14, 15, 16, 17, 19, 26, 29, 31, 34, 35, 36

Claims

1. A compound of formula (I)



5 wherein Z is O or S, and preferably Z is O;

A¹ is CH or N, and preferably N;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-
10 C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;

15

A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-
20 C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents
25 independently selected from halogen, hydroxy, and CN;

A³ is independently CR³ or N;

30 R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino,

wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

5

R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN;

10

wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and

15

R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₁₋₆alkylC₁₋₆alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN;

20

or a salt or N-oxide thereof.

2. The compound according to claim 1, wherein R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, and preferably C₁₋₆alkyl.

25

3. The compound according to claim 1 or 2, wherein R^{1b} and R^{1c} are independently selected from hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy.

4. The compound according to claim 1, wherein R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl,

30

C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and R^{1b} and R^{1c} are hydrogen.

5. The compound according to any one of the preceding claims, wherein R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN.

35

6. The compound according to any one of the preceding claims, wherein R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino, wherein

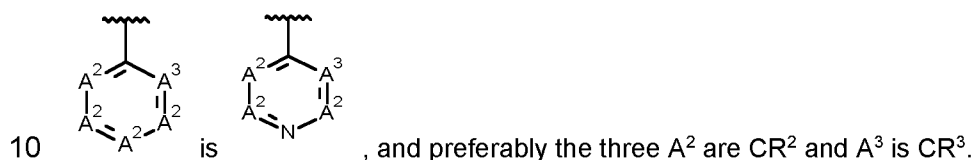
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each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN.

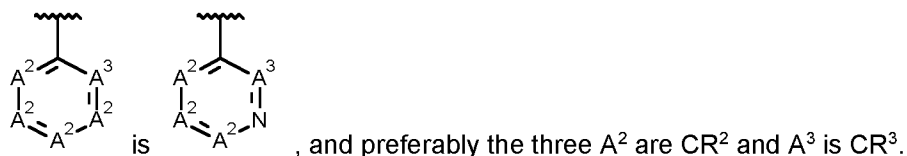
5

7. The compound according to any one of the preceding claims, wherein four A² are CR² and A³ is N.

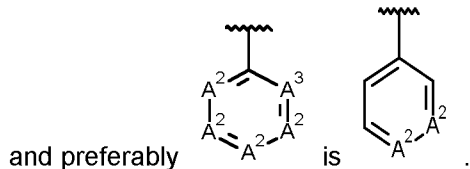
8. The compound according to any one of the claims 1 to 6, wherein



9. The compound according to any one of the claims 1 to 6, wherein



15 10. The compound according to any one of the claims 1 to 6, wherein four A² are CR² and A³ is CR³,



11. The compound according to any one of the preceding claims, wherein R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN.

12. The compound according to any one of the preceding claims, wherein R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, and C₁₋₆alkoxyC₁₋₆alkyl, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN.

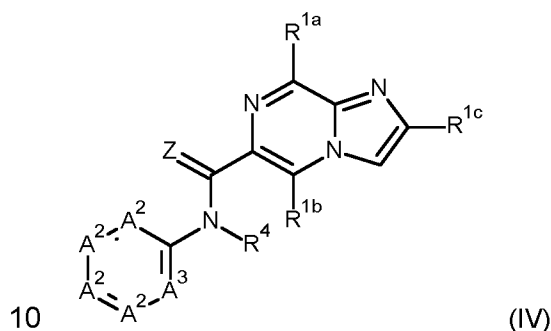
13. A composition comprising a fungicidally effective amount of a compound as defined in any one of claims 1 to 12.

30

14. A composition according to claim 13, wherein the composition further comprises at least one compound selected among an additional active ingredient, an appropriate formulation inert, a carrier, an adjuvant, and any mixtures thereof.

15. A method of combating, preventing or controlling phytopathogenic diseases which comprises applying to a phytopathogen, to the locus of a phytopathogen, to a plant susceptible to attack by a phytopathogen, or to a plant propagation material thereof, a fungicidally effective amount of a compound
 5 according to any one of claims 1 to 12, or a composition comprising a compound according to any one of claims 1 to 12, or a composition according to claim 13 or 14.

16. A compound of formula (IV)



wherein Z is O or S, and preferably Z is O;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl, and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋

15 4alkyl, and C₁₋₆alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more
 20 than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R² are independently selected from hydrogen, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, groups is optionally
 30 substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

A³ is independently CR³ or N;

R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino,
 35 6alkylsulfanyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino,

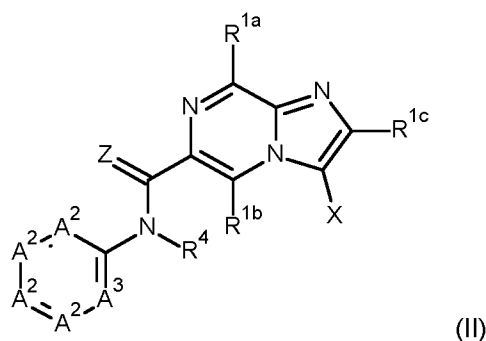
wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R³ is
 5 selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN,
 10 wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and
 15 CN; and preferably R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN; and

wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle,
 20 more preferably a 6-membered heterocycle;
 or a salt or N-oxide thereof;

or

25 a compound of formula (II)



wherein Z is O or S, and preferably Z is O;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;
 30 and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

A³ is independently CR³ or N;

R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆-alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

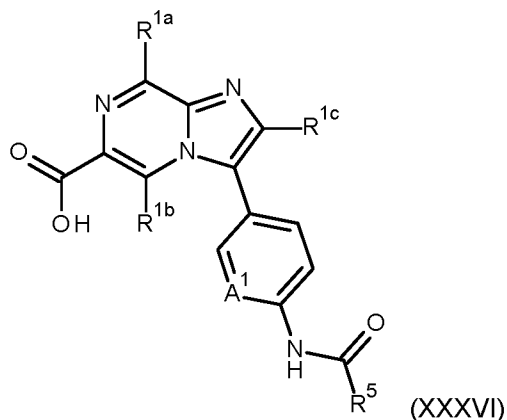
R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN; and preferably R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN;

wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and

X is Cl, Br or I;

or a salt or N-oxide thereof.

17. A compound of formula (XXXVI)



wherein A¹ is CH or N, and preferably N;

R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;

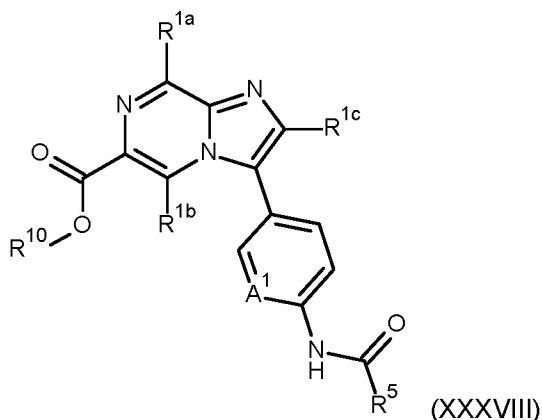
5 and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen; and

10 R⁵ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₁₋₆alkylC₁₋₆alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN;
or a salt or N-oxide thereof;

15 or

a compound of formula (XXXVIII)



wherein A¹ is CH or N, and preferably N;

20 R^{1a} is selected from hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl;
and preferably R^{1a} is selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkoxy, amino, and $NHC(O)C_{1-6}$ alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

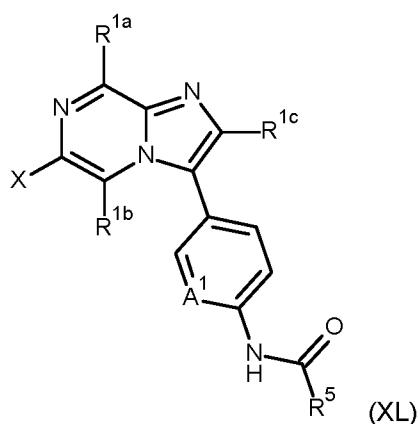
R^5 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkylamino, di- C_{1-6} alkylamino, and C_{1-6} alkyl- C_{1-6} alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN; and

R^{10} is a C_{1-6} alkyl;

or a salt or N-oxide thereof;

10 or

a compound of formula (XL)



wherein A^1 is CH or N, and preferably N;

15 R^{1a} is selected from hydroxy, halogen, CN, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkoxy, amino, and $NHC(O)C_{1-6}$ alkyl; and preferably R^{1a} is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, and C_{1-6} alkoxy;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C_{1-6} alkyl, C_{3-6} cycloalkyl,

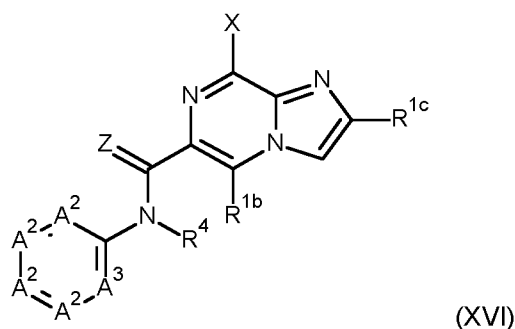
20 C_{1-6} alkoxy- C_{1-6} alkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, C_{1-6} alkylsulfanyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkoxy, amino, and $NHC(O)C_{1-6}$ alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

R^5 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-6} alkyl, C_{1-6} alkoxy- C_{1-6} alkyl, C_{1-6} alkylamino, di- C_{1-6} alkylamino, and C_{1-6} alkyl- C_{1-6} alkoxyamino, wherein each of said groups is optionally substituted with one to three substituents independently selected from halogen and CN; and

25 X is Cl, Br or I;

or a salt or N-oxide thereof.

18. A compound of formula (XVI)



wherein Z is O or S, and preferably Z is O;

R^{1b} and R^{1c} are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₃₋₆cycloalkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxy, amino, and NHC(O)C₁₋₆alkyl; and preferably R^{1b} and R^{1c} are hydrogen;

A² are independently CR² or N, with the proviso that no more than three A² are N, preferably no more than two A² are N, preferably no more than one A² is N, and more preferably the four A² are CR²;

R² are independently selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, C₁₋₆alkoxycarbonyl, C₁₋₆alkylaminocarbonyl, diC₁₋₆alkylaminocarbonyl, and C₁₋₆alkylcarbonyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R² are independently selected from hydrogen, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, and C₁₋₆alkoxy-C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

A³ is independently CR³ or N;

R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₃₋₆cycloalkylamino, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy-C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkoxy, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, C₁₋₆alkylsulfanyl, C₁₋₆alkylsulfinyl, C₁₋₆alkylsulfonyl, amino, C₁₋₆alkylamino, diC₁₋₆alkylamino, and C₃₋₆cycloalkylamino groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN, and preferably R³ is selected from hydrogen, hydroxy, halogen, CN, C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy, and C₁₋₆alkoxy-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen, hydroxy, and CN;

R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl, and CN, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆

₆alkynyl, C₁₋₆alkoxy, C₁₋₆alkylsulfanyl-C₁₋₆alkyl, C₁₋₆alkylsulfinyl-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, C₁₋₆alkoxycarbonyl-C₁₋₆alkyl, C₁₋₆alkylaminocarbonyl-C₁₋₆alkyl and diC₁₋₆alkylaminocarbonyl-C₁₋₆alkyl groups is optionally substituted with one to three substituents independently selected from halogen and CN; and preferably R⁴ is selected from C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋

5 ₄alkyl, and C₁₋₆alkoxy, wherein each of the C₁₋₆alkyl, C₁₋₆alkoxy-C₁₋₆alkyl, C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₄alkyl, and C₁₋₆alkoxy groups is optionally substituted with one to three substituents independently selected from halogen and CN;

wherein A³ and R⁴ taken together optionally form a ring, more preferably a 5-8-membered heterocycle, more preferably a 6-membered heterocycle; and

10 X is Cl, Br or I;

or a salt or N-oxide thereof.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2024/059875

A. CLASSIFICATION OF SUBJECT MATTER					
INV.	C07D487/04	A01N43/60	A01N47/08	A01N47/18	A01P3/00
	A01N43/90				
ADD.					
According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED					
Minimum documentation searched (classification system followed by classification symbols)					
C07D A01N					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched					
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)					
EPO-Internal, WPI Data					
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with indication, where appropriate, of the relevant passages				Relevant to claim No.
A	WO 02/48146 A2 (BASF AG [DE]; CULLMANN OLIVER [DE] ET AL.) 20 June 2002 (2002-06-20) the whole document; in particular the claims and table 1 on pages 43f, preparation on pages 3-5 -----				1 - 18
☐ Further documents are listed in the continuation of Box C.					
☒ See patent family annex.					
* Special categories of cited documents :					
"A" document defining the general state of the art which is not considered to be of particular relevance			"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention		
"E" earlier application or patent but published on or after the international filing date			"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone		
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)			"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art		
"O" document referring to an oral disclosure, use, exhibition or other means			"&" document member of the same patent family		
"P" document published prior to the international filing date but later than the priority date claimed					
Date of the actual completion of the international search			Date of mailing of the international search report		
4 July 2024			12/07/2024		
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016			Authorized officer Hanisch, Inken		

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2024/059875

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0248146	A2	20-06-2002	AU 2492702 A 24-06-2002
			EP 1343785 A2 17-09-2003
			US 2004058938 A1 25-03-2004
			WO 0248146 A2 20-06-2002
