

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2017/055273

International filing date (day/month/year)
07.03.2017

Priority date (day/month/year)
10.03.2016

International Patent Classification (IPC) or both national classification and IPC
INV. A01N43/42 C07D215/54

Applicant
SYNGENTA PARTICIPATIONS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Bedel, Christian

Telephone No. +49 89 2399-0



Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>6, 10-12, 14-16</u>
	No: Claims	<u>1-5, 7-9, 13</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-16</u>
Industrial applicability (IA)	Yes: Claims	<u>1-16</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

- D1 DATABASE REGISTRY
CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US;
16 December 2009 (2009-12-16),
Database accession no. 1197511-46-8
- D2 WO 2006/016708 A1 (ISHIHARA SANGYO KAISHA [JP];
NAKAMURA YUJI [JP]; MITANI SHIGERU [JP];) 16 February
2006 (2006-02-16)
- D3 EP 1 669 348 A1 (EISAI CO LTD [JP]) 14 June 2006
(2006-06-14)

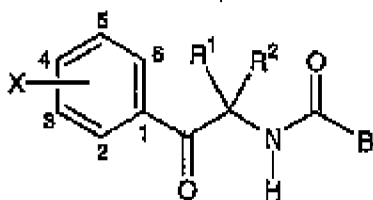
2 Novelty (Art. 33(2) PCT)

2.1 The present application does not meet the criteria of Article 33(2) PCT, because the subject-matter of claims 1-5,7-9 and 13 lacks novelty over the individual compound of D1 (no fungicide activity is reported for this compound).

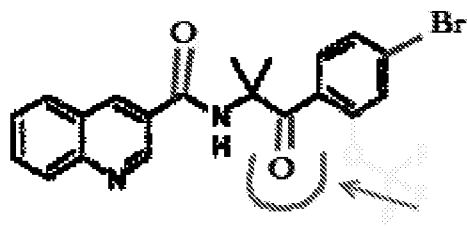
3 Inventive step (Art. 33(3) PCT)

3.1 The closest prior art D2 discloses compounds identified as fungicides.

D2 in particular discloses on page 109 the following compounds :



wherein B can be a quinoline group (B=B52 see p.106 and table on page 114). More particularly D2 discloses compound 1-195 :



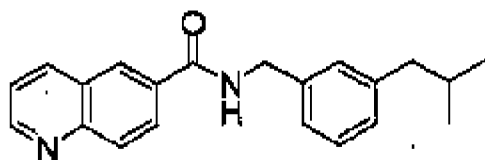
This compound differs by the presence of a carbonyl group linker before the phenyl whereas the presently claimed compounds show instead a -C(R8)(R9)- group, wherein each of R8/R9 is H, halogen, C1-C4 alkyl or alkoxy or R8/R9 together form a cycloalkyl.

Therefore D2 and the present scope do not overlap.

The problem on which the present application is based is to provide further compounds having fungicidal activity. The solution to this problem is the compounds according to claim 1 whereas the carbonyl linker of D2 is replaced by an eventually substituted methylene linker.

- 3.2 In the absence of any unexpected effect linked to this difference, it is considered as obvious for a skilled person wishing to provide alternative fungicides to the ones of D2 to slightly modify one linker (namely substitute a methylene for a carbonyl), because this feature is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.
- 3.3 Besides, such a modification is strongly encouraged by the disclosure of D3 which discloses the following compounds and their use as fungicides:

Example E-52



(see p.212).

These compounds an alkyl linker between the amido group and the phenyl and consequently present a benzyl end group as in the presently claimed compounds.

A skilled person starting from D2 would find in D3 a good motivation to replaced the carbonyl linker by a methylene linker or benzyl end-group as in D3.

Therefore claim 1 does not involve an inventive step.

Dependent claims 2-13 do not appear to contain any additional features which, in combination with the features of any claim to which it refers, meet the requirements of the PCT in respect of novelty and/or inventive step because the features concerned are either disclosed in D2 or are suggested by a combination of D2 with D3 (same reasoning as for claim 1).

- 3.4 The composition and fungicidal use lack inventive step for the same reasons (claims 14-16).

Re Item VII

Certain defects in the international application

- 1 The closest prior art D2 and D3 should be cited and discussed.

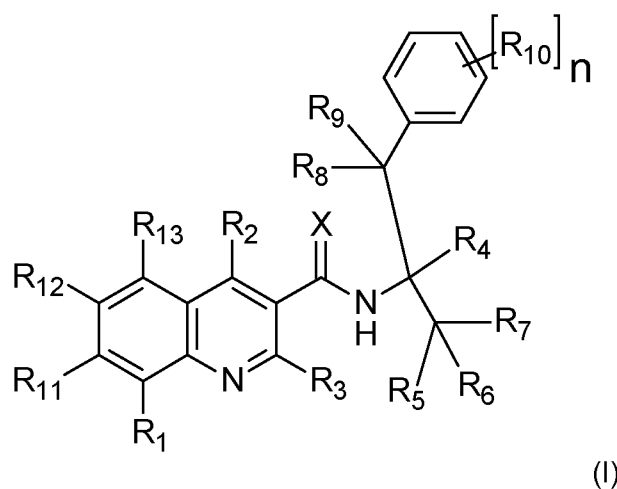
MICROBIOCIDAL QUINOLINE (THIO)CARBOXAMIDE DERIVATIVES

The present invention relates to microbiocidal quinoline (thio)carboxamide derivatives, e.g. as active ingredients, which have microbiocidal activity, in particular
 5 fungicidal activity. The invention also relates to preparation of these quinoline (thio)carboxamide derivatives, to intermediates useful in the preparation of these quinoline (thio)carboxamide derivatives, to the preparation of these intermediates, to agrochemical compositions which comprise at least one of the quinoline (thio)carboxamide derivatives, to preparation of these compositions and to the use of the quinoline (thio)carboxamide
 10 derivatives or compositions in agriculture or horticulture for controlling or preventing infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms, in particular fungi.

Certain fungicidal quinoline (thio)carboxamide compounds are described in WO04039783.

15 It has now surprisingly been found that certain novel quinoline (thio)carboxamide derivatives have favourable fungicidal properties.

The present invention therefore provides compounds of formula (I)



20 wherein

X is O or S;

R₁ is hydrogen, halogen, methyl, methoxy or cyano;

25 R₂ and R₃ are each independently hydrogen, halogen or methyl;

R₄ is hydrogen, cyano, C₁-C₄ alkyl, or C₃-C₄ cycloalkyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, C₁-C₃ alkyl, C₁-C₃ alkoxy and C₁-C₃ alkylthio;

R₅ and R₆ are each independently selected from hydrogen, halogen, C₁-C₄ alkyl, C₁-
 30 C₄ alkoxy and C₁-C₄ alkylthio; or

R_5 and R_6 together with the carbon atom to which they are attached represent $C=O$, $C=NOR_c$, C_3-C_5 cycloalkyl or C_2-C_5 alkenyl, wherein the cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, C_1-C_3 alkyl, C_1-C_3 alkoxy and C_1-C_3 alkylthio;

- 5 R_7 is hydrogen, C_1-C_5 alkyl, C_3-C_5 cycloalkyl, C_2-C_5 alkenyl, C_3-C_5 cycloalkenyl, or C_2-C_5 alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, cycloalkenyl may be optionally substituted with 1 to 4 substituents independently selected from halogen, cyano, C_1-C_3 alkyl, C_1-C_3 alkoxy, hydroxyl and C_1-C_3 alkylthio;

- R_8 and R_9 are each independently selected from hydrogen, halogen, C_1-C_4 alkyl and
10 C_1-C_4 alkoxy; or

R_8 and R_9 together with the carbon atom to which they are attached represent C_3-C_5 cycloalkyl, wherein the cycloalkyl may be optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, C_1-C_3 alkyl, C_1-C_3 alkoxy and C_1-C_3 alkylthio;

- each R_{10} independently represents halogen, nitro, cyano, formyl, C_1-C_5 alkyl, C_2-C_5
15 alkenyl, C_2-C_5 alkynyl, C_3-C_6 cycloalkyl, C_1-C_5 alkoxy, C_3-C_5 alkenyloxy, C_3-C_5 alkynyloxy, C_1-C_5 alkylthio, $-C(=NOR_c)C_1-C_5$ alkyl, or C_1-C_5 alkylcarbonyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy and alkylthio may be optionally substituted with 1 to 5 substituents independently selected from halogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, cyano and C_1-C_3 alkylthio; n is 0, 1, 2, 3, 4 or 5;

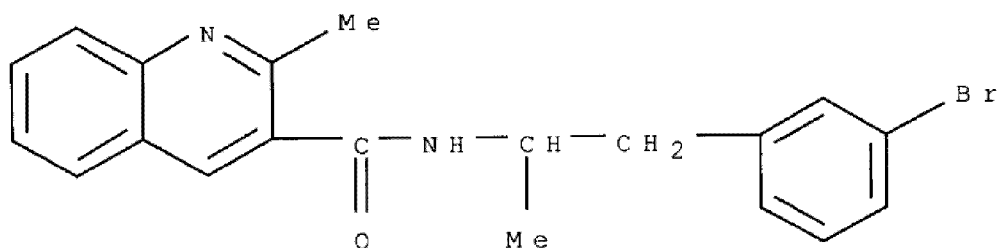
- 20 each R_c is independently selected from hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_4 alkynyl, C_3-C_4 cycloalkyl(C_1-C_2)alkyl and C_3-C_4 cycloalkyl, wherein the alkyl, cycloalkyl, alkenyl and alkynyl groups may be optionally substituted with 1 to 3 substituents independently selected from halogen and cyano;

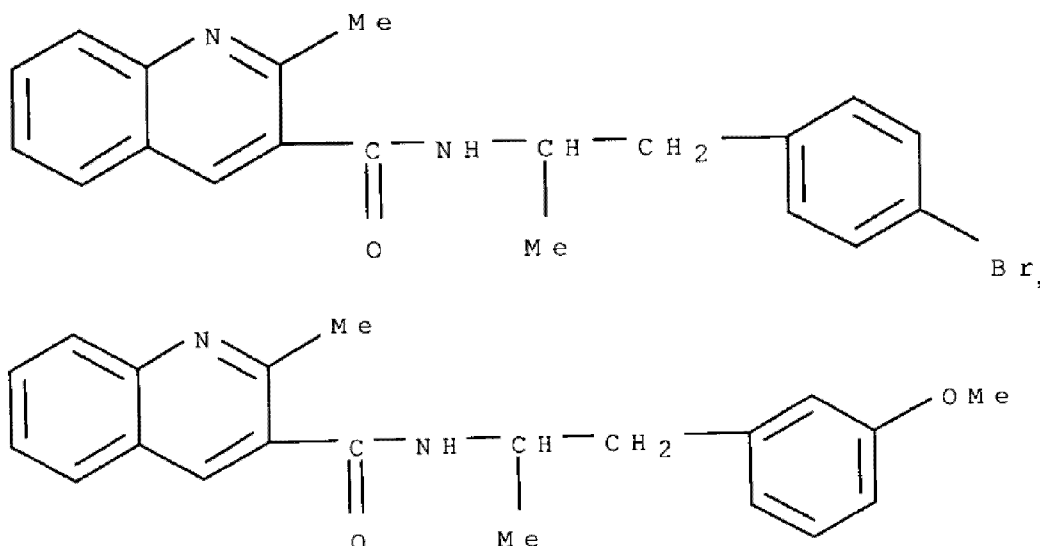
R_{11} is hydrogen, halogen, methyl, methoxy or cyano;

- 25 R_{12} and R_{13} are each independently selected from hydrogen, halogen, methyl, methoxy or hydroxyl;

and salts and/or N-oxides thereof;

provided that the compound is not one of the following compounds:





5 In a second aspect the present invention provides an agrochemical composition comprising a compound of formula (I).

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
10 the phytopathogen, or to the locus of a phytopathogen, in particular to a plant susceptible to attack by phytopathogens.

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 control a phytopathogen.

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

20 Compounds of formula (I) are particularly effective in the control of phytopathogenic fungi.

Thus, in a yet further 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.

25 In a further aspect the present invention provides a method of controlling 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.

Where substituents are indicated as being optionally substituted, this means that they
5 may or may not carry one or more identical or different substituents, e.g. one to three substituents. Normally not more than three such optional substituents are present at the same time. 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.

The term "halogen" refers to fluorine, chlorine, bromine or iodine, preferably fluorine,
10 chlorine or bromine.

Alkyl substituents (either alone or as part of a larger group, such as alkoxy-, alkylthio-) may be straight-chained or branched. Alkyl on its own or as part of another substituent is, depending upon the number of carbon atoms mentioned, for example, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl and the isomers thereof, for example, iso-propyl, iso-butyl,
15 sec-butyl, *tert*-butyl or iso-amyl.

Alkenyl substituents (either alone or as part of a larger group, eg. alkenyloxy) can be in the form of straight or branched chains, and the alkenyl moieties, where appropriate, can be of either the (*E*)- or (*Z*)-configuration. Examples are vinyl and allyl. The alkenyl groups are preferably C₂-C₆, more preferably C₂-C₄ and most preferably C₂-C₃ alkenyl groups.

20 Alkynyl substituents (either alone or as part of a larger group, eg. alkynyloxy) can be in the form of straight or branched chains. Examples are ethynyl and propargyl. The alkynyl groups are preferably C₂-C₆, more preferably C₂-C₄ and most preferably C₂-C₃ alkynyl groups.

Cycloalkyl substituents may be saturated or partially unsaturated, preferably fully
25 saturated, and are, for example, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

Haloalkyl groups (either alone or as part of a larger group, eg. haloalkyloxy) may contain one or more identical or different halogen atoms and, for example, may stand for CH₂Cl, CHCl₂, CCl₃, CH₂F, CHF₂, CF₃, CF₃CH₂, CH₃CF₂, CF₃CF₂ or CCl₃CCl₂.

Haloalkenyl groups (either alone or as part of a larger group, eg. haloalkenyloxy) are
30 alkenyl groups, respectively, which are substituted with one or more of the same or different halogen atoms and are, for example, 2,2-difluorovinyl or 1,2-dichloro-2-fluoro-vinyl.

Haloalkynyl groups (either alone or as part of a larger group, eg. haloalkynyloxy) are alkynyl groups, respectively, which are substituted with one or more of the same or different halogen atoms and are, for example, 1-chloro-prop-2-ynyl.

35 Alkoxy means a radical -OR, where R is alkyl, e.g. as defined above. Alkoxy groups include, but are not limited to, methoxy, ethoxy, 1-methylethoxy, propoxy, butoxy, 1-methylpropoxy and 2-methylpropoxy.

Cyano means a –CN group.

Amino means an –NH₂ group.

Hydroxyl or hydroxy stands for a –OH group.

Aryl groups (either alone or as part of a larger group, such as e.g. aryloxy, aryl-alkyl) are aromatic ring systems which can be in mono-, bi- or tricyclic form. Examples of such rings include phenyl, naphthyl, anthracenyl, indenyl or phenanthrenyl. Preferred aryl groups are phenyl and naphthyl, phenyl being most preferred. Where an aryl moiety is said to be substituted, the aryl moiety is preferably substituted by one to four substituents, most preferably by one to three substituents.

Heteroaryl groups (either alone or as part of a larger group, such as e.g. heteroaryloxy, heteroaryl-alkyl) are aromatic ring systems containing at least one heteroatom and consisting either of a single ring or of two or more fused rings. Preferably, single rings will contain up to three heteroatoms and bicyclic systems up to four heteroatoms which will preferably be chosen from nitrogen, oxygen and sulfur. Examples of monocyclic groups include pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl (e.g. [1,2,4] triazolyl), furanyl, thiophenyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl and thiadiazolyl. Examples of bicyclic groups include purinyl, quinolinyl, cinnolinyl, quinoxalinyl, indolyl, indazolyl, benzimidazolyl, benzothiophenyl and benzothiazolyl. Monocyclic heteroaryl groups are preferred, pyridyl being most preferred. Where a heteroaryl moiety is said to be substituted, the heteroaryl moiety is preferably substituted by one to four substituents, most preferably by one to three substituents.

Heterocyclyl groups or heterocyclic rings (either alone or as part of a larger group, such as heterocyclyl-alkyl) are non-aromatic ring structures containing up to 10 atoms including one or more (preferably one, two or three) heteroatoms selected from O, S and N. Examples of monocyclic groups include, oxetanyl, 4,5-dihydro-isoxazolyl, thietanyl, pyrrolidinyl, tetrahydrofuranyl, [1,3]dioxolanyl, piperidinyl, piperazinyl, [1,4]dioxanyl, imidazolidinyl, [1,3,5]oxadiazinanyl, hexahydro-pyrimidinyl, [1,3,5]triazinanyl and morpholinyl or their oxidised versions such as 1-oxo-thietanyl and 1,1-dioxo-thietanyl. Examples of bicyclic groups include 2,3-dihydro-benzofuranyl, benzo[1,4]dioxolanyl, benzo[1,3]dioxolanyl, chromenyl, and 2,3-dihydro-benzo[1,4]dioxinyl. Where a heterocyclyl moiety is said to be substituted, the heterocyclyl moiety is preferably substituted by one to four substituents, most preferably by one to three substituents.

The presence of one or more possible asymmetric carbon atoms in a compound of formula (I) means that the compounds may occur in optically isomeric forms, i.e. enantiomeric or diastereomeric forms. Also atropisomers may occur as a result of restricted rotation about a single bond. Formula (I) is intended to include all those possible isomeric forms and mixtures thereof. The present invention includes all those possible isomeric forms

and mixtures thereof for a compound of formula (I). Likewise, formula (I) is intended to include all possible tautomers. The present invention includes all possible tautomeric forms for a compound of formula (I).

In each case, the compounds of formula (I) according to the invention are in free
5 form, in oxidized form as a N-oxide or in salt form, e.g. an agronomically usable salt form.

N-oxides are oxidized forms of tertiary amines or oxidized forms 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.

10 Preferred values of X, R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₃, n and R_c are, in any combination thereof, as set out below:

Preferably X is O.

Preferably R₁ is hydrogen, fluoro, chloro, methyl, or cyano.

More preferably R₁ is hydrogen, fluoro, methyl, or cyano.

15 Most preferably R₁ is hydrogen or fluoro.

Preferably R₂ and R₃ are each independently hydrogen or methyl.

More preferably R₂ is hydrogen and R₃ is hydrogen or methyl; or R₂ is hydrogen or methyl and R₃ is hydrogen.

Most preferably R₂ and R₃ are both hydrogen.

20 Preferably R₄ is hydrogen, cyano, C₁-C₃ alkyl, or cyclopropyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, methoxy and methylthio.

More preferably R₄ is hydrogen, cyano, methyl or ethyl, wherein the methyl and ethyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro and
25 methoxy.

Most preferably R₄ is methyl or ethyl (wherein the methyl and ethyl may be optionally substituted with 1 to 3 fluoro substituents or methoxy).

Preferably R₅ and R₆ are each independently selected from hydrogen, fluoro, C₁-C₂ alkyl, C₁-C₂ alkoxy and C₁-C₂ alkylthio; or R₅ and R₆ together with the carbon atom to which
30 they are attached represent C=O or cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, methyl and cyano.

More preferably R₅ and R₆ are each independently selected from hydrogen, fluoro, methyl, methoxy and methylthio; or R₅ and R₆ together with the carbon atom to which they are attached represent cyclopropyl.

35 Most preferably R₅ and R₆ are each independently selected from hydrogen and fluoro.

Preferably R_7 is C_1 - C_4 alkyl, C_3 - C_4 cycloalkyl, C_2 - C_4 alkenyl, or C_2 - C_3 alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, hydroxyl and methylthio.

More preferably R_7 is C_1 - C_4 alkyl, C_3 - C_4 cycloalkyl, or C_2 - C_4 alkenyl, wherein the alkyl, 5 cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, hydroxyl, cyano and methyl.

Most preferably R_7 is methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, C_3 - C_4 cycloalkyl, or C_2 - C_4 alkenyl, wherein the methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents 10 independently selected from fluoro, chloro and methyl.

Preferably R_8 and R_9 are each independently selected from hydrogen, fluoro, C_1 - C_2 alkyl and C_1 - C_2 alkoxy; or R_8 and R_9 together with the carbon atom to which they are attached represent cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, cyano, and methyl.

15 More preferably R_8 and R_9 are each independently selected from hydrogen, fluoro and methyl; or R_8 and R_9 together with the carbon atom to which they are attached represent cyclopropyl.

Most preferably R_8 and R_9 are each independently selected from hydrogen or fluoro.

Preferably each R_{10} independently represents halogen, cyano, C_1 - C_3 alkyl, C_2 - C_3 20 alkenyl, C_2 - C_3 alkynyl, cyclopropyl, methoxy, allyloxy, propargyloxy, or C_1 - C_2 alkylthio, wherein the alkyl, cyclopropyl, alkenyl, alkynyl, methoxy, allyloxy, propargyloxy and alkylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, methyl, and cyano; n is 0, 1, 2 or 3.

More preferably each R_{10} independently represents fluoro, chloro, cyano, methyl, 25 cyclopropyl, methoxy or methylthio, wherein the methyl, cyclopropyl, methoxy and methylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro; n is 0, 1 or 2.

Most preferably each R_{10} independently represents fluoro, chloro, cyano or methyl, wherein the methyl, cyclopropyl, methoxy and methylthio may be optionally substituted with 1 30 to 3 fluoro substituents; n is 0, 1 or 2.

Preferably each R_c is independently selected from hydrogen, methyl, ethyl, allyl, propargyl, and cyclopropylmethyl, wherein the methyl, ethyl, allyl, propargyl, and cyclopropylmethyl groups may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro.

35 Most preferably each R_c is independently selected from methyl, ethyl, allyl, propargyl, and cyclopropylmethyl, wherein the methyl, ethyl, allyl, propargyl, and cyclopropylmethyl

groups may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro.

Preferably R_{11} is hydrogen, fluoro, chloro, methyl or cyano.

More preferably R_{11} is hydrogen, fluoro, methyl or chloro.

5 Most preferably R_{11} is hydrogen or fluoro.

Preferably R_{12} and R_{13} are each independently selected from hydrogen, fluoro, methyl and hydroxyl.

More preferably R_{12} and R_{13} are each independently selected from hydrogen, fluoro and methyl.

10 Most preferably R_{12} and R_{13} are both hydrogen.

Embodiments according to the invention are provided as set out below.

Embodiment 1 provides compounds of formula (I), or a salt or N-oxide thereof, as defined above.

15 Embodiment 2 provides compounds according to embodiment 1, or a salt or N-oxide thereof, wherein R_1 is hydrogen, fluoro, chloro, methyl, or cyano.

Embodiment 3 provides compounds according to embodiment 1 or 2, or a salt or N-oxide thereof, wherein R_2 and R_3 are each independently hydrogen or methyl.

Embodiment 4 provides compounds according to any one of embodiments 1, 2 or 3,
20 or a salt or N-oxide thereof, wherein R_4 is hydrogen, cyano, C_1 - C_3 alkyl, or cyclopropyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, methoxy, and methylthio.

Embodiment 5 provides compounds according to any one of embodiments 1, 2, 3 or 4, or a salt or N-oxide thereof, wherein R_5 and R_6 are each independently selected from
25 hydrogen, fluoro, C_1 - C_2 alkyl, C_1 - C_2 alkoxy and C_1 - C_2 alkylthio; or R_5 and R_6 together with the carbon atom to which they are attached represent $C=O$ or cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, methyl and cyano.

Embodiment 6 provides compounds according to any one of embodiments 1, 2, 3, 4,
30 or 5, or a salt or N-oxide thereof, wherein R_7 is C_1 - C_4 alkyl, C_3 - C_4 cycloalkyl, C_2 - C_4 alkenyl, or C_2 - C_3 alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, hydroxyl and methylthio.

Embodiment 7 provides compounds according to any one of embodiments 1, 2, 3, 4,
35 5, or 6, or a salt or N-oxide thereof, wherein R_8 and R_9 are each independently selected from hydrogen, fluoro, C_1 - C_2 alkyl and C_1 - C_2 alkoxy; or R_8 and R_9 together with the carbon atom to

which they are attached represent cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, cyano, and methyl.

Embodiment 8 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, or 7, or a salt or N-oxide thereof, wherein each R₁₀ independently represents halogen, cyano, C₁-C₃ alkyl, C₂-C₃ alkenyl, C₂-C₃ alkynyl, cyclopropyl, methoxy, allyloxy, propargyloxy, or C₁-C₂ alkylthio, wherein the alkyl, cyclopropyl, alkenyl, alkynyl, methoxy, allyloxy, propargyloxy and alkylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, methyl, and cyano; n is 0, 1, 2 or 3.

Embodiment 9 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, or 8, or a salt or N-oxide thereof, wherein each R_c is independently selected from hydrogen, methyl, ethyl, allyl, propargyl, and cyclopropylmethyl, wherein the methyl, ethyl, allyl, propargyl, and cyclopropylmethyl groups may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro.

Embodiment 10 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, or 9, or a salt or N-oxide thereof, wherein R₁ is hydrogen, fluoro, methyl, or cyano.

Embodiment 11 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, or a salt or N-oxide thereof, wherein R₂ is hydrogen and R₃ is hydrogen or methyl; or R₂ is hydrogen or methyl and R₃ is hydrogen.

Embodiment 12 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or 11, or a salt or N-oxide thereof, wherein R₄ is hydrogen, cyano, methyl or ethyl, wherein the methyl and ethyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro and methoxy.

Embodiment 13 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12, or a salt or N-oxide thereof, wherein R₅ and R₆ are each independently selected from hydrogen, fluoro, methyl, methoxy and methylthio; or R₅ and R₆ together with the carbon atom to which they are attached represent cyclopropyl.

Embodiment 14 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or 13, or a salt or N-oxide thereof, wherein R₇ is C₁-C₄ alkyl, C₃-C₄ cycloalkyl, or C₂-C₄ alkenyl, wherein the alkyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, hydroxyl, cyano and methyl.

Embodiment 15 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14, or a salt or N-oxide thereof, wherein R₈ and R₉ are each independently selected from hydrogen, fluoro and methyl; or R₈ and R₉ together with the carbon atom to which they are attached represent cyclopropyl.

Embodiment 16 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15, or a salt or N-oxide thereof, wherein each R₁₀

independently represents fluoro, chloro, cyano, methyl, cyclopropyl, methoxy or methylthio, wherein the methyl, cyclopropyl, methoxy and methylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro; n is 0, 1 or 2.

Embodiment 17 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16, or a salt or N-oxide thereof, wherein each R_c is independently selected from methyl, ethyl, allyl, propargyl, and cyclopropylmethyl, wherein the methyl, ethyl, allyl, propargyl, and cyclopropylmethyl groups may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro.

Embodiment 18 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17, or a salt or N-oxide thereof, wherein R₁ is hydrogen or fluoro.

Embodiment 19 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 or 18, or a salt or N-oxide thereof, wherein R₂ and R₃ are both hydrogen.

Embodiment 20 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 or 19, or a salt or N-oxide thereof, wherein R₄ is methyl or ethyl (wherein the methyl and ethyl may be optionally substituted with 1 to 3 fluoro substituents).

Embodiment 21 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20, or a salt or N-oxide thereof, wherein R₅ and R₆ are each independently selected from hydrogen and fluoro.

Embodiment 22 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or 21, or a salt or N-oxide thereof, wherein R₇ is methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, C₃-C₄ cycloalkyl, or C₂-C₄ alkenyl, wherein the methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro and methyl.

Embodiment 23 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22, or a salt or N-oxide thereof, wherein R₈ and R₉ are each independently selected from hydrogen or fluoro.

Embodiment 24 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22 or 23, or a salt or N-oxide thereof, wherein each R₁₀ independently represents fluoro, chloro, cyano or methyl, wherein the methyl, cyclopropyl, methoxy and methylthio may be optionally substituted with 1 to 3 fluoro substituents; n is 0, 1 or 2.

Embodiment 25 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or 24, or a salt or N-oxide

thereof, wherein R_{11} is hydrogen, fluoro, chloro, methyl or cyano. Embodiment 26 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25, or a salt or N-oxide thereof, wherein R_{12} and R_{13} are each independently selected from hydrogen, fluoro, methyl and hydroxyl.

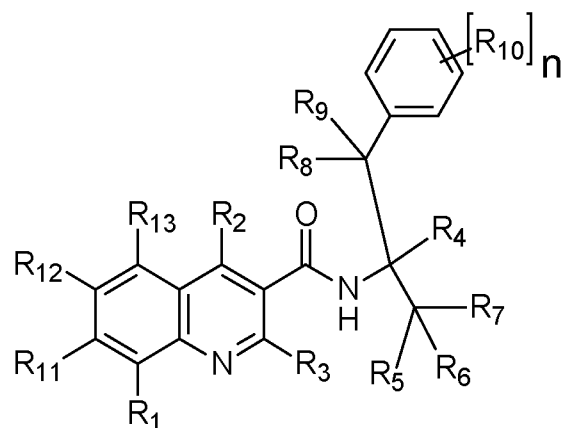
5 Embodiment 27 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or 26, or a salt or N-oxide thereof, wherein R_{11} is hydrogen, fluoro, methyl or chloro.

Embodiment 28 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26 or 27, or a salt or
10 N-oxide thereof, wherein R_{12} and R_{13} are each independently selected from hydrogen, fluoro and methyl.

Embodiment 29 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 or 28, or a salt or N-oxide thereof, wherein R_{11} is hydrogen or fluoro.

15 Embodiment 30 provides compounds according to any one of embodiments 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28 or 29, or a salt or N-oxide thereof, wherein R_{12} and R_{13} are both hydrogen.

One group of compounds according to the invention are those of formula (I'):

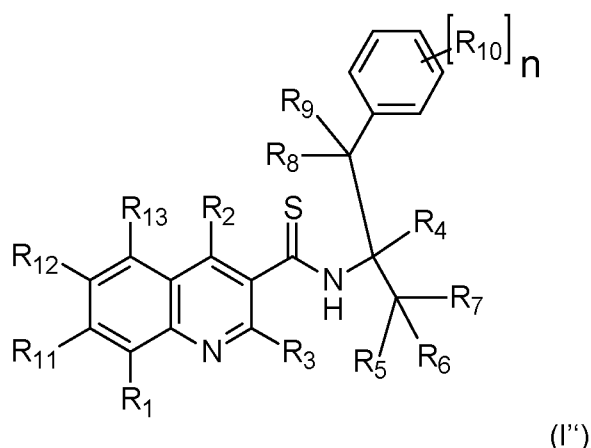


(I')

20

wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} , n and R_c are as defined for compounds of formula (I), or a salt or N-oxide thereof. Preferred definitions of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} , n and R_c are as defined for compounds of formula (I).

One group of compounds according to the invention are those of formula (I''):



wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} , n and R_c are as defined for compounds of formula (I), or a salt or N-oxide thereof. Preferred definitions of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} , n and R_c are as defined for compounds of formula (I).

5

A preferred group of compounds according to the invention are those of formula (I-1) which are compounds of formula (I) wherein X is O or S; R_1 is hydrogen, fluoro, chloro, methyl, or cyano; R_2 and R_3 are each independently hydrogen or methyl; R_4 is hydrogen, cyano, C_1 - C_3 alkyl, or cyclopropyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, methoxy, and methylthio; R_5 and R_6 are each independently selected from hydrogen, fluoro, C_1 - C_2 alkyl, C_1 - C_2 alkoxy and C_1 - C_2 alkylthio; or R_5 and R_6 together with the carbon atom to which they are attached represent $C=O$ or cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, methyl and cyano; R_7 is C_1 - C_4 alkyl, C_3 - C_4 cycloalkyl, C_2 - C_4 alkenyl, or C_2 - C_3 alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, hydroxyl and methylthio; R_8 and R_9 are each independently selected from hydrogen, fluoro, C_1 - C_2 alkyl and C_1 - C_2 alkoxy; or R_8 and R_9 together with the carbon atom to which they are attached represent cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, cyano, and methyl; each R_{10} independently represents halogen, cyano, C_1 - C_3 alkyl, C_2 - C_3 alkenyl, C_2 - C_3 alkynyl, cyclopropyl, methoxy, allyloxy, propargyloxy, or C_1 - C_2 alkylthio, wherein the alkyl, cyclopropyl, alkenyl, alkynyl, methoxy, allyloxy, propargyloxy and alkylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, methyl, and cyano; n is 0, 1, 2 or 3; R_{11} is hydrogen, fluoro, chloro, methyl or cyano; and R_{12} and R_{13} are each independently selected from hydrogen, fluoro, methyl and hydroxyl; or a salt or N-oxide thereof.

One group of compounds according to this embodiment are compounds of formula (I-1a) which are compounds of formula (I-1) wherein X is O.

Another group of compounds according to this embodiment are compounds of formula (I-1b) which are compounds of formula (I-1) wherein X is S.

A further preferred group of compounds according to the invention are those of formula (I-2) which are compounds of formula (I) wherein X is O or S; R₁ is hydrogen, fluoro, methyl, or cyano; R₂ is hydrogen and R₃ is hydrogen or methyl; or R₂ is hydrogen or methyl and R₃ is hydrogen; R₄ is hydrogen, cyano, methyl or ethyl, wherein the methyl and ethyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro and methoxy; R₅ and R₆ are each independently selected from hydrogen, fluoro, methyl, methoxy and methylthio; or R₅ and R₆ together with the carbon atom to which they are attached represent cyclopropyl; R₇ is C₁-C₄ alkyl, C₃-C₄ cycloalkyl, or C₂-C₄ alkenyl, wherein the alkyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, hydroxyl, cyano and methyl; R₈ and R₉ are each independently selected from hydrogen, fluoro and methyl; or R₈ and R₉ together with the carbon atom to which they are attached represent cyclopropyl; each R₁₀ independently represents fluoro, chloro, cyano, methyl, cyclopropyl, methoxy or methylthio, wherein the methyl, cyclopropyl, methoxy and methylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro; n is 0, 1 or 2; R₁₁ is hydrogen, fluoro, methyl or chloro; and R₁₂ and R₁₃ are each independently selected from hydrogen, fluoro and methyl; or a salt or N-oxide thereof.

One group of compounds according to this embodiment are compounds of formula (I-2a) which are compounds of formula (I-2) wherein X is O.

Another group of compounds according to this embodiment are compounds of formula (I-2b) which are compounds of formula (I-2) wherein X is S.

A further preferred group of compounds according to the invention are those of formula (I-3) which are compounds of formula (I) wherein X is O or S; R₁ is hydrogen or fluoro; R₂ and R₃ are both hydrogen; R₄ is methyl or ethyl (wherein the methyl and ethyl may be optionally substituted with 1 to 3 fluoro substituents); R₅ and R₆ are each independently selected from hydrogen and fluoro; R₇ is methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, C₃-C₄ cycloalkyl, or C₂-C₄ alkenyl, wherein the methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro and methyl; R₈ and R₉ are each independently selected from hydrogen or fluoro; each R₁₀ independently represents fluoro, chloro, cyano or methyl, wherein the methyl, cyclopropyl, methoxy and methylthio may be optionally substituted with 1 to 3 fluoro substituents; n is 0, 1 or 2; and R₁₁ is hydrogen or fluoro; R₁₂ and R₁₃ are both hydrogen; or a salt or N-oxide thereof.

One group of compounds according to this embodiment are compounds of formula (I-3a) which are compounds of formula (I-3) wherein X is O.

Another group of compounds according to this embodiment are compounds of formula (I-3b) which are compounds of formula (I-3) wherein X is S.

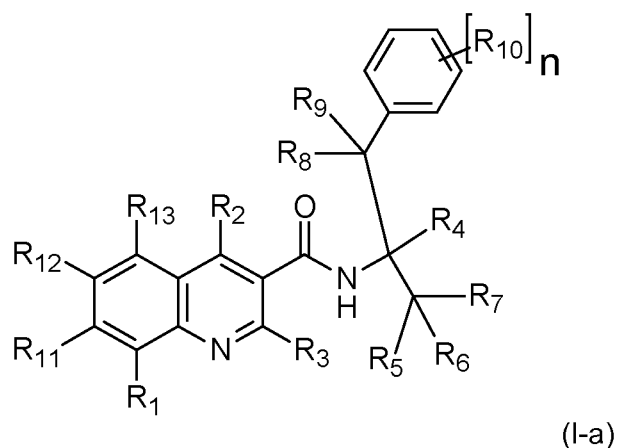
Compounds according to the invention may possess any number of benefits

- 5 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).

10

Specific examples of compounds of formula (I) are illustrated in the Tables A1 to A13 below:

Table A1 provides 248 compounds of formula (I-a)



wherein R₁, R₂ and R₃ are all H and R₁₁, R₁₂, R₁₃ are all H

- 15 and wherein the values of R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ and n (if R₁₀ and n are present) are as defined in Table Z below:

Table Z

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
1	H	H	H	CH ₃	H	H	—
2	H	H	H	CH ₂ CH ₃	H	H	—
3	H	H	H	CH ₂ CH ₂ CH ₃	H	H	—
4	H	H	H	CH ₂ CH ₂ CF ₃	H	H	—
5	H	H	H	CH(CH ₃) ₂	H	H	—
6	H	H	H	CH=CH ₂	H	H	—
7	H	H	H	C(CH ₃)=CH ₂	H	H	—
8	H	H	H	C(Cl)=CH ₂	H	H	—
9	H	H	H	C(CH ₃)=CF ₂	H	H	—
10	H	H	H	C(F)=CH ₂	H	H	—

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
11	H	H	H	C(CH ₃) ₃	H	H	—
12	H	H	H	CF(CH ₃) ₂	H	H	—
13	H	H	H	C(OH)(CH ₃) ₂	H	H	—
14	H	H	H	C(CN)(CH ₃) ₂	H	H	—
15	H	H	H	C(SCH ₃)(CH ₃) ₂	H	H	—
16	H	H	H	CF ₃	H	H	—
17	H	H	H	CHF ₂	H	H	—
18	H	H	H	CF ₂ CH ₃	H	H	—
19	H	H	H	CF ₂ Cl	H	H	—
20	H	H	H	CH=CF ₂	H	H	—
21	H	H	H	CH=C(CH ₃)H	H	H	—
22	H	H	H	CH=C(CH ₃) ₂	H	H	—
23	H	H	H	cyclopropyl	H	H	—
24	H	H	H	1-methylcyclopropyl	H	H	—
25	H	H	H	1-fluorocyclopropyl	H	H	—
26	H	H	H	1-cyanocyclopropyl	H	H	—
27	H	H	H	1-Methylthiocyclopropyl	H	H	—
28	H	H	H	cyclobutyl	H	H	—
29	H	H	H	1-fluorocyclobutyl	H	H	—
30	H	H	H	3,3-difluorocyclobutyl	H	H	—
31	CH ₃	H	H	CH ₃	H	H	—
32	CH ₃	H	H	CH ₂ CH ₃	H	H	—
33	CH ₃	H	H	CH ₂ CH ₂ CH ₃	H	H	—
34	CH ₃	H	H	CH ₂ CH ₂ CF ₃	H	H	—
35	CH ₃	H	H	CH(CH ₃) ₂	H	H	—
36	CH ₃	H	H	CH=CH ₂	H	H	—
37	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	—
38	CH ₃	H	H	C(Cl)=CH ₂	H	H	—
39	CH ₃	H	H	C(CH ₃)=CF ₂	H	H	—
40	CH ₃	H	H	C(F)=CH ₂	H	H	—
41	CH ₃	H	H	C(CH ₃) ₃	H	H	—
42	CH ₃	H	H	CF(CH ₃) ₂	H	H	—
43	CH ₃	H	H	C(OH)(CH ₃) ₂	H	H	—
44	CH ₃	H	H	C(CN)(CH ₃) ₂	H	H	—
45	CH ₃	H	H	C(SCH ₃)(CH ₃) ₂	H	H	—
46	CH ₃	H	H	CF ₃	H	H	—
47	CH ₃	H	H	CHF ₂	H	H	—

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
48	CH ₃	H	H	CF ₂ CH ₃	H	H	—
49	CH ₃	H	H	CF ₂ Cl	H	H	—
50	CH ₃	H	H	CH=CF ₂	H	H	—
51	CH ₃	H	H	CH=C(CH ₃)H	H	H	—
52	CH ₃	H	H	CH=C(CH ₃) ₂	H	H	—
53	CH ₃	H	H	cyclopropyl	H	H	—
54	CH ₃	H	H	1-methylcyclopropyl	H	H	—
55	CH ₃	H	H	1-fluorocyclopropyl	H	H	—
56	CH ₃	H	H	1-cyanocyclopropyl	H	H	—
57	CH ₃	H	H	1-Methylthiocyclopropyl	H	H	—
58	CH ₃	H	H	cyclobutyl	H	H	—
59	CH ₃	H	H	1-fluorocyclobutyl	H	H	—
60	CH ₃	H	H	3,3-difluorocyclobutyl	H	H	—
61	H	CH ₃	H	CH ₃	H	H	—
62	H	CH ₃	CH ₃	CH ₃	H	H	—
63	H	cyclopropyl		CH ₃	H	H	
64	H	CH ₃	CH ₃	CH ₂ CH ₃	H	H	—
65	H	cyclopropyl		CH ₂ CH ₃	H	H	
66	CH ₃	H	H	H	H	H	—
67	CH ₃	H	H	F	H	H	—
68	CH ₃	H	H	Cl	H	H	—
69	CH ₂ CH ₃	H	H	H	H	H	—
70	CH ₂ CH ₃	H	H	F	H	H	—
71	CH ₂ CH ₃	H	H	Cl	H	H	—
72	CH ₂ CH ₃	H	H	CH ₃	H	H	—
73	CH ₂ CH ₃	H	H	CH ₂ CH ₃	H	H	—
74	CH ₂ CH ₃	H	H	CH ₂ CH ₂ CH ₃	H	H	—
75	CH ₂ CH ₃	H	H	CH(CH ₃) ₂	H	H	—
76	CH ₂ CH ₃	H	H	CH=CH ₂	H	H	—
77	CH ₂ CH ₃	H	H	C(CH ₃)=CH ₂	H	H	—
78	CH ₂ CH ₃	H	H	C(CH ₃) ₃	H	H	—
79	CH ₂ CH ₃	H	H	CF(CH ₃) ₂	H	H	—
80	CH ₂ CH ₃	H	H	C(CN)(CH ₃) ₂	H	H	—
81	CH ₂ CH ₃	H	H	C(SCH ₃)(CH ₃) ₂	H	H	—
82	CH ₂ CH ₃	H	H	CF ₃	H	H	—
83	CH ₂ CH ₃	H	H	CHF ₂	H	H	—

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
84	CH ₂ CH ₃	H	H	CF ₂ CH ₃	H	H	—
85	CH ₂ CH ₃	H	H	cyclopropyl	H	H	—
86	CH ₂ CH ₃	H	H	1-methylcyclopropyl	H	H	—
87	CH ₂ CH ₃	H	H	1-fluorocyclopropyl	H	H	—
88	CH ₂ CH ₃	H	H	1-cyanocyclopropyl	H	H	—
89	CH ₂ CH ₃	H	H	1-Methylthiocyclopropyl	H	H	—
90	CH ₂ CH ₃	H	H	cyclobutyl	H	H	—
91	CH ₂ CH ₃	H	H	1-fluorocyclobutyl	H	H	—
92	CH ₂ CH ₃	H	H	3,3-difluorocyclobutyl	H	H	—
93	CN	H	H	CH ₃	H	H	—
94	CN	H	H	CH ₂ CH ₃	H	H	—
95	CN	H	H	CH ₂ CH ₂ CH ₃	H	H	—
96	CN	H	H	CH(CH ₃) ₂	H	H	—
97	CN	H	H	C(CH ₃) ₃	H	H	—
98	CN	H	H	CF(CH ₃) ₂	H	H	—
99	CN	H	H	CF ₃	H	H	—
100	CH ₂ OCH ₃	H	H	CH ₃	H	H	—
101	CH ₂ OCH ₃	H	H	CH ₂ CH ₂ CF ₃	H	H	—
102	CH ₂ OCH ₃	H	H	CH(CH ₃) ₂	H	H	—
103	CH ₂ OCH ₃	H	H	CH=CH ₂	H	H	—
104	CH ₂ OCH ₃	H	H	C(CH ₃)=CH ₂	H	H	—
105	CH ₂ OCH ₃	H	H	C(CH ₃) ₃	H	H	—
106	CH ₂ OCH ₃	H	H	CF(CH ₃) ₂	H	H	—
107	CH ₂ OCH ₃	H	H	CF ₃	H	H	—
108	CH ₂ OCH ₃	H	H	CHF ₂	H	H	—
109	CH ₂ OCH ₃	H	H	CF ₂ CH ₃	H	H	—
110	CH ₂ OCH ₃	H	H	CF ₂ Cl	H	H	—
111	CH ₂ OCH ₃	H	H	CH=CF ₂	H	H	—
112	CH ₂ OCH ₃	H	H	cyclopropyl	H	H	—
113	CH ₂ OCH ₃	H	H	1-methylcyclopropyl	H	H	—
114	CH ₂ OCH ₃	H	H	1-fluorocyclopropyl	H	H	—
115	CH ₂ OCH ₃	H	H	1-cyanocyclopropyl	H	H	—
116	CH ₃	F	F	H	H	H	—
117	CH ₃	F	F	F	H	H	—
118	CH ₃	F	F	CH ₃	H	H	—
119	CH ₃	F	F	CH ₂ CH ₃	H	H	—

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
120	CH ₃	F	F	CH ₂ CH ₂ CH ₃	H	H	—
121	CH ₃	F	F	CH(CH ₃) ₂	H	H	—
122	CH ₃	F	F	C(CH ₃) ₃	H	H	—
123	CH ₃	F	F	cyclopropyl	H	H	—
124	CH ₃	F	F	1-methylcyclopropyl	H	H	—
125	CH ₃	F	F	cyclobutyl	H	H	—
126	CH ₃	CH ₃	CH ₃	H	H	H	—
127	CH ₃	CH ₃	CH ₃	F	H	H	—
128	CH ₃	CH ₃	CH ₃	CH ₃	H	H	—
129	CH ₃	CH ₃	CH ₃	CH ₂ CH ₃	H	H	—
130	CH ₃	CH ₃	CH ₃	CH(CH ₃) ₂	H	H	—
131	CH ₃	CH ₃	CH ₃	CH=CH ₂	H	H	—
132	CH ₃	CH ₃	CH ₃	C(CH ₃)=CH ₂	H	H	—
133	CH ₃	CH ₃	CH ₃	cyclopropyl	H	H	—
134	CH ₃	cyclopropyl		H	H	H	—
135	CH ₃	cyclopropyl		F	H	H	—
136	CH ₃	cyclopropyl		Cl	H	H	—
137	CH ₃	cyclopropyl		CH ₃	H	H	—
138	CH ₃	cyclopropyl		CH ₂ CH ₃	H	H	—
139	CH ₃	cyclopropyl		CH(CH ₃) ₂	H	H	—
140	CH ₃	cyclopropyl		CH=CH ₂	H	H	—
141	CH ₃	cyclopropyl		C(CH ₃)=CH ₂	H	H	—
142	CH ₃	cyclopropyl		cyclopropyl	H	H	—
143	CH ₂ CH ₃	F	F	H	H	H	—
144	CH ₂ CH ₃	F	F	F	H	H	—
145	CH ₂ CH ₃	F	F	CH ₃	H	H	—
146	CH ₂ CH ₃	F	F	CH ₂ CH ₃	H	H	—
147	CH ₂ CH ₃	F	F	CH ₂ CH ₂ CH ₃	H	H	—
148	CH ₂ CH ₃	F	F	CH(CH ₃) ₂	H	H	—
149	CH ₂ CH ₃	F	F	C(CH ₃) ₃	H	H	—
150	CH ₂ CH ₃	F	F	cyclopropyl	H	H	—
151	CH ₂ CH ₃	F	F	1-methylcyclopropyl	H	H	—
152	CH ₂ CH ₃	F	F	cyclobutyl	H	H	—
153	CH ₂ CH ₃	CH ₃	CH ₃	H	H	H	—
154	CH ₂ CH ₃	CH ₃	CH ₃	F	H	H	—
155	CH ₂ CH ₃	CH ₃	CH ₃	Cl	H	H	—

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
156	CH ₂ CH ₃	CH ₃	CH ₃	CH ₃	H	H	—
157	CH ₂ CH ₃	CH ₃	CH ₃	CH ₂ CH ₃	H	H	—
158	CH ₂ CH ₃	CH ₃	CH ₃	CH(CH ₃) ₂	H	H	—
159	CH ₂ CH ₃	CH ₃	CH ₃	CH=CH ₂	H	H	—
160	CH ₂ CH ₃	CH ₃	CH ₃	C(CH ₃)=CH ₂	H	H	—
161	CH ₂ CH ₃	CH ₃	CH ₃	cyclopropyl	H	H	—
162	CH ₂ CH ₃	cyclopropyl		H	H	H	—
163	CH ₂ CH ₃	cyclopropyl		F	H	H	—
164	CH ₂ CH ₃	cyclopropyl		Cl	H	H	—
165	CH ₂ CH ₃	cyclopropyl		CH ₃	H	H	—
166	CH ₂ CH ₃	cyclopropyl		CH ₂ CH ₃	H	H	—
167	CH ₂ CH ₃	cyclopropyl		CH(CH ₃) ₂	H	H	—
168	CH ₂ CH ₃	cyclopropyl		CH=CH ₂	H	H	—
169	CH ₂ CH ₃	cyclopropyl		C(CH ₃)=CH ₂	H	H	—
170	CH ₂ CH ₃	cyclopropyl		cyclopropyl	H	H	—
171	CH ₃	H	H	CH(CH ₃) ₂	H	H	2-F
172	CH ₃	H	H	CH(CH ₃) ₂	H	H	3-F
173	CH ₃	H	H	CH(CH ₃) ₂	H	H	4-F
174	CH ₃	H	H	CH(CH ₃) ₂	H	H	2-Cl
175	CH ₃	H	H	CH(CH ₃) ₂	H	H	3-Cl
176	CH ₃	H	H	CH(CH ₃) ₂	H	H	4-Cl
177	CH ₃	H	H	CH(CH ₃) ₂	H	H	2-CH ₃
178	CH ₃	H	H	CH(CH ₃) ₂	H	H	3-CH ₃
179	CH ₃	H	H	CH(CH ₃) ₂	H	H	4-CH ₃
180	CH ₃	H	H	CH(CH ₃) ₂	H	H	2-CN
181	CH ₃	H	H	CH(CH ₃) ₂	H	H	3-CN
182	CH ₃	H	H	CH(CH ₃) ₂	H	H	4-CN
183	CH ₃	H	H	CH(CH ₃) ₂	H	H	2-SCH ₃
184	CH ₃	H	H	CH(CH ₃) ₂	H	H	3-SCH ₃
185	CH ₃	H	H	CH(CH ₃) ₂	H	H	4-SCH ₃
186	CH ₃	H	H	CH(CH ₃) ₂	F	F	—
187	CH ₃	H	H	CH(CH ₃) ₂	CH ₃	CH ₃	—
188	CH ₃	H	H	CH(CH ₃) ₂	cyclopropyl		—
189	CH ₃	H	H	CF ₃	H	H	2-F
190	CH ₃	H	H	CF ₃	H	H	3-F
191	CH ₃	H	H	CF ₃	H	H	4-F

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
192	CH ₃	H	H	CF ₃	H	H	2-Cl
193	CH ₃	H	H	CF ₃	H	H	3-Cl
194	CH ₃	H	H	CF ₃	H	H	4-Cl
195	CH ₃	H	H	CF ₃	H	H	2-CH ₃
196	CH ₃	H	H	CF ₃	H	H	3-CH ₃
197	CH ₃	H	H	CF ₃	H	H	4-CH ₃
198	CH ₃	H	H	CF ₃	H	H	2-CN
199	CH ₃	H	H	CF ₃	H	H	3-CN
200	CH ₃	H	H	CF ₃	H	H	4-CN
201	CH ₃	H	H	CF ₃	H	H	2-SCH ₃
202	CH ₃	H	H	CF ₃	H	H	3-SCH ₃
203	CH ₃	H	H	CF ₃	H	H	4-SCH ₃
204	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	2-F
205	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	3-F
206	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	4-F
207	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	2-Cl
208	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	3-Cl
209	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	4-Cl
210	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	2-CH ₃
211	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	3-CH ₃
212	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	4-CH ₃
213	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	2-CN
214	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	3-CN
215	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	4-CN
216	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	2-SCH ₃
217	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	3-SCH ₃
218	CH ₃	H	H	C(CH ₃)=CH ₂	H	H	4-SCH ₃
219	CH ₃	H	H	CF(CH ₃) ₂	H	H	2-F
220	CH ₃	H	H	CF(CH ₃) ₂	H	H	3-F
221	CH ₃	H	H	CF(CH ₃) ₂	H	H	4-F
222	CH ₃	H	H	CF(CH ₃) ₂	H	H	2-Cl
223	CH ₃	H	H	CF(CH ₃) ₂	H	H	3-Cl
224	CH ₃	H	H	CF(CH ₃) ₂	H	H	4-Cl
225	CH ₃	H	H	CF(CH ₃) ₂	H	H	2-CH ₃
226	CH ₃	H	H	CF(CH ₃) ₂	H	H	3-CH ₃
227	CH ₃	H	H	CF(CH ₃) ₂	H	H	4-CH ₃

Entry	R ₄	R ₅	R ₆	R ₇	R ₈	R ₉	R ₁₀
228	CH ₃	H	H	CF(CH ₃) ₂	H	H	2-CN
229	CH ₃	H	H	CF(CH ₃) ₂	H	H	3-CN
230	CH ₃	H	H	CF(CH ₃) ₂	H	H	4-CN
231	CH ₃	H	H	CF(CH ₃) ₂	H	H	2-SCH ₃
232	CH ₃	H	H	CF(CH ₃) ₂	H	H	3-SCH ₃
233	CH ₃	H	H	CF(CH ₃) ₂	H	H	4-SCH ₃
234	CH ₃	H	H	CF ₂ CH ₃	H	H	2-F
235	CH ₃	H	H	CF ₂ CH ₃	H	H	3-F
236	CH ₃	H	H	CF ₂ CH ₃	H	H	4-F
237	CH ₃	H	H	CF ₂ CH ₃	H	H	2-Cl
238	CH ₃	H	H	CF ₂ CH ₃	H	H	3-Cl
239	CH ₃	H	H	CF ₂ CH ₃	H	H	4-Cl
240	CH ₃	H	H	CF ₂ CH ₃	H	H	2-CH ₃
241	CH ₃	H	H	CF ₂ CH ₃	H	H	3-CH ₃
242	CH ₃	H	H	CF ₂ CH ₃	H	H	4-CH ₃
243	CH ₃	H	H	CF ₂ CH ₃	H	H	2-CN
244	CH ₃	H	H	CF ₂ CH ₃	H	H	3-CN
245	CH ₃	H	H	CF ₂ CH ₃	H	H	4-CN
246	CH ₃	H	H	CF ₂ CH ₃	H	H	2-SCH ₃
247	CH ₃	H	H	CF ₂ CH ₃	H	H	3-SCH ₃
248	CH ₃	H	H	CF ₂ CH ₃	H	H	4-SCH ₃

Table A2 provides 248 compounds of formula (I-a) wherein R₁₁, R₁₂, R₁₃ are all H,

- 5 R₁ is fluoro, R₂ and R₃ are H and wherein the values of R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ are as defined in Table Z above.

Table A3 provides 248 compounds of formula (I-a) wherein R₁₁, R₁₂, R₁₃ are all H, R₁ is chloro, R₂ and R₃ are H and wherein the values of R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ are as defined in Table Z above.

- 10 Table A4 provides 248 compounds of formula (I-a) wherein R₁₁, R₁₂, R₁₃ are all H, R₁ is bromo, R₂ and R₃ are H and wherein the values of R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ are as defined in Table Z above.

Table A5 provides 248 compounds of formula (I-a) wherein R₁₁, R₁₂, R₁₃ are all H, R₁ is methyl, R₂ and R₃ are H and wherein the values of R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ are as

- 15 defined in Table Z above.

Table A6 provides 248 compounds of formula (I-a) wherein R_{11} , R_{12} , R_{13} are all H, R_1 is cyano, R_2 and R_3 are H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A7 provides 248 compounds of formula (I-a) wherein R_{11} is fluoro, R_1 is H, R_2 and R_3 are H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A8 provides 248 compounds of formula (I-a) wherein R_{11} , R_{12} , R_{13} are all H, R_2 is methyl, R_1 and R_3 are H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

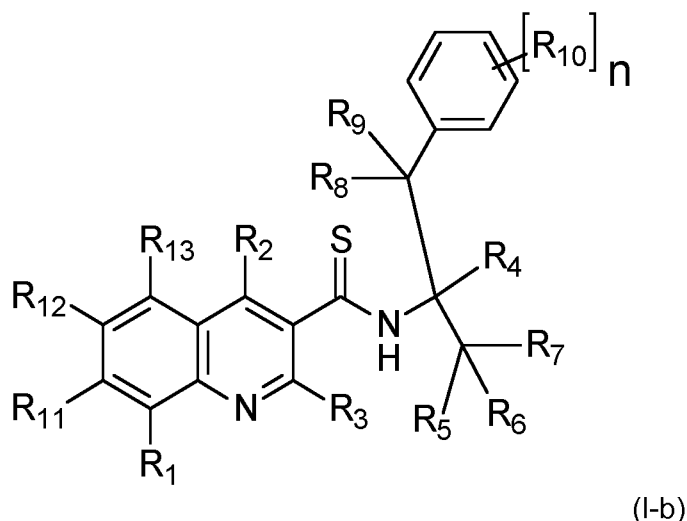
Table A9 provides 248 compounds of formula (I-a) wherein R_{11} , R_{12} , R_{13} are all H, R_3 is methyl, R_1 and R_2 are H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A10 provides 248 compounds of formula (I-a) wherein R_{11} , R_{12} , R_{13} are all H, R_2 is methyl, R_1 is fluoro and R_3 is H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A11 provides 248 compounds of formula (I-a) wherein R_{11} , R_{12} , R_{13} are all H, R_3 is methyl, R_1 is fluoro and R_2 is H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A12 provides 248 compounds of formula (I-a) wherein R_{12} , R_{13} are H, R_2 and R_3 are H, R_1 and R_{11} are fluoro, and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A13 provides 248 compounds of formula (I-b)



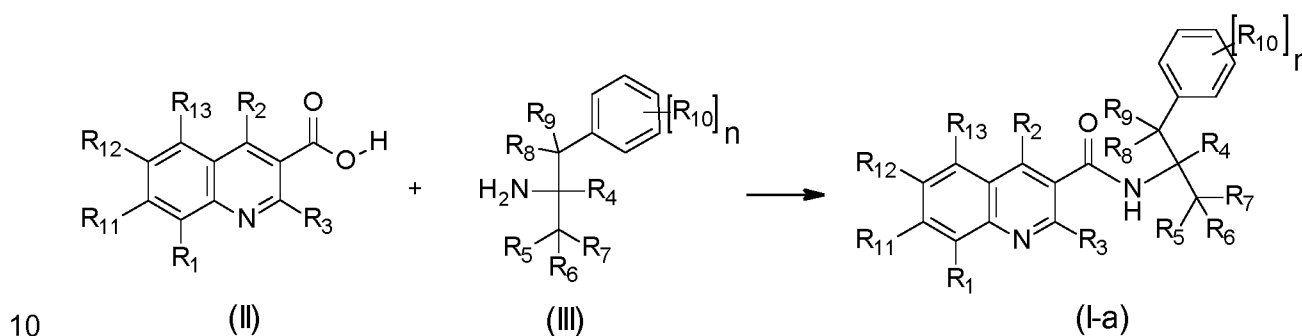
wherein R_{11} , R_{12} , R_{13} , R_1 , R_2 and R_3 are all H

and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Table A14 provides 248 compounds of formula (I-b) wherein R_1 is fluoro, R_{11} , R_{12} , R_{13} , R_2 and R_3 are H and wherein the values of R_4 , R_5 , R_6 , R_7 , R_8 , R_9 and R_{10} are as defined in Table Z above.

Compounds of the present invention can be made as shown in the following schemes, in which, unless otherwise stated, the definition of each variable is as defined above for a compound of formula (I).

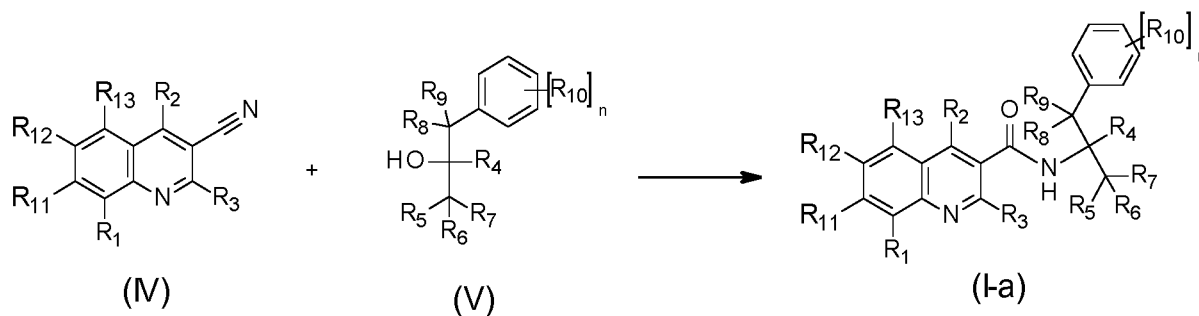
- 5 A shown in scheme 1, compounds of general formula (I-a) wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} and n are as defined for compounds of formula (I) and X is O can be prepared by the reaction of compounds of formula (II) wherein R_1 , R_2 , R_3 , R_{11} , R_{12} and R_{13} are as defined for compounds of formula (I) with amines of formula (III) wherein R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} and n are as defined for compounds of formula (I).



Scheme 1

- Among the various reported methods for this transformation, the most widely applied involve treatment of carboxylic acid (II) with an activating agent like thionyl chloride or an amide coupling reagent like dicyclohexylcarbodiimide in an inert organic solvent like tetrahydrofuran (THF) or dimethylformamide (DMF) and reaction with amine (III) in the presence of a catalyst like dimethylaminopyridine as described in *Chem. Soc. Rev.*, **2009**, 606-631 or *Tetrahedron* **2005**, 10827–10852.
- 15

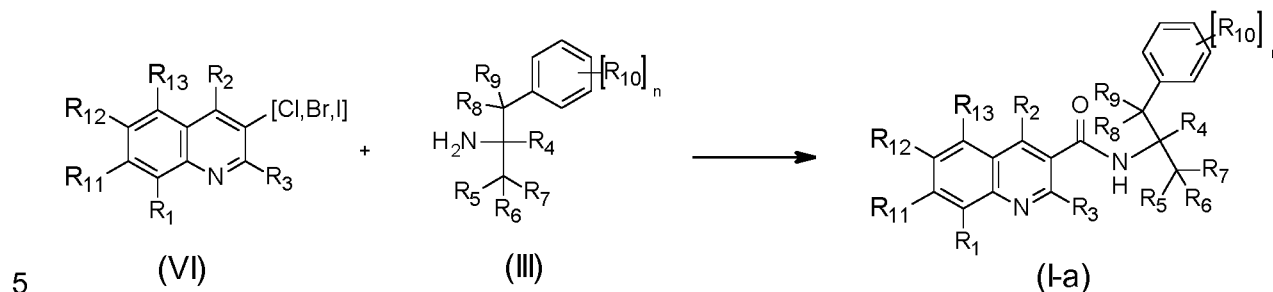
- As shown in scheme 2, compounds of general formula (I-a) wherein X is O can also be prepared by the reaction of compounds of formula (IV) and (V) in the presence of a Brönsted acid like sulphuric acid or trifluoromethane sulfonic acid, in a solvent like dichloromethane or acetic acid at temperatures between $-20\text{ }^{\circ}\text{C}$ and $+50\text{ }^{\circ}\text{C}$ as described in *Eur. J. Org. Chem.* **2015**, 2727–2732 and *Synthesis* **2000**, 1709–1712.
- 20



Scheme 2

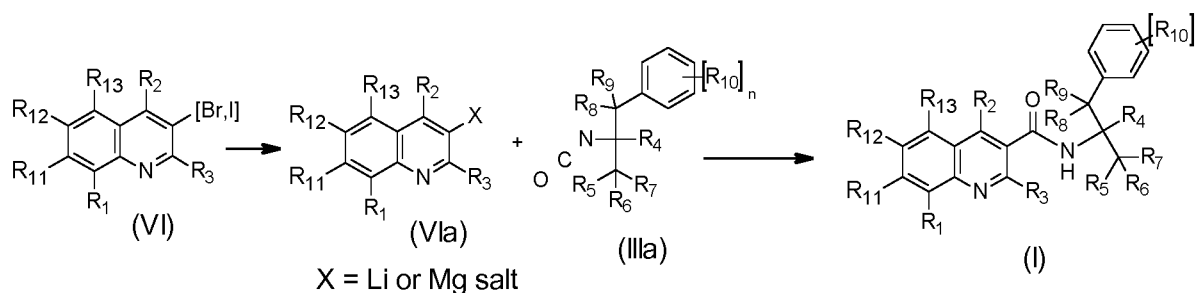
- 25 Alternatively, compounds of general formula (I-a) wherein X is O can also be prepared by the reaction of compounds of formula (VI) with amines of formula (III), carbon monoxide, a

base like triethylamine or potassium carbonate and a suitably supported transitional metal catalyst like palladium in an inert organic solvent like 1,4-dioxane at a temperature between 20 °C and 110 °C as described in *Org. Lett.*, **2014**, 4296–4299 (and references therein) and shown in scheme 3.



Scheme 3

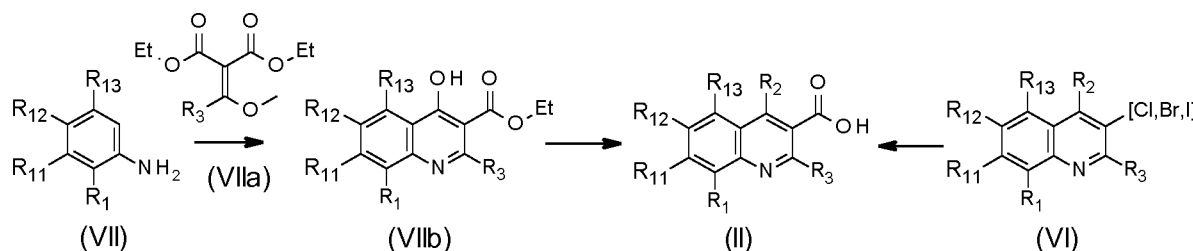
Alternatively, compounds of general formula (I-a) wherein X is O can also be prepared by the reaction of organometallic compounds of formula (VIa) with isocyanates of formula (IIIa) in an inert organic solvent like diethyl ether or THF at temperatures between -78 °C and +40 °C as described in *Angew. Chem. Int. Ed.* **2012**, 9173 –9175 and shown in scheme 4.



Scheme 4

The preparation of organometallic compounds of formula (VIa) from compounds of formula (VI) by lithium-halogen exchange with an alkyl lithium reagent like s-butyl lithium or magnesium-halogen exchange with tri n-butyl magnesate in an ethereal solvent like THF at temperatures between -90 °C and +20 °C is generally known to a person skilled in the art, and is described in synthetic chemistry texts such as *March's Advanced Organic Chemistry*.

As shown in scheme 5, carboxylic acids of formula (II) can be prepared by various methods and many are commercially available. Among the many reported methods for their preparation, the following have been widely applied:



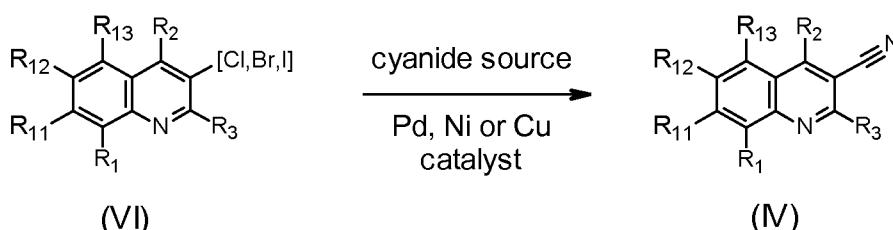
Scheme 5

1) Transformation of anilines of formula (VII) to quinolones of formula (VIIb) by reaction with a malonate derivative of formula (VIIa) in an inert solvent like diphenyl ether at temperatures between 100 °C and 260 °C as described in *US 20070015758*, followed by well-known functional group interconversion which is generally known to a person skilled in the art and also described in WO 2007133637.

2) Transformation of compounds of formula (VI) to organometallic intermediates of formula (VIa) by lithium-halogen exchange with an alkyl lithium reagent like s-butyl lithium or magnesium-halogen exchange with tri n-butyl magnesate in an ethereal solvent like THF at temperatures between -90 °C and +20 °C and subsequent reaction with CO₂.

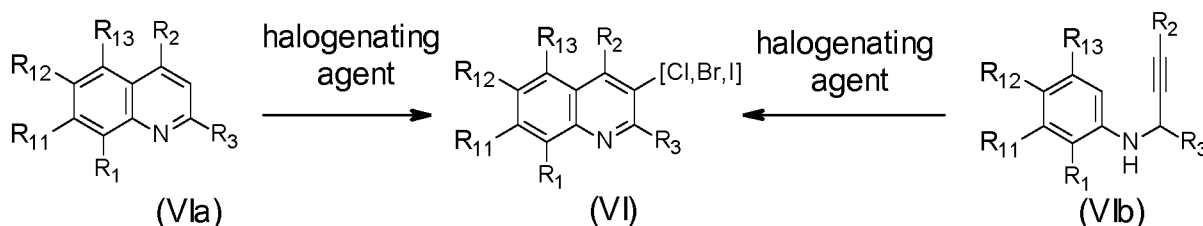
3) Transformation of compounds of formula (VI) in the presence of a carbon monoxide source, a base like triethylamine, water or an equivalent thereof and a suitably ligated transition metal catalyst containing for example palladium as described in *J. Am. Chem. Soc.* **2013**, 2891-2894 (and references therein) or *Tetrahedron* **2003**, 8629-8640.

As shown in scheme 6, compounds of formula (IV) can be prepared from compounds of formula (VI) by treatment with a cyanide source like zinc cyanide in the presence of a palladium, nickel or copper catalyst in an inert solvent like DMF at temperatures between 20 °C and 150 °C as described in *J. Org. Chem.* **2011**, 665-668 or *Bull. Chem. Soc. Jpn.* **1993**, 2776-8.



Scheme 6

As shown in scheme 7, compounds of formula (VI) can be prepared by treatment of compounds of formula (VIa) with a halogenating agent like N-iodosuccinimide, bromine or chlorine in an inert solvent as described in WO 2005113539 or JP 2001322979. Alternatively, compounds of formula (VI) can be prepared by treatment of propargylated anilines of formula (VIb) with a halogenating agent like iodine in an inert solvent like acetonitrile and a base like sodium hydrogen carbonate at temperatures between 0 °C and 80 °C as described in *Org. Lett.* **2005**, 763-766.

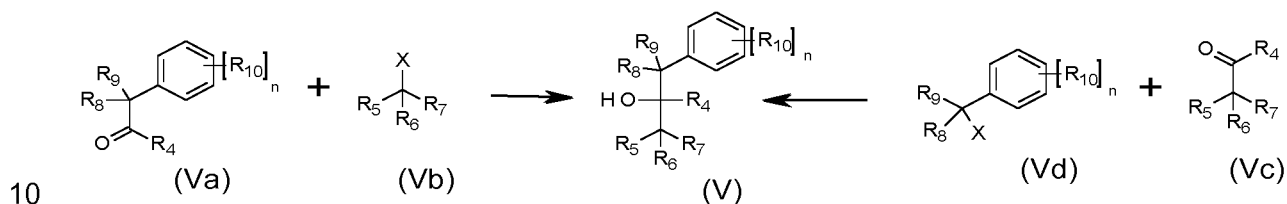


Scheme 7.

The preparation of propargylated anilines of formula (VIb) from the corresponding commercially available anilines is trivial to a person skilled in the art and described in *March's Advanced Organic Chemistry*, Smith and March, 6th edition, Wiley, 2007.

The synthesis of compounds of formula (VIa) is generally known to a person skilled in the art and a large selection of compounds is commercially available.

As shown in scheme 8, compounds of formula (V) can be prepared from carbonyl compounds of formula (Va) or (Vc) by treatment with an organometallic species of formula (Vb) or (Vd) respectively where X is lithium, an aluminum- or a magnesium-salt, in an inert solvent like diethyl ether at temperatures between -90 °C and 60 °C.

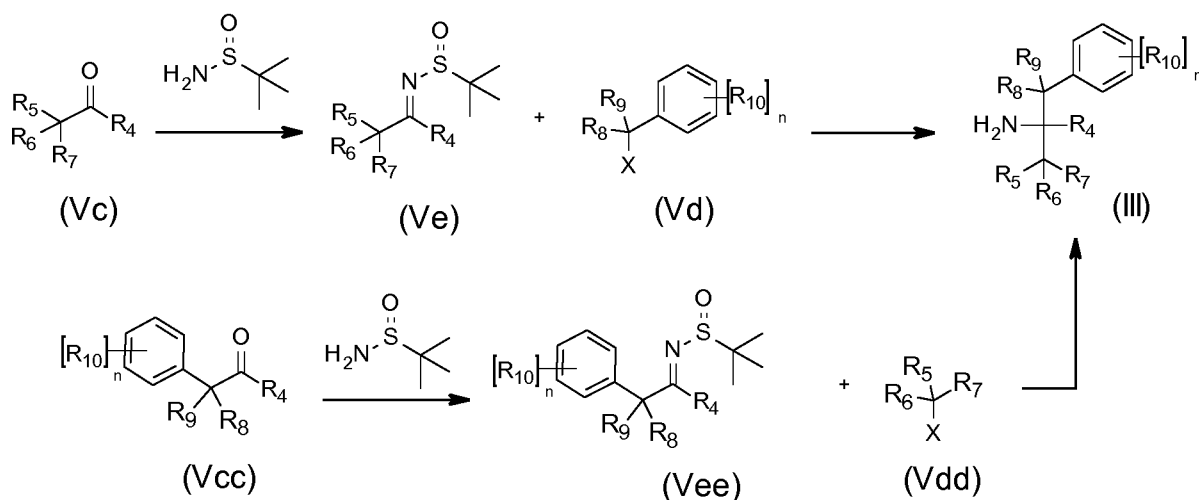


Scheme 8

The general preparation, handling and reactivity of reagents with formula (Vb) and (Vd) is described in *March's Advanced Organic Chemistry*, Smith and March, 6th edition, Wiley, 2007 and is generally known to a person skilled in the art. A large selection of compounds of formula (Va) and (Vc), where R₄, R₅, R₆, R₇, R₈, R₉ and R₁₀ as defined in the above, are also commercially available and their syntheses are well described in the scientific literature and synthetic chemistry text (such as *March's Advanced Organic Chemistry*) and, further, are generally known to a person skilled in the art.

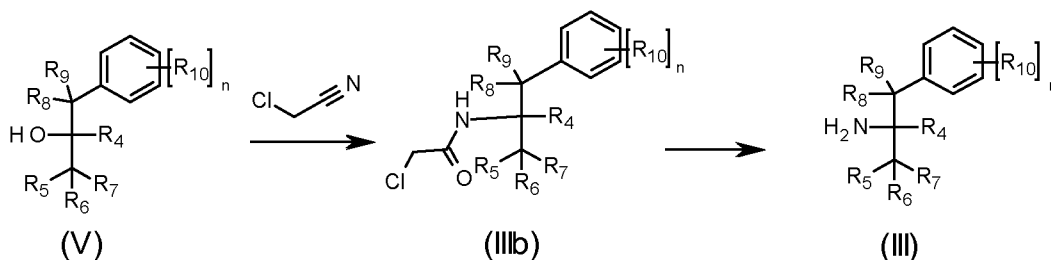
As shown in scheme 9, amines of formula (III) can be prepared from compounds of formula (Vc) by condensation with tertbutyl sulfinamide in the presence of a dehydrating agent like Ti(OEt)₄ to form sulfinamines of formula (Ve) which can then be treated with an organometallic reagent of formula (Vd), where X is lithium, an aluminum- or a magnesium-salt, in an inert solvent like THF at temperatures between -78 °C and + 70 °C, followed by an acidic hydrolysis of the sulfonamide; a sequence generally known to a person skilled in the art and also described in *Chem. Rev.* **2010**, 3600–3740.

Alternatively, amines of formula (III) can be prepared from compounds of formula (Vcc) by condensation with tertbutyl sulfinamide in the presence of a dehydrating agent like Ti(OEt)₄ to form sulfinamines of formula (Vee) which can then be treated with an organometallic reagent of formula (Vdd), where X is lithium, an aluminum- or a magnesium-salt, in an inert solvent like THF at temperatures between -78 °C and + 70 °C, followed by an acidic hydrolysis of the sulfonamide.



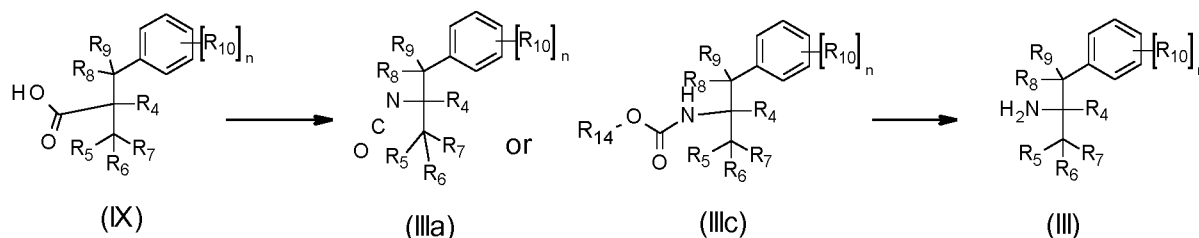
Scheme 9

Alternatively, amines of formula (III) can be also prepared from alcohols of formula (V) by treatment with a strong acid like sulfuric acid in the presence of chloroacetonitrile in an organic solvent like acetic acid at temperatures between -10 °C and 50 °C to give amides of formula (IIIb) which can be deprotected with thiourea in an organic solvent like ethanol or acetic acid at temperatures between 20 °C and 100 °C as described in *Synthesis* **2000**, 1709 – 1712 and shown in scheme 10.



Scheme 10

Alternatively, amines of formula (III) can be also prepared from carboxylic acids of formula (IX) through an intermediary isocyanate of formula (IIIa) or a carbamate of formula (IIIc), where R₁₄ is C₁-C₄ alkyl, which can be hydrolyzed with aqueous acid or base at temperatures between 0 °C and 100 °C as shown in scheme 11.



Scheme 11

Among the various protocols reported for the transformation of acid (IX) to isocyanate (IIIa), the following have found wide spread application:

1) Treatment of acid (IX) with diphenylphosphoryl azide and an amine base like tributylamine in an inert organic solvent like toluene at temperatures between 50 °C and 120 °C to give isocyanate (IIIa) as described in *Aust. J. Chem.*, **1973**, 1591-3.

2) Treatment of acid (IX) with an activating agent like thionyl chloride or propylphosphonic anhydride in the presence of an azide source like sodium azide and an amine base like triethyl amine in an inert solvent like THF at temperatures between 20 °C and 100 °C as described in *Synthesis* **2011**, 1477–1483.

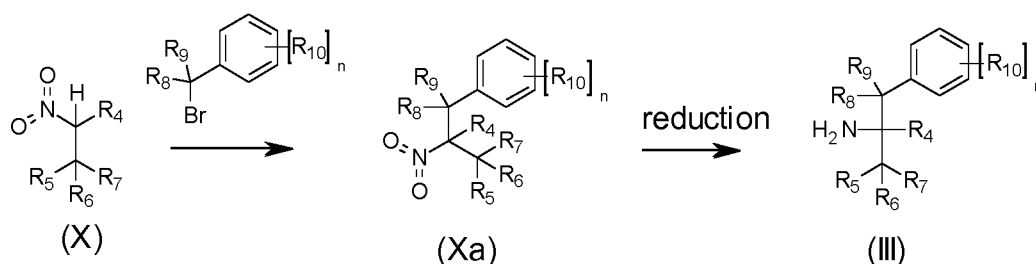
3) Conversion of acid (IX) to the corresponding hydroxamic acids which can then be treated with a dehydrating agent like para-toluenesulfonyl chloride and a base like triethylamine in an inert organic solvent like toluene at temperatures between 20 °C and 120 °C.

4) Conversion of acid (IX) to the corresponding primary carboxamide which can then be treated with an oxidizing agent such as diacetoxyiodobenzene and an acid such as trifluoroacetic acid or para-toluenesulfonic acid in a solvent like acetonitrile at temperatures between 0 °C and 100 °C as described in *J. Org. Chem.* **1984**, 4212-4216.

5) Conversion of acid (IX) to the corresponding primary carboxamide which can then be treated with an oxidizing agent such as bromine and a base such as sodium hydroxide in a solvent like water or methanol at temperatures between 0 °C and 100 °C.

A person skilled in the art will appreciate that carboxylic acids of formula (IX) can be prepared from the corresponding esters. Similarly a person skilled in the art will appreciate that the *alpha* position of these esters can be functionalized by deprotonation with a strong base like lithium diisopropylamine in an inert solvent like THF at temperatures between -78 °C and 20 °C followed by reaction with an electrophilic reagent like an alkyl iodide as described in *March's Advanced Organic Chemistry*, Smith and March, 6th edition, Wiley, 2007. This reaction can be repeated to prepare acids of formula (IX) from commercially available esters.

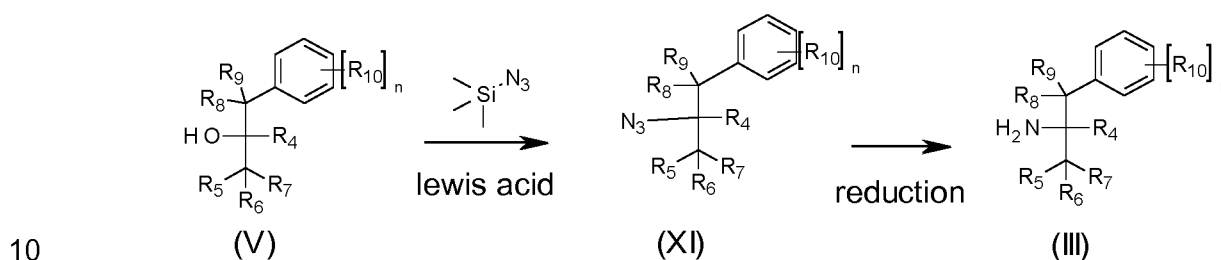
Alternatively, amines of formula (III) can be also prepared by reduction of nitro compounds of formula (Xa) with a reducing agent like iron in an organic solvent like acetic acid at temperatures between 20 °C and 120 °C as shown in scheme 12. Nitro compounds of formula (Xa) in turn can be prepared from simpler nitro compounds of formula (X) by treatment with a benzyl bromide and a base like sodium tert-butoxide in the presence of a copper catalyst in an inert solvent like hexanes at temperatures between 20 °C and 100 °C as described in *J. Am. Chem. Soc.* **2012**, 9942–9945.



Scheme 12

The synthesis of compounds of formula (X) is generally known to a person skilled in the art and a large selection is commercially available.

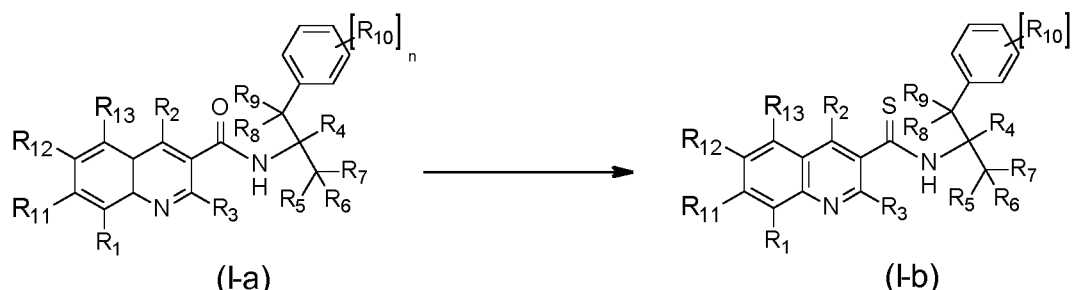
Alternatively, amines of formula (III) can be also prepared by treatment of compounds of formula (V) with trimethylsilyl azide and a lewis acid catalyst like $B(C_6F_5)_3$ in an inert solvent like toluene at temperatures between 0 °C and 100 °C as described in *J. Am. Chem. Soc.* **2015**, 9555–9558, followed by reduction of the intermediary azides of formula (XI) with a reducing agent like hydrogen/palladium in an organic solvent like methanol at temperatures between 0 °C and 80 °C as shown in scheme 13.



Scheme 13

As shown in scheme 14, compounds of general formula (I-b) wherein X is S can be prepared from compounds of general formula (I-a) wherein X is O by treatment with a deoxygenating agent like P_4S_{10} or Lawesson reagent in an inert organic solvent like toluene at temperatures between 20 °C and 150 °C.

15

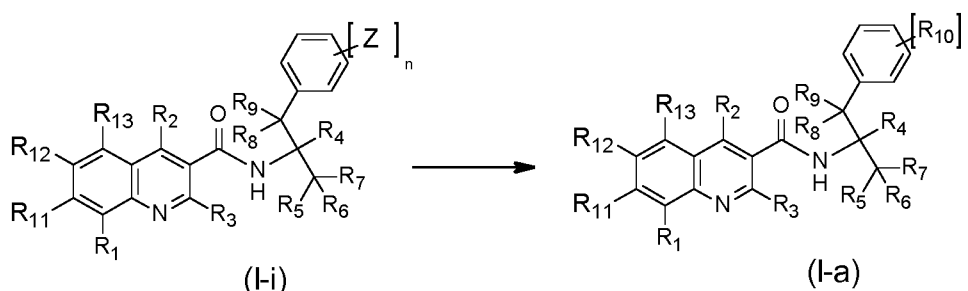


Scheme 14

Alternatively, the compounds of formula (I-a), wherein wherein $R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}$ and n are as defined for compounds of formula (I) and X is O, can be obtained by transformation of a compound of formula I-i, wherein $R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{11}, R_{12}, R_{13}$ and n are as defined for formula (I) and X is O and Z represents chlorine, bromine or iodine in a solvent, in the presence of or absence of a base, and in the presence of a coupling reagent and a metal catalyst. There are no particular limitations on the coupling agent, catalyst, solvent and bases, provided it is used in ordinary coupling reactions, such as those described in “Cross-Coupling Reactions: A Practical Guide (Topics in Current Chemistry)”, edited by Norio Miyaura und S.L. Buchwald (editions Springer), or “Metal-Catalyzed Cross-Coupling Reactions”, edited by Armin de Meijere and François Diederich (editions WILEY-VCH). This is shown in Scheme 15.

20

25



Scheme 15

- Alternatively, the compounds of formula (I-a) wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} and n are as defined for compounds of formula (I) and X is O, can be obtained by transformation of another, closely related, compound of formula (I-a) 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, and halogenation reactions.

Certain intermediates described in the above schemes are novel and as such form a further aspect of the invention.

- The compounds of formula (I) can be used in the agricultural sector and related fields of use e.g. as active ingredients for controlling plant pests 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) can be used to inhibit or destroy the pests 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.

- It is also possible to use compounds of formula (I) 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 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) before planting: seed, for example, can be dressed before being sown. The compounds of formula (I) 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 according to 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) 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. lusitaniae*, *C. parapsilosis*, *C. tropicalis*, *Cephalosporium fragrans*, *Ceratocystis* spp, *Cercospora* spp. including *C. arachidicola*, *Cercosporidium personatum*, *Cladosporium* spp, *Claviceps purpurea*, *Coccidioides immitis*, *Cochliobolus* spp, *Colletotrichum* spp. including *C. musae*, *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*, *Gymnosporangium juniperi-virginianae*, *Helminthosporium* spp, *Hemileia* spp, *Histoplasma* spp. including *H. capsulatum*, *Laetisaria fuciformis*, *Leptographium lindbergii*, *Leveillula taurica*, *Lophodermium seeditiosum*, *Microdochium nivale*,

- Microsporium 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, *Peronosclerospora* spp. Including *P. maydis*, *P. philippinensis* and *P. sorghi*, *Peronospora* spp, *Phaeosphaeria*
- 5 *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. cubensis*, *P. humuli*, *Pseudopeziza tracheiphila*,
- 10 *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*, *Sclerotinia* spp, *Sclerotium* spp, *Septoria* spp, including *S. nodorum*, *S. tritici*,
- 15 *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,
- 20 *Venturia* spp. including *V. inaequalis*, *Verticillium* spp, and *Xanthomonas* spp.

In particular, compounds of formula (I) 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, Chytridiomycete, Glomeromycete and/or Mucoromycete classes.

- 25 These pathogens may include:

- Oomycetes, including *Phytophthora* diseases such as those caused by *Phytophthora capsici*, *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*
- 30 *aphanidermatum*, *Pythium arrhenomanes*, *Pythium graminicola*, *Pythium irregulare* 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*, *Labyrinthula zosterae*, *Peronosclerospora sorghi* and
- 35 *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*, *Ophiobolus graminis*, *Leptosphaeria maculans*, *Hendersonia creberrima*, *Helminthosporium tritici-repentis*, *Setosphaeria turcica*, *Drechslera glycines*,
- 5 *Didymella bryoniae*, *Cycloconium oleagineum*, *Corynespora cassiicola*, *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*, *Cercospora arachidicola*, *Cercospora soja*, *Cercospora zeae-maydis*, *Cercospora capsellae* and
- 10 *Cercospora herpotrichoides*, *Cladosporium carpophilum*, *Cladosporium effusum*, *Passalora fulva*, *Cladosporium oxysporum*, *Dothistroma septosporum*, *Isariopsis clavispora*, *Mycosphaerella fijiensis*, *Mycosphaerella graminicola*, *Mycovellosiella koepkei*, *Phaeoisariopsis bataticola*, *Pseudocercospora vitis*, *Pseudocercospora herpotrichoides*, *Ramularia beticola*, *Ramularia collo-cygni*, Magnaporthales such as *Gaeumannomyces*
- 15 *graminis*, *Magnaporthe grisea*, *Pyricularia oryzae*, Diaporthales such as *Anisogramma anomala*, *Apiognomonia errabunda*, *Cytospora platani*, *Diaporthe phaseolorum*, *Discula destructiva*, *Gnomonia fructicola*, *Greenaria uvicola*, *Melanconium juglandinum*, *Phomopsis viticola*, *Sirococcus clavigignenti-juglandacearum*, *Tubakia dryina*, *Dicarpella* spp., *Valsa ceratosperma*, and others such as *Actinothyrium graminis*, *Ascochyta pisi*, *Aspergillus flavus*,
- 20 *Aspergillus fumigatus*, *Aspergillus nidulans*, *Asperisporium caricae*, *Blumeriella jaapii*, *Candida* spp., *Capnodium ramosum*, *Cephaloascus* spp., *Cephalosporium gramineum*, *Ceratocystis paradoxa*, *Chaetomium* spp., *Hymenoscyphus pseudoalbidus*, *Coccidioides* spp., *Cylindrosporium padi*, *Diplocarpon malae*, *Drepanopeziza campestris*, *Elsinoe ampelina*, *Epicoccum nigrum*, *Epidermophyton* spp., *Eutypa lata*, *Geotrichum candidum*,
- 25 *Gibellina cerealis*, *Gloeocercospora sorghi*, *Gloeodes pomigena*, *Gloeosporium perennans*; *Gloeotinia temulenta*, *Griphosphaeria corticola*, *Kabatiella lini*, *Leptographium microsporum*, *Leptosphaerulina crassiasca*, *Lophodermium seeditiosum*, *Marssonina graminicola*, *Microdochium nivale*, *Monilinia fructicola*, *Monographella albescens*, *Monosporascus cannonballus*, *Naemacyclus* spp., *Ophiostoma novo-ulmi*, *Paracoccidioides brasiliensis*,
- 30 *Penicillium expansum*, *Pestalotia rhododendri*, *Petriellidium* spp., *Pezicula* spp., *Phialophora gregata*, *Phyllachora pomigena*, *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*
- 35 *sclerotiorum*, *Sclerotinia minor*, *Sclerotium* spp., *Typhula ishikariensis*, *Seimatosporium mariae*, *Lepteutypa cupressi*, *Septocytia ruborum*, *Sphaceloma perseae*, *Sporonema phacidoides*, *Stigmina 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 fuliginea*, *Podosphaera leucotricha*, *Podosphaera macularis*, *Golovinomyces cichoracearum*, *Leveillula taurica*, *Microsphaera diffusa*, *Oidiopsis gossypii*,
- 5 *Phyllactinia guttata* and *Oidium arachidis*; molds for example those caused by Botryosphaeriales such as *Dothiorella aromatica*, *Diplodia seriata*, *Guignardia bidwellii*, *Botrytis cinerea*, *Botryotinia allii*, *Botryotinia fabae*, *Fusicoccum amygdali*, *Lasiodiplodia theobromae*, *Macrophoma theicola*, *Macrophomina phaseolina*, *Phyllosticta cucurbitacearum*; anthracnoses for example those caused by Glomerellales such as
- 10 *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 subglutinans*, *Fusarium oxysporum* f.sp. *cubense*, *Gerlachia nivale*, *Gibberella fujikuroi*,
- 15 *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 *Ustilaginoidea virens*, *Ustilago nuda*, *Ustilago tritici*, *Ustilago zeae*, rusts for example those caused by Pucciniales such as *Cerotelium fici*, *Chrysomyxa arctostaphyli*, *Coleosporium*
- 20 *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 ampelosidis*, *Tranzschelia discolor* and
- 25 *Uromyces 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*, *Itersonilia perplexans*, *Corticium invisum*, *Laetisaria fuciformis*, *Waitea circinata*, *Rhizoctonia solani*, *Thanetophorus cucurmeris*, *Entyloma dahliae*, *Entylomella microspora*, *Neovossia molinae* and *Tilletia caries*.

- 30 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.

- 35 In addition to their fungicidal activity, the compounds and compositions comprising them may also have activity against bacteria such as *Erwinia amylovora*, *Erwinia caratovora*,

Xanthomonas campestris, *Pseudomonas syringae*, *Strptomyces scabies* and other related species as well as certain protozoa.

Within the scope of present invention, target crops and/or useful plants to be protected typically comprise perennial and annual crops, such as berry plants for example
5 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, nectarine, peach, pear
10 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
15 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, potato, pumpkin, rhubarb, spinach and tomato; and vines for example grapes.

The useful plants and / or target crops in accordance with the invention include
20 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 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
25 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 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)
30 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, 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
35 genetic engineering methods include glyphosate- and glufosinate-resistant maize varieties commercially available under the trade names RoundupReady® , Herculex I® and LibertyLink®.

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 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 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 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 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 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, 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 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
5 Cry9C, or vegetative insecticidal proteins (Vip), for example Vip1, Vip2, Vip3 or Vip3A, expressly also hybrid toxins, truncated toxins and modified 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
10 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-recognition sequence is inserted into a Cry3A toxin (see WO03/018810).

More examples of such toxins or transgenic plants capable of synthesising such
15 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.

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
20 WO 95/34656, EP-A-0 367 474, EP-A-0 401 979 and WO 90/13651.

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).

25 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
30 variety that expresses a Cry9C toxin); Herculex I® (maize variety that 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
35 a Vip3A and a Cry1Ab toxin); NewLeaf® (potato variety that expresses a Cry3A toxin); NatureGard®, Agrisure® GT 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, 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, 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, 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, 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, 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.

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.

The term "plants" refers to all physical parts of a plant, including seeds, seedlings, 5 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. 10 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.

Pesticidal agents referred to herein using their common name are known, for 15 example, from "The Pesticide Manual", 15th Ed., British Crop Protection Council 2009.

The compounds of formula (I) 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 20 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. The compositions may also contain further adjuvants such as stabilizers, antifoams, viscosity regulators, binders or 25 tackifiers as well as fertilizers, micronutrient donors or other formulations for obtaining special effects.

Suitable carriers and 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 30 carriers are for example described in WO 97/33890.

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 35 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.

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

5 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.

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

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, diacetonolcohol, 1,2-dichloropropane, diethanolamine,
15 p-diethylbenzene, diethylene glycol, diethylene glycol abietate, diethylene glycol butyl ether, diethylene glycol ethyl ether, diethylene glycol methyl ether, N,N-dimethyl 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
20 glycol, ethylene glycol butyl ether, ethylene glycol methyl ether, gamma-butyrolactone, glycerol, glycerol diacetate, glycerol monoacetate, glycerol triacetate, hexadecane, hexylene glycol, isoamyl acetate, isobornyl 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
25 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, triethylene glycol, xylene sulfonic acid, paraffin, mineral oil, trichloroethylene, perchloroethylene, ethyl acetate, amyl acetate, butyl acetate, methanol, ethanol, isopropanol, and higher molecular
30 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.

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

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 ethoxylate; alcohol-alkylene oxide addition products, such as tridecyl alcohol-C.sub. 16 ethoxylate; soaps, such as sodium stearate; alkyl naphthalenesulfonate salts, such as sodium dibutyl naphthalenesulfonate; 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 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-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 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 and/or plant growth regulators.

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 acibenzolar-S-methyl.

The compounds of formula (I) 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 preparations, which influence the growth of plants. They can also be selective herbicides or non-selective herbicides as well as insecticides, fungicides, bactericides,

nematicides, 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.

The compounds of formula (I) may be used in the form of (fungicidal) compositions for
5 controlling or protecting against phytopathogenic microorganisms, comprising as active ingredient at least one compound of formula (I) 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.

The invention therefore provides a composition, preferably a fungicidal composition,
10 comprising at least one compound formula (I) 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 comprise at least one or more pesticidally active compounds, for example an additional fungicidal active ingredient in addition to the compound of formula (I).

15 The compound of formula (I) may be the sole active ingredient of a composition or it may be admixed with one or more additional active ingredients such as a pesticide, fungicide, synergist, herbicide or plant growth regulator where appropriate. An additional active ingredient may, in some cases, result in unexpected synergistic activities.

Examples of suitable additional active ingredients include the following: 1,2,4-
20 thiadiazoles, 2,6-dinitroanilines, acylalanines, aliphatic nitrogenous compounds, amidines, aminopyrimidinols, anilides, anilino-pyrimidines, anthraquinones, antibiotics, aryl-phenylketones, benzamides, benzene-sulfonamides, benzimidazoles, benzothiazoles, benzothiadiazoles, benzothiophenes, benzoylpyridines, benzthiadiazoles, benzylcarbamates, butylamines, carbamates, carboxamides, carpropamids, chloronitriles, cinnamic acid amides,
25 copper containing compounds, cyanoacetamideoximes, cyanoacrylates, cyanoimidazoles, cyanomethylene-thiazolidines, dicarbonitriles, dicarboxamides, dicarboximides, dimethylsulphamates, dinitrophenol carbonates, dinitrophenyl, dinitrophenyl crotonates, diphenyl phosphates, dithiino compounds, dithiocarbamates, dithioethers, dithiolanes, ethyl-amino-thiazole carboxamides, ethyl-phosphonates, furan carboxamides, glucopyranosyls,
30 glucopyranoxyls, glutaronitriles, guanidines, herbicides/plant growth regulator, hexopyranosyl antibiotics, hydroxy(2-amino)pyrimidines, hydroxyanilides, hydroxyisoxazoles, imidazoles, imidazolinones, insecticides/plant growth regulators, isobenzofuranones, isoxazolidinyl-pyridines, isoxazolines, maleimides, mandelic acid amides, mectin derivatives, morpholines, norpholines, n-phenyl carbamates, organotin compounds, oxathiin
35 carboxamides, oxazoles, oxazolidine-diones, phenols, phenoxy quinolines, phenyl-acetamides, phenylamides, phenylbenzamides, phenyl-oxo-ethyl-thiophenes amides, phenylpyrroles, phenylureas, phosphorothiolates, phosphorus acids, phthalamic acids,

phthalimides, picolinamides, piperazines, piperidines, plant extracts, polyoxins, propionamides, pthalimides, pyrazole-4-carboxamides, pyrazolinones, pyridazinones, pyridines, pyridine carboxamides, pyridinyl-ethyl benzamides, pyrimdinamines, pyrimidines, pyrimidine-amines, pyrimidione-hydrazone, pyrrolidines, pyrrolquinoliones, quinazolinones, 5 quinolines, quinoline derivatives, quinoline-7-carboxylic acids, quinoxalines, spiroketalamines, strobilurins, sulfamoyl triazoles, sulphamides, tetrazolyloximes, thiadiazines, thiadiazole carboxamides, thiazole carboxanides, thiocyanates, thiophene carboxamides, toluamides, triazines, triazobenthiazoles, triazoles, triazole-thiones, triazolo-pyrimidylamine, valinamide carbamates, ammonium methyl phosphonates, arsenic- 10 containing compounds, benyimidazolylcarbamates, carbonitriles, carboxanilides, carboximidamides, carboxylic phenylamides, diphenyl pyridines, furanilides, hydrazine carboxamides, imidazoline acetates, isophthalates, isoxazolones, mercury salts, organomercury compounds, organophosphates, oxazolidinediones, pentylsulfonyl benzenes, phenyl benzamides, phosphonothionates, phosphorothioates, pyridyl carboxamides, pyridyl 15 furfuryl ethers, pyridyl methyl ethers, SDHIs, thiadiazinanethiones, thiazolidines..

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, 20 especially fungal organisms, which comprises the application of a compound of formula (I) 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 25 or spoilage 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, or insects which comprises the application of a compound of formula (I), or an agrochemical composition which contains 30 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) 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 solid form to the soil, e.g. in granular form (soil application). In 35 crops of water rice such granulates can be applied to the flooded rice field. The compounds of formula (I) 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.

A formulation, e.g. a composition containing the compound of formula (I), and, if desired, a solid or liquid adjuvant or monomers for encapsulating the compound of formula (I), 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).

The application methods for the compositions, that is the methods of controlling pests 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 pests of the abovementioned type are other subjects of the invention. 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.

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) according to the present invention is applied either preventative, meaning prior to disease development or curative, meaning after disease development.

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 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 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 inert (diluent, solvents, fillers and optionally other formulating ingredients such 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 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 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.

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) together with component (B) and (C), and optionally other active agents, particularly microbiocides or 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 use dilute formulations.

EXAMPLES

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, using lower application rates if necessary, for example 50 ppm, 12.5 ppm, 6 ppm, 3 ppm, 1.5 ppm, 0.8 ppm or 0.2 ppm.

Throughout this description, temperatures are given in degrees Celsius and "m.p." means melting point. LC/MS means Liquid Chromatography Mass Spectroscopy and the description of the apparatus and the methods are:

Method G:

Spectra were recorded on a Mass Spectrometer from Waters (SQD, SQDII Single quadrupole mass spectrometer) equipped with an electrospray source (Polarity: positive and negative ions), Capillary: 3.00 kV, Cone range: 30 V, Extractor: 2.00 V, Source Temperature: 150°C, Desolvation Temperature: 350°C, Cone Gas Flow: 50 l/h, Desolvation Gas Flow: 650 l/h, Mass range: 100 to 900 Da) and an Acquity UPLC from Waters: Binary pump, heated column compartment, diode-array detector and ELSD detector. Column: Waters UPLC HSS T3, 1.8 µm, 30 x 2.1 mm, Temp: 60 °C, DAD Wavelength range (nm): 210 to 500, Solvent Gradient: A = water + 5% MeOH + 0.05 % HCOOH, B= Acetonitrile + 0.05 % HCOOH, gradient: 10-100% B in 1.2 min; Flow (ml/min) 0.85

10

Method H:

Spectra were recorded on a Mass Spectrometer from Waters (SQD, SQDII Single quadrupole mass spectrometer) equipped with an electrospray source (Polarity: positive and negative ions), Capillary: 3.00 kV, Cone range: 30V, Extractor: 2.00 V, Source Temperature: 150°C, Desolvation Temperature: 350°C, Cone Gas Flow: 50 l/h, Desolvation Gas Flow: 650 l/h, Mass range: 100 to 900 Da) and an Acquity UPLC from Waters: Binary pump, heated column compartment, diode-array detector and ELSD detector. Column: Waters UPLC HSS T3, 1.8 µm, 30 x 2.1 mm, Temp: 60 °C, DAD Wavelength range (nm): 210 to 500, Solvent Gradient: A = water + 5% MeOH + 0.05 % HCOOH, B= Acetonitrile + 0.05 % HCOOH, gradient: 10-100% B in 2.7 min; Flow (ml/min) 0.85

20

Method W:

Spectra were recorded on a Mass Spectrometer (ACQUITY UPLC) from Waters (SQD, 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), DAD Wavelength range (nm): 210 to 400, and an Acquity UPLC from Waters: 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 500, 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

35 Formulation Examples

Wettable powders

a) b) c)

active ingredient [compound of formula (I)]	25 %	50 %	75 %
sodium lignosulfonate	5 %	5 %	-
sodium lauryl sulfate	3 %	-	5 %
sodium diisobutyl naphthalenesulfonate	-	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.

<u>Powders for dry seed treatment</u>	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

- 5 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 (4-5 mol of ethylene oxide)	3 %
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 %

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 %

- 5 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.
- 10

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
- 15

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 %
tristyrenephenole 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 %

5

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

10 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-
 15 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.

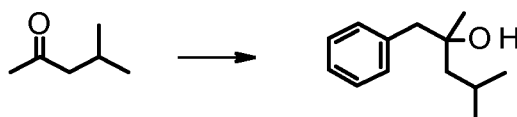
20 The obtained capsule suspension is stabilized by adding 0.25 parts of a thickener and 3 parts of a dispersing agent. The capsule suspension formulation contains 28% of the active ingredients. The medium capsule diameter is 8-15 microns.

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

25 Preparation examples

Example 1: Preparation of N-(1-benzyl-1,3-dimethyl-butyl)quinoline-3-carboxamide

Step 1: preparation of 2,4-dimethyl-1-phenyl-pentan-2-ol



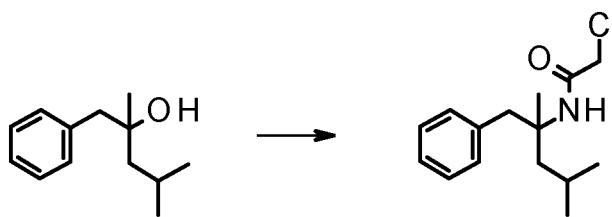
A solution of 4-methyl-2-pentanone (3.0 g, 29.4 mmol) in diethyl ether (25 mL) was added drop wise to benzyl magnesium chloride in tetrahydrofuran (2 M in tetrahydrofuran, 22 mL, 44 mmol) at RT. The reaction mixture was then warmed to 35 °C and aged for 3 h at this

5 temperature. After cooling to RT, aqueous HCl (2 M) was added to the reaction and the mixture was portioned between water and ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄, filtrated and concentrated in vacuo. The residue was purified by chromatography on silica gel to afford the title compound as colorless liquid.

¹H NMR (400 MHz, CDCl₃) δ 7.18-7.34 (m, 5H), 2.65-2.85 (m, 2H), 1.81-1.99 (m, 1H),

10 1.42 (dd, 2H), 1.15 (s, 3H), 0.98 (dd, 6H).

Step 2: preparation of N-(1-benzyl-1,3-dimethyl-butyl)-2-chloro-acetamide



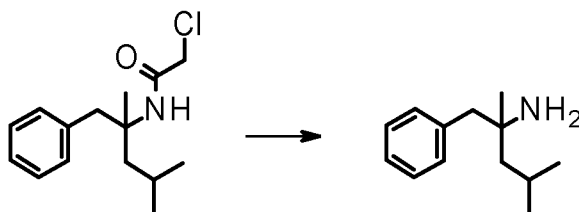
To a solution of 2,4-dimethyl-1-phenyl-pentan-2-ol (3.6 g, 19 mmol) and

15 chloroacetonitrile (2.4 mL, 37 mmol) in acetic acid (11 mL) cooled to 0-5 °C was added drop wise concentrated sulfuric acid (3.1 mL, 56 mmol). The resulting slurry was warmed to 20 °C and stirred for 3 h at this temperature. The reaction mixture was then diluted with water and extracted with ethyl acetate. The organic layer was washed with aqueous NaHCO₃, brine, dried over MgSO₄, filtrated and concentrated in vacuo. The residue was purified by

20 chromatography on silica gel to afford the title compound as colorless solid.

¹H NMR (400 MHz, CDCl₃) δ 7.20-7.34 (m, 3H), 7.08-7.16 (m, 2H), 6.13 (br. s., 1H), 3.94 (s, 2H), 3.21 (d, 1H), 2.90 (d, 1H), 1.86-1.95 (m, 1H), 1.73-1.86 (m, 1H), 1.54 (dd, 1H), 1.31 (s, 3H), 0.96 (dd, 6H).

25 Step 3: preparation of 2,4-dimethyl-1-phenyl-pentan-2-amine



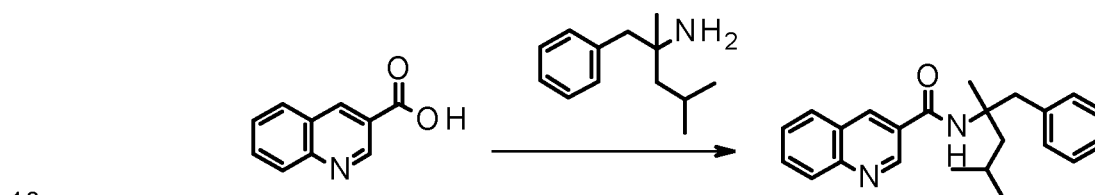
A solution of N-(1-benzyl-1,3-dimethyl-butyl)-2-chloro-acetamide (3.0 g, 11.2 mmol), acetic acid (3.9 mL, 67 mmol) and thiourea (1.02 g, 13.4 mmol) in ethanol (30 mL) was

warmed to 80 °C and stirred for 18 h at this temperature. The reaction mixture was then cooled to 20 °C, diluted with aqueous HCl (0.5 M) filtrated through a short pad of Celite. The filtrate was washed with ethyl acetate; the aqueous layer was then basified with 4 M NaOH and extracted with n-hexanes. The n-hexanes layer was washed with brine, dried over

5 Na₂SO₄, filtrated and concentrated in vacuo to afford the title compound as light brown oil.

¹H NMR (400 MHz, CDCl₃) δ 7.14-7.34 (m, 5H), 2.59-2.71 (m, 2H), 1.78-1.94 (m, 1H), 1.26-1.41 (m, 2H), 1.05 (s, 3H), 1.03 (br.s, 2H), 0.98 (dd, 6H).

Step 4: preparation of N-(1-benzyl-1,3-dimethyl-butyl)quinoline-3-carboxamide



To a solution of quinoline-3-carboxylic acid (0.20 g, 1.15 mmol), 2,4-dimethyl-1-phenyl-pentan-2-amine (0.22 g, 1.15 mmol), triethylamine (0.14 g, 1.4 mmol) and 1-hydroxy-7-azabenzotriazole (0.16 g, 1.15 mmol) in dry dimethylformamide (5 mL) was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide HCl (0.22 g, 1.15 mmol) at RT and the resulting

15 solution was aged for 18 h at 20 °C. Water was added and the mixture was extracted with ethyl acetate. The organic phase was washed with brine, dried over Na₂SO₄, filtrated and concentrated in vacuo. The residue was purified by chromatography on silica gel to afford the title compound as white solid, m.p. 121 °C.

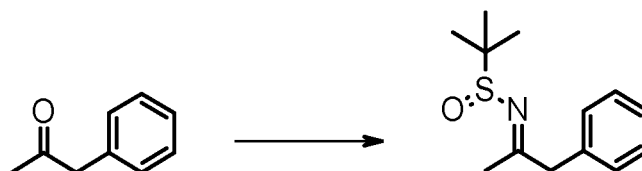
¹H NMR (400 MHz, CDCl₃) δ 9.12 (d, 1H), 8.40 (d, 1H), 8.13 (d, 1H), 7.86 (d, 1H), 7.74-7.82 (m, 1H), 7.56-7.64 (m, 1H), 7.16-7.30 (m, 5H), 5.73 (s, 1H), 3.46 (d, 1H), 2.98 (d, 1H), 2.17 (dd, 1H), 1.84-1.99 (m, 1H), 1.67 (dd, 1H), 1.43 (s, 3H), 1.02 (d, 6H).

20

Example 2: Preparation of N-(1-benzyl-1,3-dimethyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide

25

Step 1: preparation of 2-methyl-N-(1-methyl-2-phenyl-ethylidene)propane-2-sulfinamide



1-Phenylpropan-2-one (8.30 g, 61.9 mmol) was dissolved in tetrahydrofuran (75 mL), titanium(IV)ethoxide (32.6 g, 92.8 mmol) and 2-methylpropane-2-sulfinamide (7.50 g, 61.9 mmol) was added sequentially at room temperature and the resulting mixture was warmed to

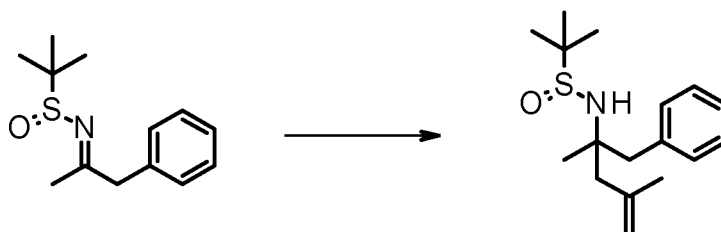
30 60 °C. After stirring for 2 h at 60 °C, the reaction was cooled to room temperature and

quenched with aqueous NaHCO_3 . The resulting mixture was filtrated and the filter cake was washed with ethyl acetate. The combined filtrates were extracted with ethyl acetate, the organic layer was washed with brine, dried over sodium sulfate, filtrated and concentrated in vacuo to afford the title compound as light yellow oil (purity >80%, ca. 4:1 ratio of cis-trans

5 isomers) which was used as such for the next step.

^1H NMR (400 MHz, CDCl_3 , major isomer) δ 7.17-7.43 (m, 5H), 3.72 (d, 1H), 3.70 (d, 1H), 2.32 (s, 3H), 1.23 (s, 9H)

Step 2: preparation of N-(1-benzyl-1,3-dimethyl-but-3-enyl)-2-methyl-propane-2-sulfinamide



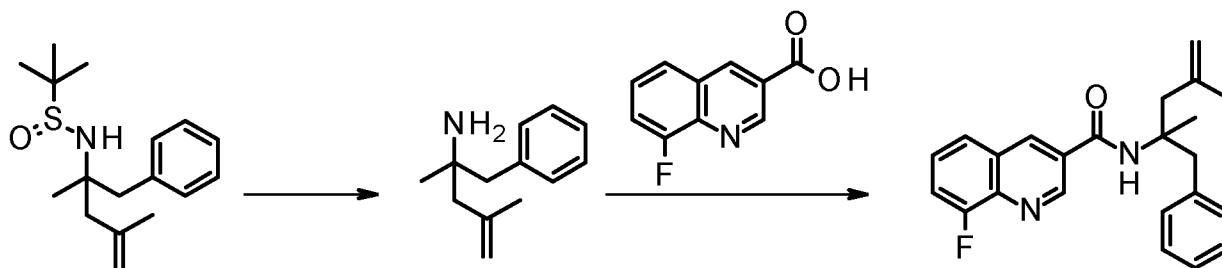
10

A solution of crude 2-methyl-N-(1-methyl-2-phenyl-ethylidene)propane-2-sulfinamide (80% purity, 7.4 g, 24.9 mmol) in dichloromethane (100 mL) was added slowly to a commercially available solution of 2-methylallylmagnesium chloride in THF (0.5 M, 75 mL, 37.4 mmol) maintained at -50°C . The reaction mixture was gradually warmed to 20°C over 4 h and

15 stirred overnight at 20°C . Saturated NH_4Cl solution was then added, the mixture was extracted with ethyl acetate and the organic layer was washed with brine, dried over sodium sulfate, filtrated and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to afford the title compound as mixture diastereoisomers.

20 ^1H NMR (400 MHz, CDCl_3 , major isomer) δ 6.94-7.18 (m, 5H), 4.82 (s, 1H), 4.71 (s, 1H), 3.39 (s, 1H), 2.76 (d, 1H), 2.55 (d, 1H), 2.21 (d, 2H), 1.63 (s, 3H), 1.06 (s, 3H), 0.94 (s, 9H).

Step 3: preparation of N-(1-benzyl-1,3-dimethyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide



25 To an ice cold solution of N-(1-benzyl-1,3-dimethyl-but-3-enyl)-2-methyl-propane-2-sulfinamide (5.2 g, 15.9 mmol) in methanol (16 mL) was added HCl in 1,4-dioxane (4 M, 6 mL, 24 mmol) and the resulting solution was stirred for 2 h at $0 - 5^\circ\text{C}$. All volatiles were then removed in vacuo to afford a brown, gummy residue which was triturated with a mixture of

diethyl ether/heptanes. The resulting light brown solid was dried in vacuo and used as such for the next step.

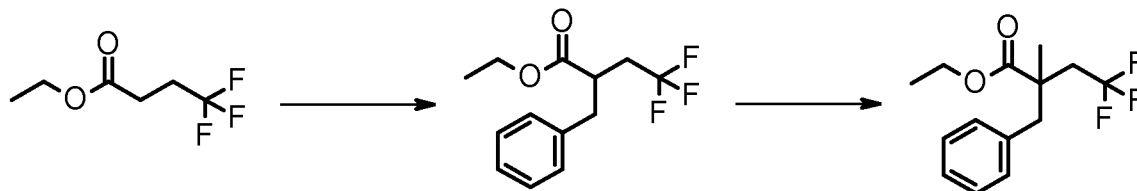
A part of the solid hydrochloride salt obtained above (2 g, 8.0 mmol) was suspended in dichloromethane (40 mL) and 8-fluoroquinoline-3-carboxylic acid (1.68 g, 8.8 mmol), triethylamine (2.8 mL, 19.9 mmol), 1-hydroxy-7-azabenzotriazol (1.2 g, 8.8 mmol) and N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide-HCl (1.72 g, 8.8 mmol) was added sequentially at ambient temperature. The resulting mixture was aged for 2 h at 20 °C. Water was then added and the mixture was extracted with dichloromethane. The organic layer was washed with brine, dried over sodium sulfate, filtrated and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to afford the title compound as white solid, m.p. 115-117°C

¹H NMR (400 MHz, CDCl₃) δ 9.11-9.26 (m, 1H), 8.50 (s, 1H), 7.72 (d, 1H), 7.45-7.64 (m, 2H), 7.19-7.37 (m, 5H), 5.96 (s, 1H), 5.01 (s, 1H), 4.84 (s, 1H), 3.57 (d, 1H), 3.08 (dd, 2H), 2.46 (d, 1H), 1.89 (s, 3H), 1.47 (s, 3H).

¹⁹F NMR (377 MHz, CDCl₃) δ -124.64 (s).

Example 3: N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7,8-difluoro-quinoline-3-carboxamide

Step 1: preparation of ethyl 2-benzyl-4,4,4-trifluoro-2-methyl-butanoate



20

n-Butyl lithium (2.5 M in hexanes, 100 mL, 248.9 mmol) was added slowly to a solution of diisopropyl amine (35.2 mL, 248.9 mmol) in tetrahydrofuran (400 mL) at -70°C. The resulting solution was aged for 30 min at -70 °C and then ethyl 4,4,4-trifluorobutyrate (36 g, 207.4 mmol) was added drop wise. The reaction was stirred for 2 h at -70 °C, benzyl bromide (43.2 g, 248.9 mmol) was added and the reaction mixture was gradually warmed to room temperature over ca. 2 h. Saturated NH₄Cl solution was added and the mixture was extracted with methyl tertbutyl ether. The organic layer was washed with water, brine, dried over MgSO₄, filtrated and concentrated in vacuo. The residual oil was passed through a short pad of silica gel, the pad was rinsed with cyclohexane:ethyl acetate (2:1) and the filtrate was concentrated in vacuo, affording ethyl 4,4,4-trifluoro-2-methyl-butanoate as light orange oil.

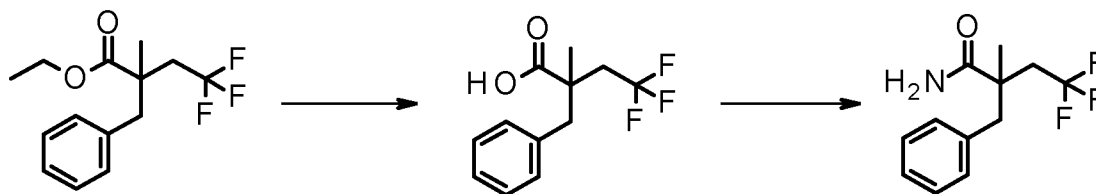
30

n-Butyl lithium (2.5 M in hexanes, 99 mL, 247.2 mmol) was added slowly to a solution of diisopropyl amine (35 mL, 247.2 mmol) in tetrahydrofuran (380 mL) at -70°C. The resulting solution was aged for 30 min at -70 °C and then the crude product obtained above (49.5 g,

190.2 mmol, diluted with tetrahydrofuran (30 mL)) was added slowly at – 70 °C. The resulting dark solution was stirred for 2 h at -70 °C before methyl iodide (13.1 mL, 209.3 mmol) was added. The reaction mixture was gradually warmed to 20 °C over ca. 3 h, then quenched with saturated NH₄Cl solution and extracted with methyl tertbutylether. The organic layer was washed with water, brine, dried over MgSO₄, filtrated and concentrated in vacuo. The residual oil was passed through a short pad of silica gel, the pad was rinsed with cyclohexane:ethyl acetate (2:1) and the filtrate was concentrated in vacuo, affording the title compound as light brown oil (ca. 80% pure).

¹H NMR (400 MHz, CDCl₃) δ 7.05-7.33 (m, 5H), 4.13 (q, 2H), 2.98 (d, 1H), 2.81-2.72 (m, 2H), 2.11-2.32 (m, 1H), 1.28 (s, 3H), 1.21 (t, 3H).

Step 2: preparation of 2-benzyl-4,4,4-trifluoro-2-methyl-butanamide

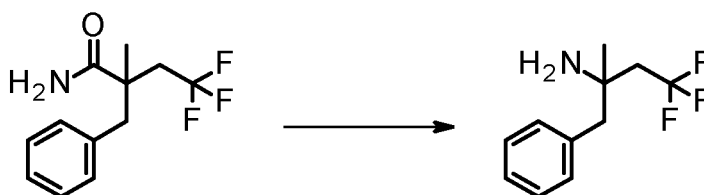


A solution of ethyl 2-benzyl-4,4,4-trifluoro-2-methylbutanoate (25.5 g, 93.0 mmol) in 1,4-dioxane (45 mL) / ethanol (45 mL) was treated with NaOH (7.6 g, 186 mmol) at room temperature, the resulting solution was warmed to 90 °C and aged for 1 h at 90 °C. After cooling to room temperature, the reaction mixture was concentrated to about 50% of the original volume. The residue was diluted with water and washed with cyclohexane. The water layer was then acidified with HCl (conc.) under ice cooling at temp < 25 °C and the mixture was extracted with DCM. The organic layer were washed with brine, dried with Na₂SO₄, filtrated and concentrated in vacuo to afford 2-benzyl-4,4,4-trifluoro-2-methylbutanoic acid as dark yellow oil.

To a solution of crude 2-benzyl-4,4,4-trifluoro-2-methylbutanoic acid (6.7 g, 27.2 mmol) and dimethyl formamide (0.1 mL, 1.4 mmol) in dichloromethane (25 mL) was slowly added oxalyl chloride (2.5 mL, 28.6 mmol) at 20 °C. The resulting solution was stirred for 1 h at 20 °C and then all volatiles were removed in vacuo. The residue was dissolved in dichloromethane (25 mL) and the resulting solution was slowly added to ice cooled, rapidly stirred aqueous ammonia solution (25-wt%, 21 mL). The resulting mixture was gradually warmed to room temperature and stirred for 30 min. Water was then added and the mixture was extracted with dichloromethane. The organic layer was washed with water, brine, dried with Na₂SO₄, filtrated and concentrated in vacuo to afford the title compound as light brown oil.

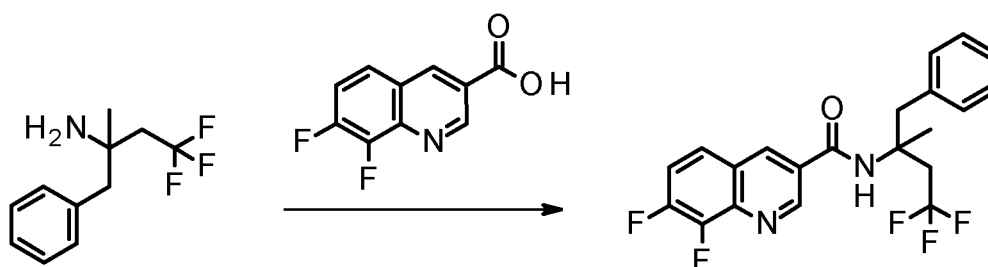
¹H NMR (400 MHz, CDCl₃) δ 7.13-7.44 (m, 5H), 5.42 (br s, 2H), 3.13 (d, 1H), 2.97-3.09 (m, 1H), 2.67 (d, 1H), 2.18 (qd, 1H), 1.33 (s, 3H).

Step 3: preparation of 4,4,4-trifluoro-2-methyl-1-phenyl-butan-2-amine



To a solution of 2-benzyl-4,4,4-trifluoro-2-methyl-butanamide (6.6 g, 26.9 mmol) in acetonitrile (25 mL) / water (25 mL) was added diacetoxyiodobenzene (9.73 g, 29.6 mmol) and trifluoroacetic acid (4.6 mL, 59.2 mmol) at room temperature and the resulting mixture was stirred for 18 h at room temperature. Acetonitrile was then removed in vacuo, the remaining aqueous emulsion was adjusted to pH1 with concentrated HCl and washed with methyl tertbutylether. The aqueous layer was basified to pH12 with NaOH (8 M) and extracted with methyl tertbutylether. The organic layer was washed with brine, dried over Na₂SO₄, filtrated and concentrated in vacuo to afford the title compound as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.16-7.50 (m, 5H), 2.81 (s, 2H), 2.13-2.41 (m, 2H), 1.28 (s, 3H).

Step 4: preparation of N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7,8-difluoro-quinoline-3-carboxamide



To a solution of 7,8-difluoroquinoline-3-carboxylic acid (0.35 g, 1.67 mmol), 4,4,4-trifluoro-2-methyl-1-phenyl-butan-2-amine (0.40 g, 0.84 mmol), triethylamine (0.6 mL, 4.2 mmol) and 1-hydroxy-7-azabenzotriazol (0.27 g, 2.0 mmol) in dichloromethane (10 mL) was added N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide-HCl (0.39 g, 2.0 mmol) at room temperature. The resulting mixture was stirred for 15 h at room temperature and then quenched with water. The mixture was extracted with dichloromethane, the organic layer was washed with water, brine, dried over Na₂SO₄, filtrated and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to afford the title compound as white solid, m.p. 158-160°C. ¹H NMR (400 MHz, CDCl₃) δ 9.07 (d, 1H), 8.38 (t, 1H), 7.62 (ddd, 1H), 7.47 (dt, 1H), 7.11-7.38 (m, 5H), 6.14 (s, 1H), 3.62 (d, 1H), 3.46 (dd, 1H), 2.96 (d, 1H), 2.58 (qd, 1H), 1.50 (s, 3H). ¹⁹F NMR (377 MHz, CDCl₃) δ -59.75 (s, 1F), -132.03 (d, 1F), -150.23 (d, 1F).

Example 4: Preparation of the single isomers:

N-[(1*S*)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-7,8-difluoro-quinoline-3-carboxamide and
N-[(1*R*)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-7,8-difluoro-quinoline-3-carboxamide

5

The racemic N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7,8-difluoro-quinoline-3-carboxamide mixture was submitted to chiral resolution by preparative HPLC chromatography using the conditions outlined hereafter.

Analytical HPLC method10 SFC:Waters Acquity UPC²/QDaPDA Detector Waters Acquity UPC²

Column: Daicel SFC CHIRALPAK® OZ, 3µm, 0.3cm x 10cm, 40°C Mobile phase: A: CO₂ B: iPr gradient: 10% B in 2.8 min

ABPR: 1800 psi

15 Flow rate: 2.0 ml/min

Detection: 233 nm

Sample concentration: 1 mg/mL in ACN/iPr 50/50

Injection: 1 µL

20 Preparative HPLC method:

Autopurification System from Waters: 2767 sample Manager, 2489 UV/Visible Detector, 2545 Quaternary Gradient Module.

Column: Daicel CHIRALPAK® IF, 5µm, 1.0 cm x 25cm

Mobile phase: TBME/EtOH 98/02

25 Flow rate: 10 ml/min Detection: UV 265 nm

Sample concentration: 165mg/mL in EE/ACN

Injection: 30-90µl, 5-15mg

Results:

First eluting enantiomer	Second eluting enantiomer
Retention time (min) ~ 1.05	Retention time (min) ~ 1.51
Chemical purity (area% at 220 nm) 99	Chemical purity (area% at 220 nm) 99
Enantiomeric excess (%) > 99	Enantiomeric excess (%) > 99

The compound with the elution time of 1.05 minute is N-[(1*R*)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-7,8-difluoro-quinoline-3-carboxamide, corresponding to compound F-38.

30

The compound with the elution time of 1.51 minutes is N-[(1*S*)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-7,8-difluoro-quinoline-3-carboxamide, corresponding to compound F-37.

Example 5: Preparation of the single isomers:

N-[(1*S*)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide

N-[(1*R*)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide

The racemic N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-fluoro-quinoline-3-
5 carboxamide mixture was submitted to chiral resolution by preparative HPLC
chromathography using the conditions outlined hereafter.

Analytical HPLC method

SFC: Waters Acquity UPC²/QDa

10 PDA Detector Waters Acquity UPC²

Column: Daicel SFC CHIRALPAK® ID, 3µm, 0.3cm x 10cm, 40°C

Mobile phase: A: CO₂ B: iPr gradient: 15% B in 2.8 min

ABPR: 1800 psi

Flow rate: 2.0 ml/min

15 Detection: 235 nm

Sample concentration: 1 mg/mL in ACN/iPr 50/50

Injection: 1 µL

Preparative HPLC method:

Autopurification System from Waters: 2767 sample Manager, 2489 UV/Visible Detector,
20 2545 Quaternary Gradient Module.

Column: Daicel CHIRALPAK® IF, 5µm, 1.0 cm x 25cm

Mobile phase: Hept/EtOH 95/05

Flow rate: 10 ml/min

Detection: UV 265 nm

25 Sample concentration: 10 mg/mL in MeOH/DCM (1/1)

Injection: 500µl

Results:

First eluting enantiomer	Second eluting enantiomer
Retention time (min) ~ 1.49	Retention time (min) ~ 1.88
Chemical purity (area% at 235 nm) 99	Chemical purity (area% at 235 nm) 99
Enantiomeric excess (%) > 99	Enantiomeric excess (%) > 99

The compound with the elution time of 1.49 minute is N-[(1*S*)-1-benzyl-3,3,3-trifluoro-1-
30 methyl-propyl]-8-fluoro-quinoline-3-carboxamide, corresponding to compound F-11.

The compound with the elution time of 1.88 minutes is N-[(1*R*)-1-benzyl-3,3,3-trifluoro-1-
methyl-propyl]-8-fluoro-quinoline-3-carboxamide, corresponding to compound F-12.

Example 6: Preparation of the single isomers:

N-[(1*R*)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide and

N-[(1*S*)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide

The racemic N-(1-benzyl-1,3-dimethyl-butyl)-8-fluoro-quinoline-3-carboxamide

- 5 mixture was submitted to chiral resolution by preparative HPLC chromatography using the conditions outlined hereafter.

Analytical HPLC method:

SFC: Waters Acquity UPC²/QDa

- 10 PDA Detector Waters Acquity UPC²

Column: Daicel SFC CHIRALPAK® IA, 3μm, 0.3cm x 10cm, 40°C

Mobile phase: A: CO₂ B: MeOH gradient: 25% B in 1.8 min

ABPR: 1800 psi

Flow rate: 2.0 ml/min

- 15 Detection: 240 nm

Sample concentration: 1 mg/mL in Hept/EtOH 90/10

Injection: 3 μL

Preparative HPLC method:

Autopurification System from Waters: 2767 sample Manager, 2489 UV/Visible Detector,

- 20 2545 Quaternary Gradient Module.

Column: Daicel CHIRALPAK® IE, 5μm, 1.0 cm x 25cm

Mobile phase: Hept/EtOH 90/10

Flow rate: 10 ml/min

Detection: UV 265 nm

- 25 Sample concentration: 100 mg/mL in MeOH/DCM (1/3) (filtered)

Injection: 150μl - 250μl

First eluting enantiomer	Second eluting enantiomer
Retention time (min) ~ 0.97	Retention time (min) ~ 1.32
Chemical purity (area% at 240 nm) 99	Chemical purity (area% at 240 nm) 99
Enantiomeric excess (%) > 99	Enantiomeric excess (%) > 99

The compound with the elution time of 0.97 minute is N-[(1*S*)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide, corresponding to compound F-1.

- 30 The compound with the elution time of 1.88 minutes is N-[(1*R*)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide, corresponding to compound F-2.

Example 7: Preparation of the single isomers:

N-[(1*R*)-1-benzyl-3-fluoro-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide and
N-[(1*S*)-1-benzyl-3-fluoro-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide

The racemic N-(1-benzyl-3-fluoro-1,3-dimethyl-butyl)-8-fluoro-quinoline-3-carboxamide mixture was submitted to chiral resolution by preparative HPLC

5 chromatography using the conditions outlined hereafter.

Analytical HPLC method:

SFC: Waters Acquity UPC²/QDa

PDA Detector Waters Acquity UPC²

10 Column: Daicel SFC CHIRALPAK® IA, 3µm, 0.3cm x 10cm, 40°C

Mobile phase: A: CO₂ B: MeOH gradient: 30% B in 1.8 min

ABPR: 1800 psi

Flow rate: 2.0 ml/min

Detection: 230 nm

15 Sample concentration: 1 mg/mL in ACN/iPr 50/50

Injection: 1 µL Preparative HPLC method:

Autopurification System from Waters: 2767 sample Manager, 2489 UV/Visible Detector, 2545 Quaternary Gradient Module.

Column: Daicel CHIRALPAK® IA, 5µm, 1.0 cm x 25cm

20 Mobile phase: Hept/EtOH 90/10

Flow rate: 10 ml/min

Detection: UV 265 nm

Sample concentration: 127mg/mL in EE

Injection: 40-160µl, 5-20mg

First eluting enantiomer	Second eluting enantiomer
Retention time (min) ~ 0.88	Retention time (min) ~ 1.51
Chemical purity (area% at 235 nm) 99	Chemical purity (area% at 235 nm) 99
Enantiomeric excess (%) > 99	Enantiomeric excess (%) > 99

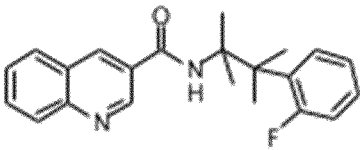
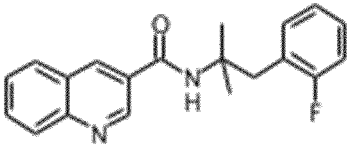
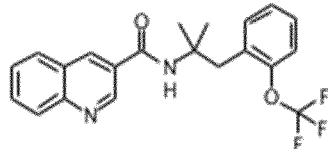
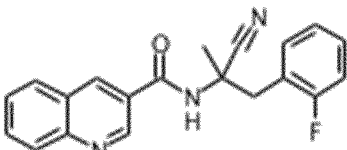
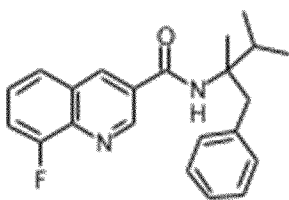
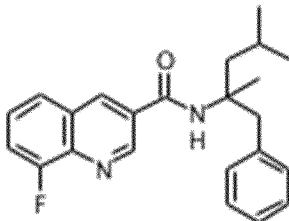
25

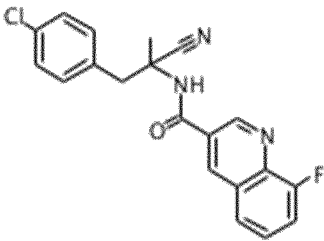
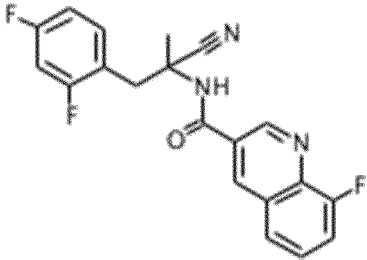
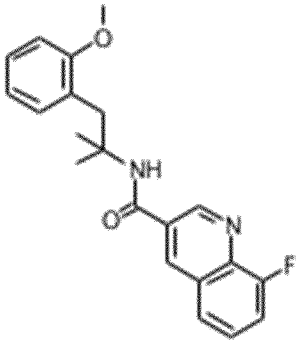
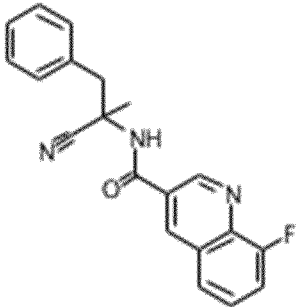
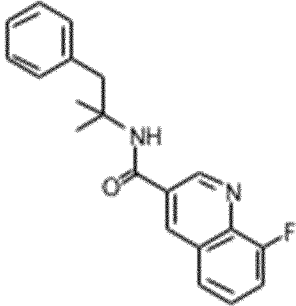
The compound with the elution time of 0.88 minute is N-[(1*R*)-1-benzyl-3-fluoro-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide, corresponding to compound F-23.

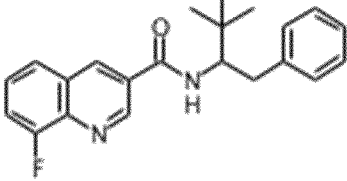
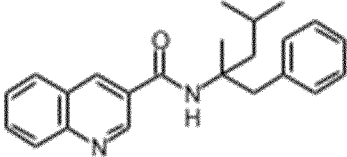
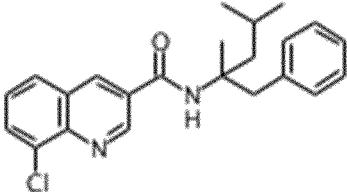
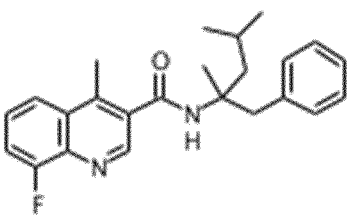
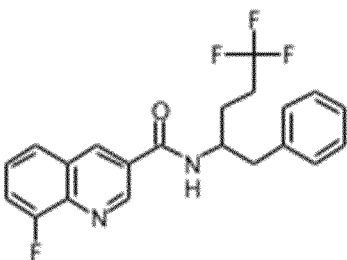
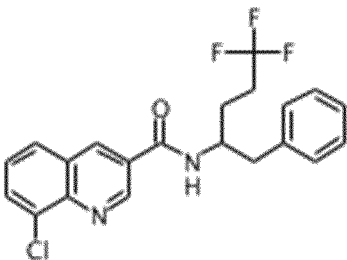
The compound with the elution time of 1.51 minutes is N-[(1*S*)-1-benzyl-3-fluoro-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide, corresponding to compound F-24.

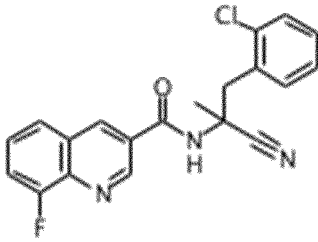
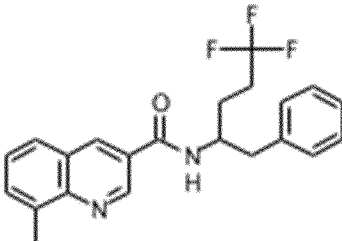
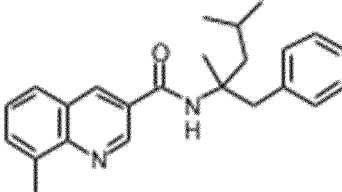
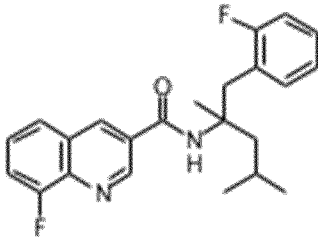
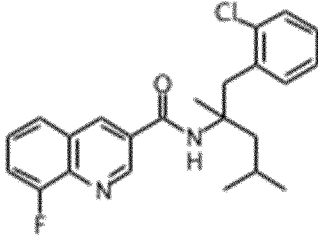
30

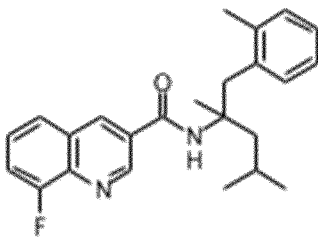
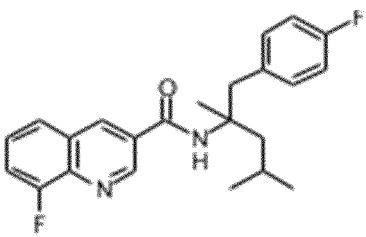
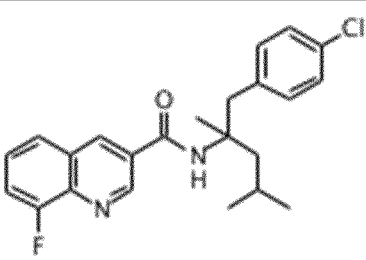
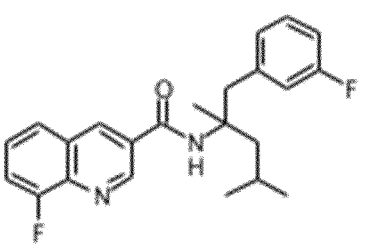
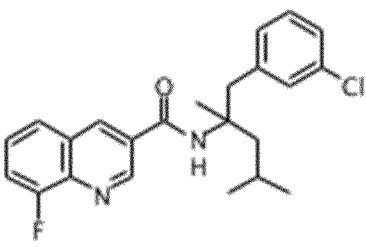
Table E: Physical data of compounds of formula (I)

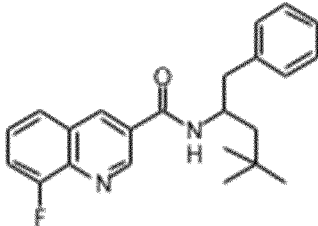
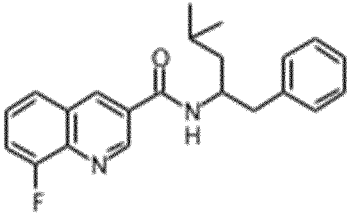
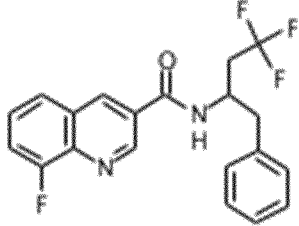
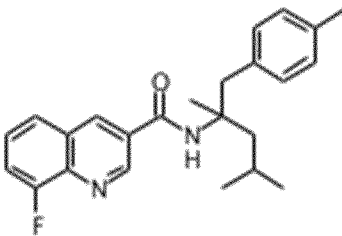
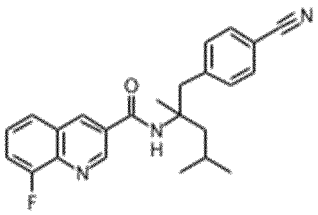
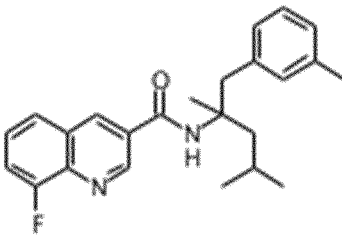
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-1	N-[2-(2-fluorophenyl)-1,1,2-trimethylpropyl]quinoline-3-carboxamide		1.08	351	G	
E-2	N-[2-(2-fluorophenyl)-1,1-dimethylethyl]quinoline-3-carboxamide		1.00	323	G	
E-3	N-[1,1-dimethyl-2-[2-(trifluoromethoxy)phenyl]ethyl]quinoline-3-carboxamide		1.79	389	G	145 - 149
E-4	N-[1-cyano-2-(2-fluorophenyl)-1-methylethyl]quinoline-3-carboxamide		1.35	334	G	134 - 139
E-5	N-(1-benzyl-1,2-dimethylpropyl)-8-fluoroquinoline-3-carboxamide		1.12	351	G	
E-6	N-(1-benzyl-1,3-dimethylbutyl)-8-fluoroquinoline-3-carboxamide		1.17	365	H	110 - 112

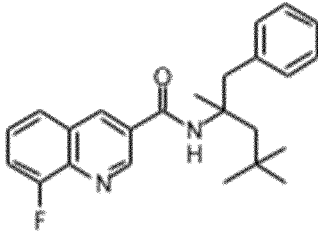
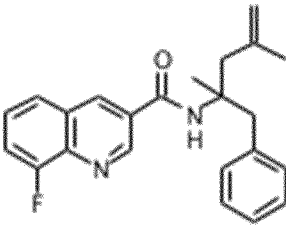
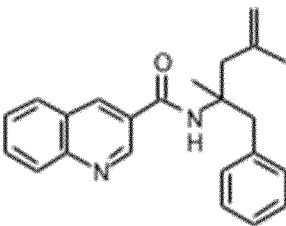
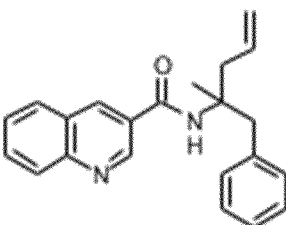
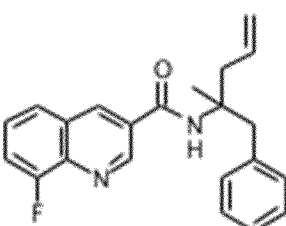
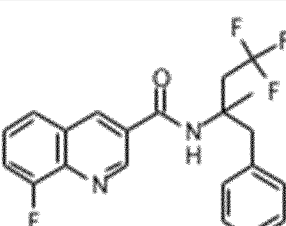
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-7	N-[2-(4-chlorophenyl)-1-cyano-1-methyl-ethyl]-8-fluoro-quinoline-3-carboxamide		1.51	368	W	
E-8	N-[1-cyano-2-(2,4-difluorophenyl)-1-methyl-ethyl]-8-fluoro-quinoline-3-carboxamide		1.43	370	W	
E-9	8-fluoro-N-[2-(2-methoxyphenyl)-1,1-dimethyl-ethyl]quinoline-3-carboxamide		1.64	353	W	
E-10	N-(1-cyano-1-methyl-2-phenyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.37	334	W	
E-11	N-(1,1-dimethyl-2-phenyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.56	323	W	

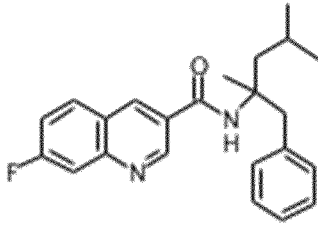
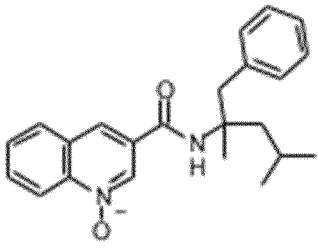
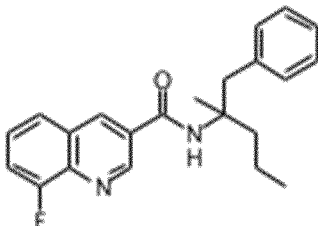
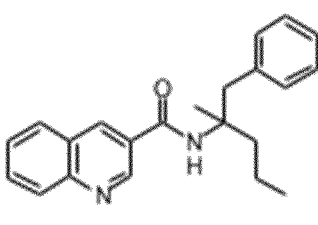
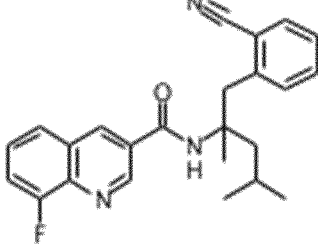
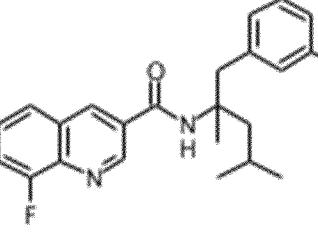
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-12	N-(1-benzyl-2,2-dimethyl-propyl)-8-fluoro-quinoline-3-carboxamide		1.03	351	H	163 - 164
E-13	N-(1-benzyl-1,3-dimethyl-butyl)quinoline-3-carboxamide		1.13	347	H	
E-14	N-(1-benzyl-1,3-dimethyl-butyl)-8-chloro-quinoline-3-carboxamide		1.19	381	H	147 - 148
E-15	N-(1-benzyl-1,3-dimethyl-butyl)-8-fluoro-4-methyl-quinoline-3-carboxamide		1.14	379	H	92 - 94
E-16	N-(1-benzyl-4,4,4-trifluoro-butyl)-8-fluoro-quinoline-3-carboxamide		1.64	391	H	157 - 161
E-17	N-(1-benzyl-4,4,4-trifluoro-butyl)-8-chloro-quinoline-3-carboxamide		1.75	407	H	163 - 167

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-18	N-[2-(2-chlorophenyl)-1-cyano-1-methyl-ethyl]-8-fluoro-quinoline-3-carboxamide		0.96	368-370	G	198 - 203
E-19	N-(1-benzyl-4,4,4-trifluorobutyl)-8-methyl-quinoline-3-carboxamide		1.79	387	H	158 - 161
E-20	N-(1-benzyl-1,3-dimethyl-butyl)-8-methyl-quinoline-3-carboxamide		1.24	361	H	132 - 133
E-21	8-fluoro-N-[1-[(2-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide		1.16	383	G	105 - 106
E-22	N-[1-[(2-chlorophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.21	399-401	G	109 - 110

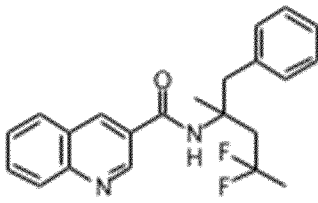
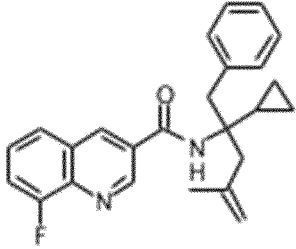
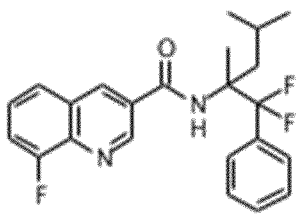
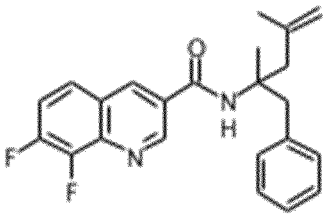
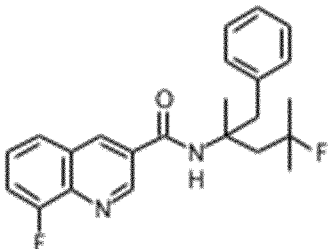
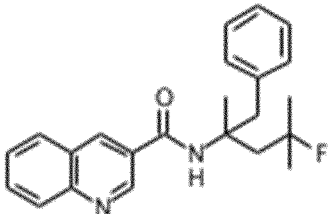
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-23	N-[1,3-dimethyl-1-(o-tolylmethyl)butyl]-8-fluoro-quinoline-3-carboxamide		1.19	379	G	125 - 126
E-24	8-fluoro-N-[1-[(4-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide		1.15	383	G	38 - 39
E-25	N-[1-[(4-chlorophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.21	399-401	G	57 - 59
E-26	8-fluoro-N-[1-[(3-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide		1.15	383	G	45 - 47
E-27	N-[1-[(3-chlorophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.20	399-401	G	41 - 42

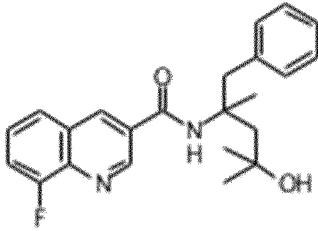
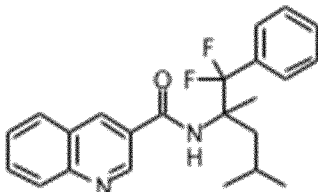
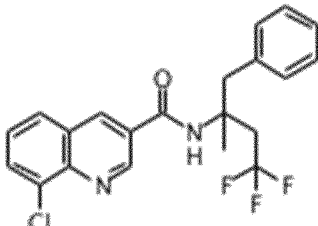
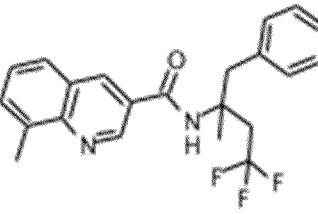
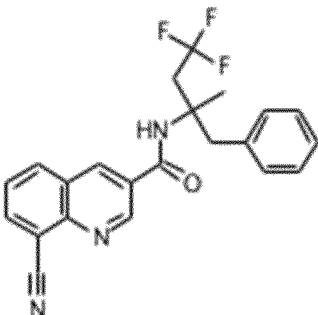
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-28	N-(1-benzyl-3,3-dimethyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.10	365	G	178 - 180
E-29	N-(1-benzyl-3-methyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.07	351	G	136- 139
E-30	N-(1-benzyl-3,3,3-trifluoropropyl)-8-fluoro-quinoline-3-carboxamide		0.98	377	G	140 - 142
E-31	N-[1,3-dimethyl-1-(p-tolylmethyl)butyl]-8-fluoro-quinoline-3-carboxamide		1.21	379	G	116 - 118
E-32	N-[1-[(4-cyanophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.10	390	G	67 - 69
E-33	N-[1,3-dimethyl-1-(m-tolylmethyl)butyl]-8-fluoro-quinoline-3-carboxamide		1.20	379	G	94 - 96

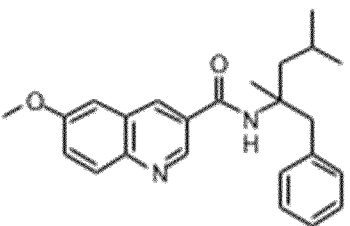
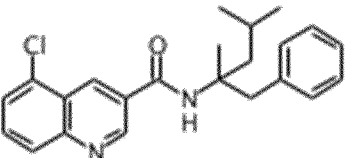
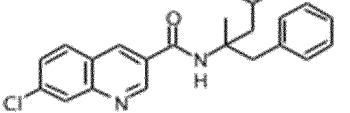
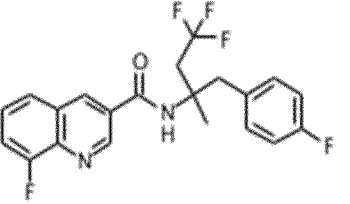
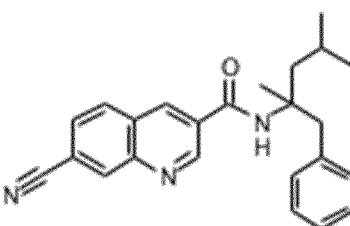
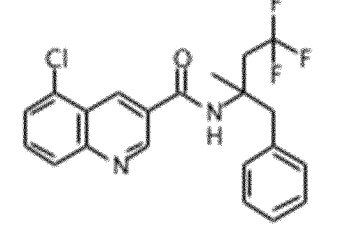
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-34	N-(1-benzyl-1,3,3-trimethyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.19	379	G	48 - 50
E-35	N-(1-benzyl-1,3-dimethyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide		1.12	363	G	115 - 117
E-36	N-(1-benzyl-1,3-dimethyl-but-3-enyl)quinoline-3-carboxamide		1.11	345	G	99 - 103
E-37	N-(1-benzyl-1-methyl-but-3-enyl)quinoline-3-carboxamide		1.07	331	G	
E-38	N-(1-benzyl-1-methyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide		1.08	349	G	
E-39	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-fluoro-quinoline-3-carboxamide		1.06	391	G	158 - 160

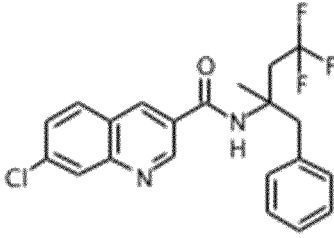
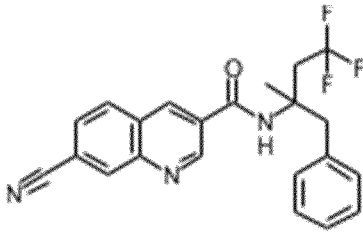
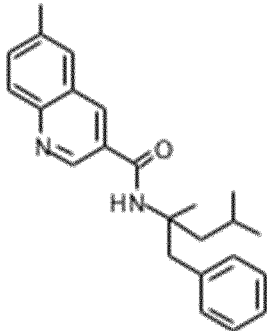
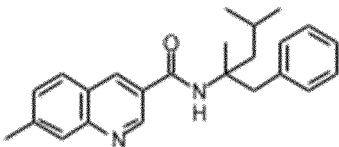
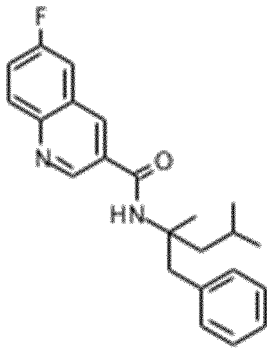
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-40	N-(1-benzyl-1,3-dimethyl-butyl)-7-fluoro-quinoline-3-carboxamide		1.15	365	G	142 - 144
E-41	N-(1-benzyl-1,3-dimethyl-butyl)-1-oxido-quinolin-1-ium-3-carboxamide		1.06	363	G	
E-42	N-(1-benzyl-1-methyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.12	351	G	
E-43	N-(1-benzyl-1-methyl-butyl)quinoline-3-carboxamide		1.10	333	G	
E-44	N-[1-[(2-cyanophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.10	390	G	43 - 44
E-45	N-[1-[(3-bromophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.22	443-445	G	87 - 89

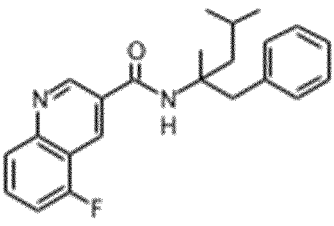
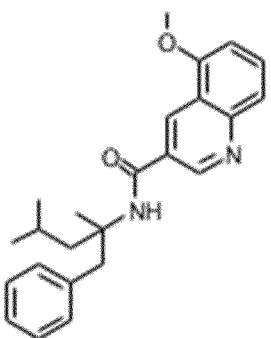
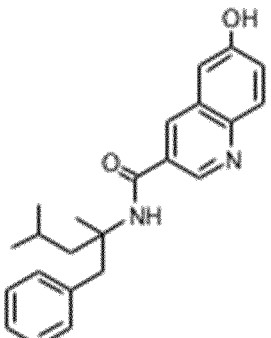
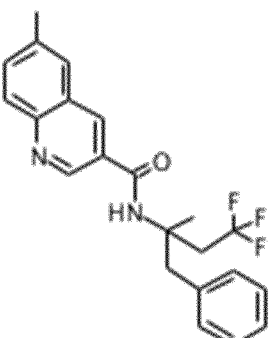
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-46	N-[1-[(3-cyanophenyl)methyl]-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.10	390	G	45 - 46
E-47	N-[1-benzyl-1-methyl-2-(1-methylcyclopropyl)ethyl]-8-fluoro-quinoline-3-carboxamide		1.16	377	G	126 - 129
E-48	N-(1-benzyl-1,3-dimethyl-butyl)-7,8-difluoro-quinoline-3-carboxamide		1.19	383	G	114 - 116
E-49	N-(1-benzyl-2-cyclopropyl-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.11	363	G	
E-50	N-(1-benzyl-3,3-difluoro-1-methyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.06	387	G	
E-51	N-[1-(difluoro(phenyl)methyl)-1,3-dimethyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide		1.11	399	G	

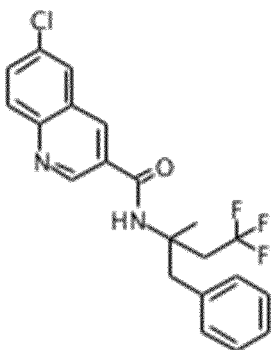
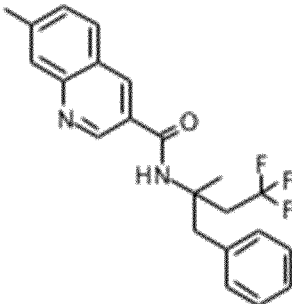
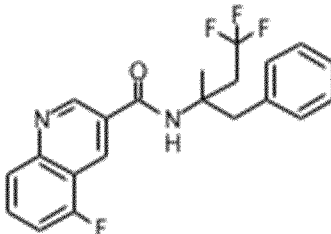
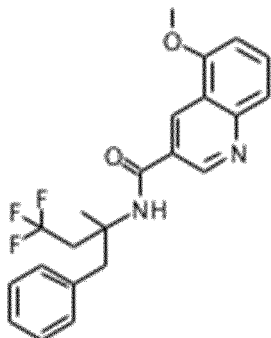
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-52	N-(1-benzyl-3,3-difluoro-1-methyl-butyl)quinoline-3-carboxamide		1.05	369	G	131 - 133
E-53	N-(1-benzyl-1-cyclopropyl-3-methyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide		2.01	389	H	
E-54	N-[1-(difluoro(phenyl)methyl)-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.15	401	G	
E-55	N-(1-benzyl-1,3-dimethyl-but-3-enyl)-7,8-difluoro-quinoline-3-carboxamide		1.16	381	G	94 - 96
E-56	N-(1-benzyl-3-fluoro-1,3-dimethyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.08	383	G	
E-57	N-(1-benzyl-3-fluoro-1,3-dimethyl-butyl)quinoline-3-carboxamide		1.07	365	G	

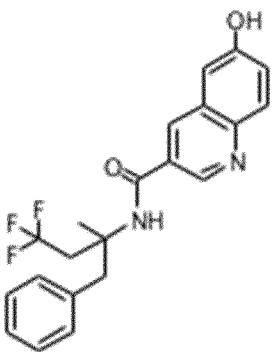
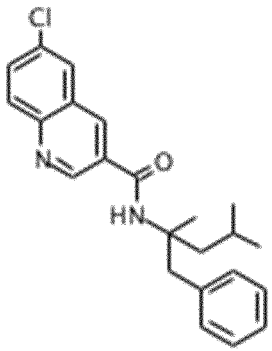
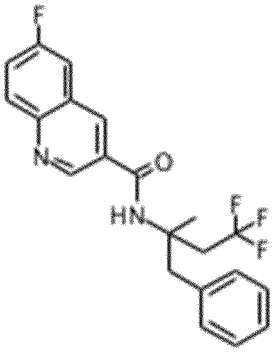
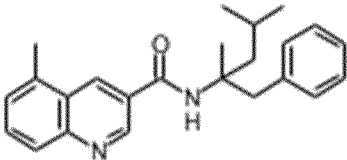
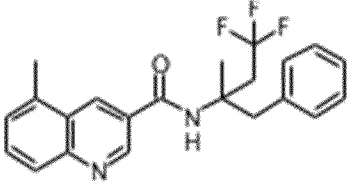
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-58	N-(1-benzyl-3-hydroxy-1,3-dimethyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.02	381	G	
E-59	N-[1-(difluoro(phenyl)methyl)-1,3-dimethyl-butyl]quinoline-3-carboxamide		1.12	383	G	
E-60	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-chloro-quinoline-3-carboxamide		1.11	408	G	141 - 144
E-61	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-methyl-quinoline-3-carboxamide		1.14	387	G	120 - 123
E-62	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-cyano-quinoline-3-carboxamide		1.06	398	G	175 - 179

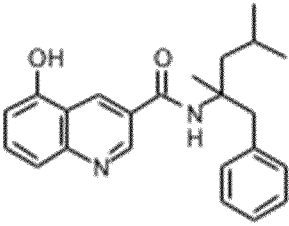
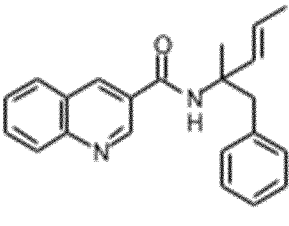
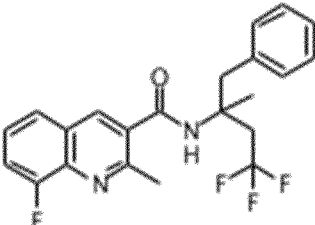
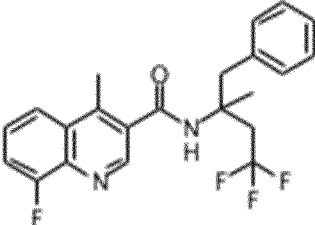
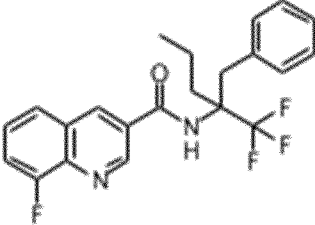
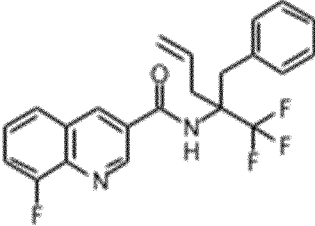
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-63	N-(1-benzyl-1,3-dimethyl-butyl)-6-methoxy-quinoline-3-carboxamide		1.13	377	G	102 - 105
E-64	N-(1-benzyl-1,3-dimethyl-butyl)-5-chloro-quinoline-3-carboxamide		1.23	381-383	G	50 - 60
E-65	N-(1-benzyl-1,3-dimethyl-butyl)-7-chloro-quinoline-3-carboxamide		1.22	381-383	G	172 - 174
E-66	8-fluoro-N-[3,3,3-trifluoro-1-[(4-fluorophenyl)methyl]-1-methyl-propyl]quinoline-3-carboxamide		1.07	409	G	146 - 147
E-67	N-(1-benzyl-1,3-dimethyl-butyl)-7-cyano-quinoline-3-carboxamide		1.14	372	G	170 - 172
E-68	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-5-chloro-quinoline-3-carboxamide		1.14	407-409	G	85 - 88

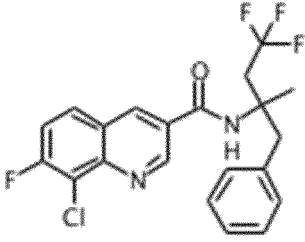
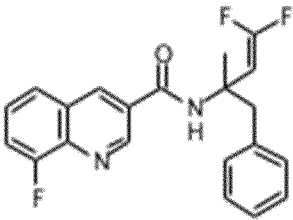
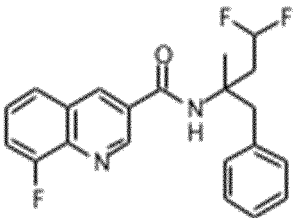
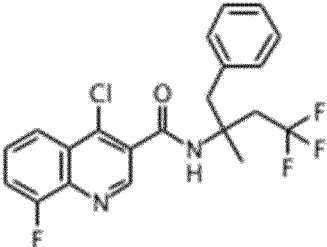
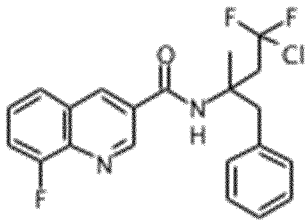
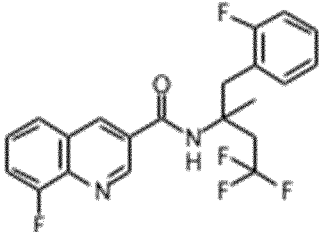
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-69	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7-chloro-quinoline-3-carboxamide		1.14	407-409	G	174 - 176
E-70	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7-cyano-quinoline-3-carboxamide		1.06	398	G	172 - 174
E-71	N-(1-benzyl-1,3-dimethyl-butyl)-6-methyl-quinoline-3-carboxamide		1.87	361	W	
E-72	N-(1-benzyl-1,3-dimethyl-butyl)-7-methyl-quinoline-3-carboxamide		1.84	361	W	
E-73	N-(1-benzyl-1,3-dimethyl-butyl)-6-fluoro-quinoline-3-carboxamide		1.86	365	W	

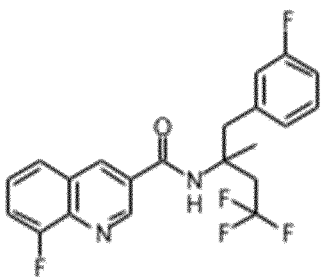
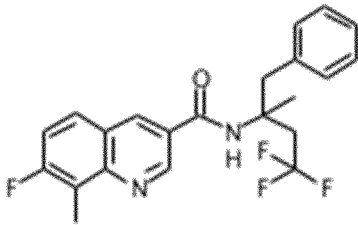
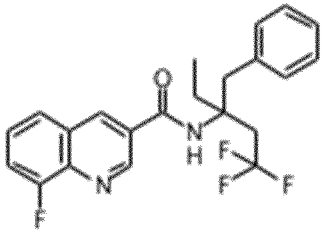
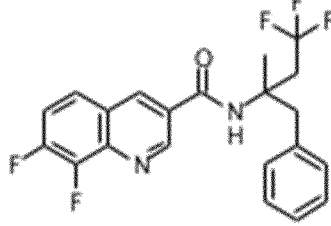
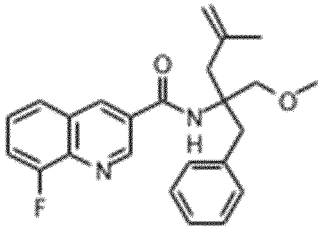
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-74	N-(1-benzyl-1,3-dimethyl-butyl)-5-fluoro-quinoline-3-carboxamide		1.89	365	W	
E-75	N-(1-benzyl-1,3-dimethyl-butyl)-5-methoxy-quinoline-3-carboxamide		1.82	377	W	
E-76	N-(1-benzyl-1,3-dimethyl-butyl)-6-hydroxy-quinoline-3-carboxamide		1.52	363	W	
E-77	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-6-methyl-quinoline-3-carboxamide		1.70	387	W	

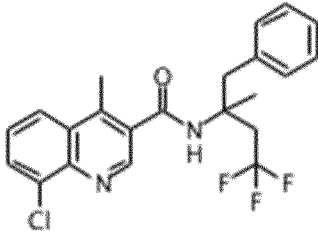
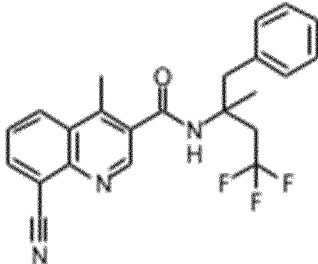
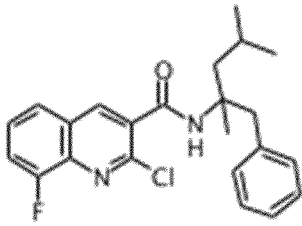
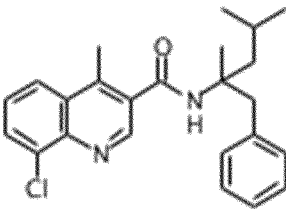
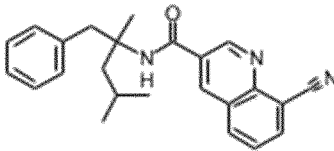
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-78	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-6-chloro-quinoline-3-carboxamide		1.81	407	W	
E-79	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7-methyl-quinoline-3-carboxamide		1.68	387	W	
E-80	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-5-fluoro-quinoline-3-carboxamide		1.72	391	W	
E-81	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-5-methoxy-quinoline-3-carboxamide		1.66	403	W	

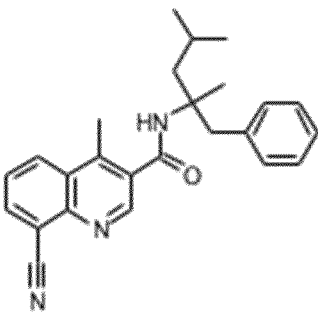
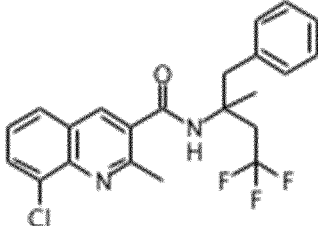
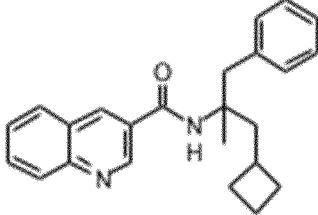
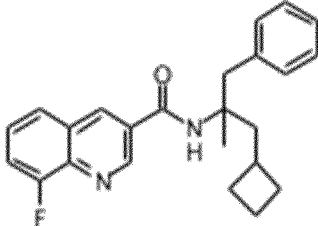
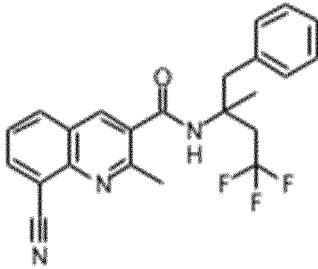
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-82	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-6-hydroxy-quinoline-3-carboxamide		1.37	389	W	
E-83	N-(1-benzyl-1,3-dimethyl-butyl)-6-chloro-quinoline-3-carboxamide		1.98	381	W	
E-84	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-6-fluoro-quinoline-3-carboxamide		1.69	391	W	
E-85	N-(1-benzyl-1,3-dimethyl-butyl)-5-methyl-quinoline-3-carboxamide		1.17	361	G	79 - 81
E-86	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-5-methyl-quinoline-3-carboxamide		1.09	387	G	101 - 103

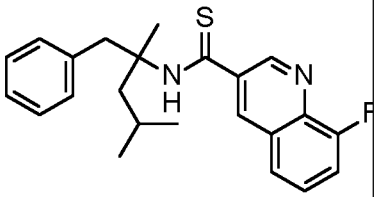
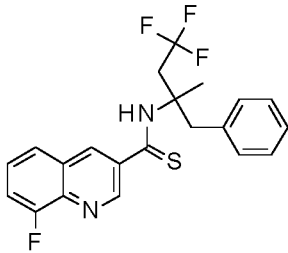
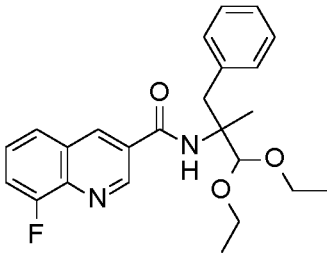
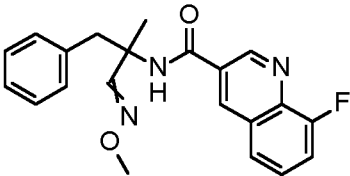
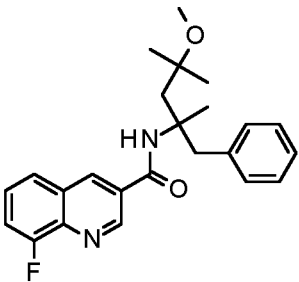
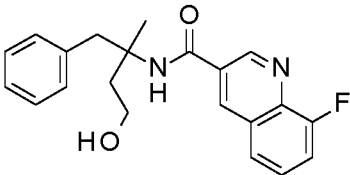
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-87	N-(1-benzyl-1,3-dimethyl-butyl)-5-hydroxy-quinoline-3-carboxamide		1.01	363	G	90 - 95
E-88	N-[(E)-1-benzyl-1-methyl-but-2-enyl]quinoline-3-carboxamide		1.05	331	G	
E-89	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-fluoro-2-methyl-quinoline-3-carboxamide		1.09	405	G	
E-90	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-fluoro-4-methyl-quinoline-3-carboxamide		1.08	404	G	154 - 158
E-91	N-[1-benzyl-1-(trifluoromethyl) butyl]-8-fluoro-quinoline-3-carboxamide		1.15	405	G	
E-92	N-[1-benzyl-1-(trifluoromethyl) but-3-enyl]-8-fluoro-quinoline-3-carboxamide		1.13	403	G	

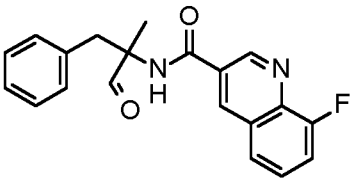
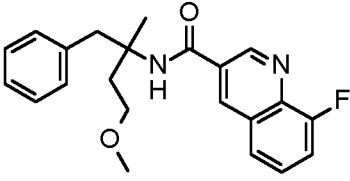
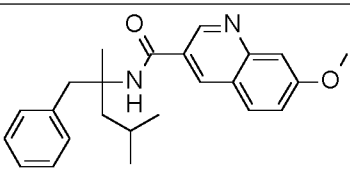
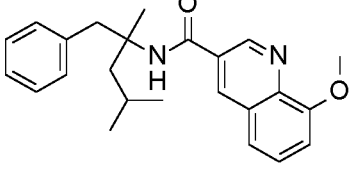
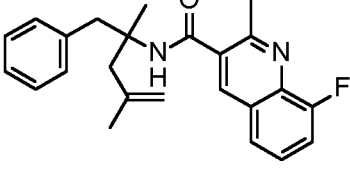
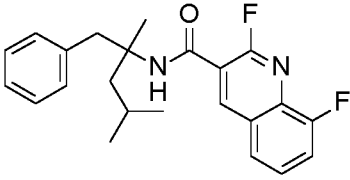
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-93	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-chloro-7-fluoro-quinoline-3-carboxamide					150 - 152
E-94	N-(1-benzyl-3,3-difluoro-1-methyl-allyl)-8-fluoro-quinoline-3-carboxamide		1.05	371	G	99 - 101
E-95	N-(1-benzyl-3,3-difluoro-1-methyl-propyl)-8-fluoro-quinoline-3-carboxamide		1.01	373	G	
E-96	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-4-chloro-8-fluoro-quinoline-3-carboxamide		1.13	425	G	
E-97	N-(1-benzyl-3-chloro-3,3-difluoro-1-methyl-propyl)-8-fluoro-quinoline-3-carboxamide		1.10	407-409	G	
E-98	8-fluoro-N-[3,3,3-trifluoro-1-[(2-fluorophenyl)methyl]-1-methyl-		1.07	409	G	131 - 133

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
	propyl]quinoline-3-carboxamide					
E-99	8-fluoro-N-[3,3,3-trifluoro-1-[(3-fluorophenyl)methyl]-1-methyl-propyl]quinoline-3-carboxamide		1.07	409	G	149 - 151
E-100	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7-fluoro-8-methyl-quinoline-3-carboxamide		1.17	405	G	127 - 129
E-101	N-(1-benzyl-1-ethyl-3,3,3-trifluoro-propyl)-8-fluoro-quinoline-3-carboxamide		1.11	405	G	127 - 129
E-102	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-7,8-difluoro-quinoline-3-carboxamide		1.10	409	G	158 - 160
E-103	N-[1-benzyl-1-(methoxymethyl)-3-methyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide		1.13	393	G	147 - 149

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-104	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-chloro-4-methyl-quinoline-3-carboxamide		1.13	421	G	184 - 186
E-105	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-cyano-4-methyl-quinoline-3-carboxamide		1.07	412	G	194 - 197
E-106	N-(1-benzyl-1,3-dimethyl-butyl)-2-chloro-8-fluoro-quinoline-3-carboxamide		1.21	399	G	106 - 108
E-107	N-(1-benzyl-1,3-dimethyl-butyl)-8-chloro-4-methyl-quinoline-3-carboxamide		1.21	395-397	G	65 - 70
E-108	N-(1-benzyl-1,3-dimethyl-butyl)-8-cyano-quinoline-3-carboxamide		1.14	372	G	160 - 162

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-109	N-(1-benzyl-1,3-dimethyl-butyl)-8-cyano-4-methyl-quinoline-3-carboxamide		1.15	386	G	
E-110	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-chloro-2-methyl-quinoline-3-carboxamide		1.16	422	G	176 - 179
E-111	N-(1-benzyl-2-cyclobutyl-1-methyl-ethyl)quinoline-3-carboxamide		1.16	359	G	88 - 90
E-112	N-(1-benzyl-2-cyclobutyl-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.18	377	G	125 - 127
E-113	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-cyano-2-methyl-quinoline-3-carboxamide		1.10	412	G	136 - 140

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-114	N-(1-benzyl-1,3-dimethyl-butyl)-8-fluoro-quinoline-3-carbothioamide		1.28	382	G	150-153
E-115	N-(1-benzyl-3,3,3-trifluoro-1-methyl-propyl)-8-fluoro-quinoline-3-carbothioamide		1.19	408	G	173-175
E-116	N-(1-benzyl-2,2-diethoxy-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.07	411	G	
E-117	N-(1-benzyl-2-methoxyimino-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.01	366	G	
E-118	N-(1-benzyl-3-methoxy-1,3-dimethyl-butyl)-8-fluoro-quinoline-3-carboxamide		1.14	395	G	118-120
E-119	N-(1-benzyl-3-hydroxy-1-methyl-propyl)-8-fluoro-quinoline-3-carboxamide		0.88	353	G	

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measure d	Method	MP °C
E-120	N-(1-benzyl-1-methyl-2-oxoethyl)-8-fluoroquinoline-3-carboxamide		0.92	337	G	
E-121	N-(1-benzyl-3-methoxy-1-methyl-propyl)-8-fluoroquinoline-3-carboxamide		1.02	367	G	
E-122	N-(1-benzyl-1,3-dimethyl-butyl)-7-methoxyquinoline-3-carboxamide		1.14	377	G	136-138
E-123	N-(1-benzyl-1,3-dimethyl-butyl)-8-methoxyquinoline-3-carboxamide		1.11	377	G	155-156
E-124	N-(1-benzyl-1,3-dimethyl-but-3-enyl)-8-fluoro-2-methylquinoline-3-carboxamide		1.14	377	G	
E-125	N-(1-benzyl-1,3-dimethyl-butyl)-2,8-difluoroquinoline-3-carboxamide		1.23	383	G	

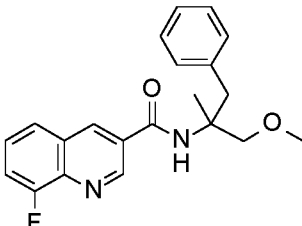
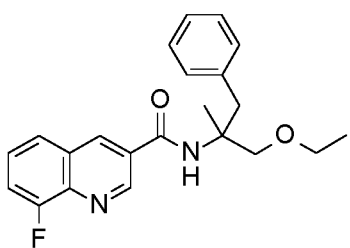
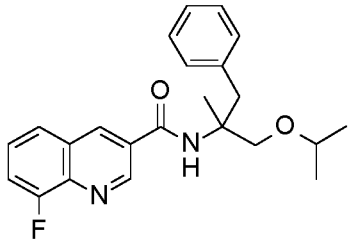
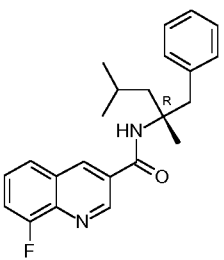
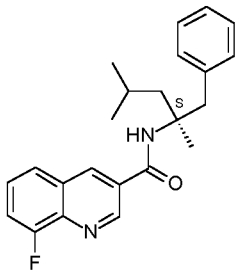
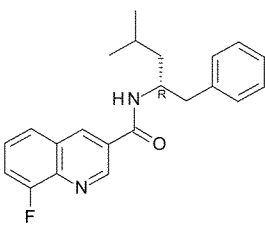
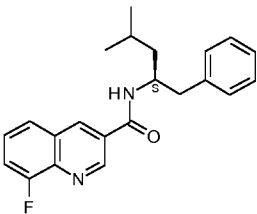
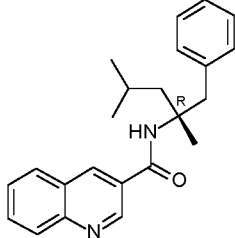
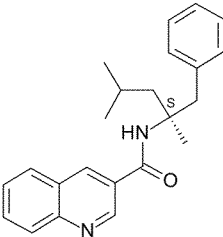
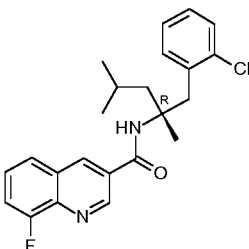
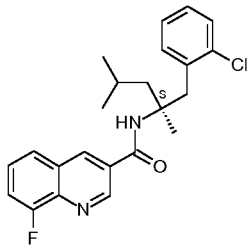
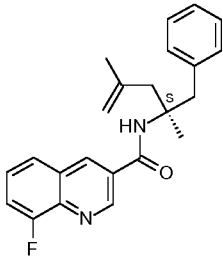
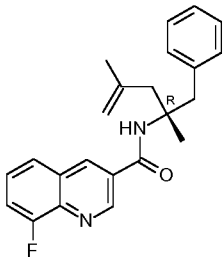
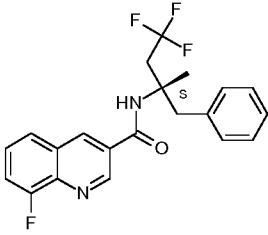
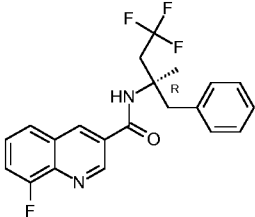
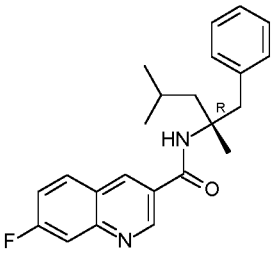
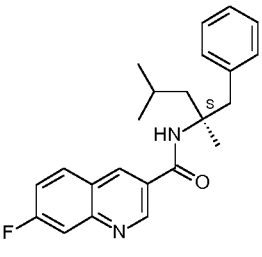
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	Method	MP °C
E-126	N-(1-benzyl-2-methoxy-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.00	353	G	
E-127	N-(1-benzyl-2-ethoxy-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.06	367	G	
E-128	N-(1-benzyl-2-isopropoxy-1-methyl-ethyl)-8-fluoro-quinoline-3-carboxamide		1.13	381	G	

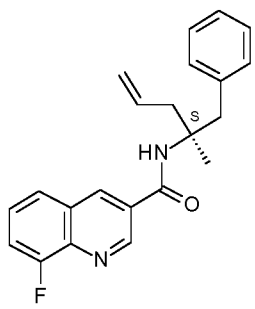
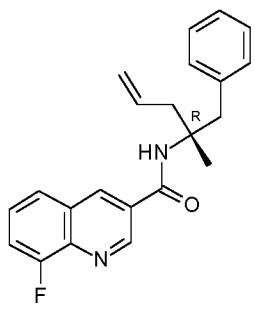
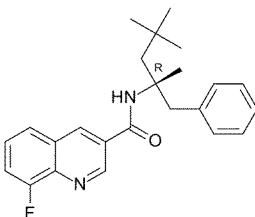
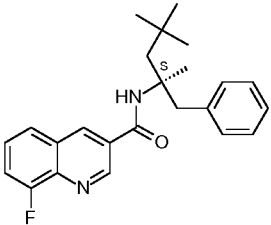
Table F: Physical data of compounds of formula (I) as individual enantiomers

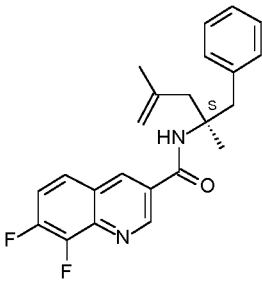
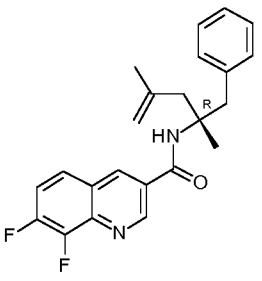
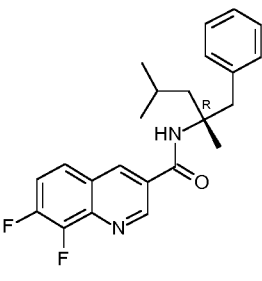
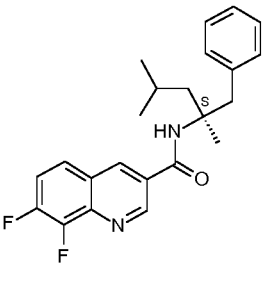
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-1	N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide		1.32	365	-90.79°	SFC: Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IA,

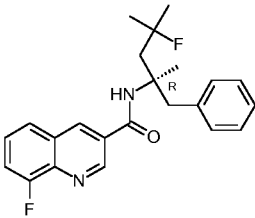
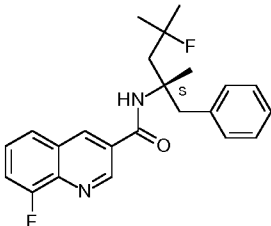
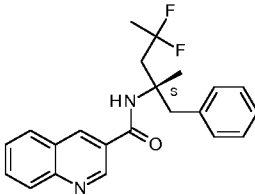
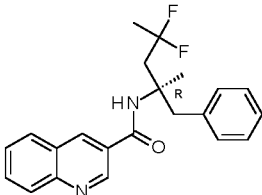
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-2	N-[(1S)-1-benzyl-1,3-dimethylbutyl]-8-fluoroquinoline-3-carboxamide		0.97	365	+92.65°	3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 25% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 240 nm Sample concentration: 1 mg/mL in Hept/EtOH 90/10 Injection: 3 μL
F-3	N-[(1R)-1-benzyl-3-methyl-butyl]-8-fluoroquinoline-3-carboxamide		3.43	351		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® ID
F-4	N-[(1S)-1-benzyl-3-methyl-butyl]-8-fluoroquinoline-3-carboxamide		2.61	351		3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: iPr gradient: 15% B in 4.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 235 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-5	N-[(1R)-1-benzyl-1,3-dimethylbutyl]quinoline-3-carboxamide		1.59	348		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC

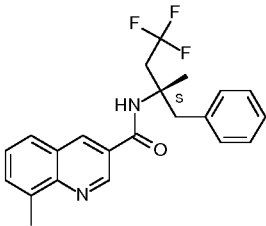
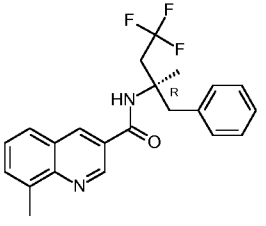
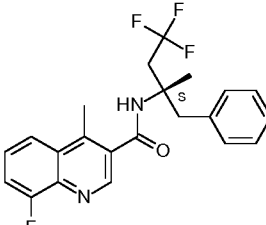
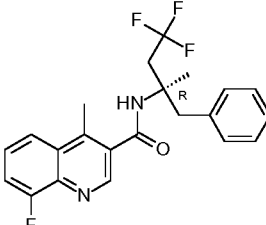
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-6	N-[(1S)-1-benzyl-1,3-dimethylbutyl]quinoline-3-carboxamide		1.02	348		CHIRALPAK® IA 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: EtOH gradient: 30% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 232 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-7	N-[(1R)-1-[(2-chlorophenyl)methyl]-1,3-dimethylbutyl]-8-fluoroquinoline-3-carboxamide		1.61	399		SFC:Waters Acquity UPC ³ /QDa PDA Detector Waters Acquity UPC ³ Column: Daicel SFC CHIRALPAK® IA 3μm, 0.3cm x 10cm, 40°C
F-8	N-[(1S)-1-[(2-chlorophenyl)methyl]-1,3-dimethylbutyl]-8-fluoroquinoline-3-carboxamide		1.21	399		Mobile phase: A: CO ₂ B: MeOH gradient: 20-40% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 235 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-9	N-[(1S)-1-benzyl-1,3-dimethylbut-3-enyl]-8-fluoroquinoline-3-carboxamide		8.10	363		Waters UPLC – Hclass DAD Detector Waters UPLC Column: Daicel CHIRALPAK® IA, 3μm, 0.46cm x

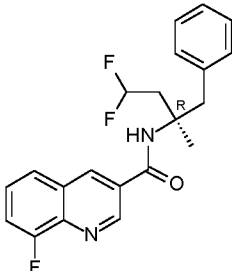
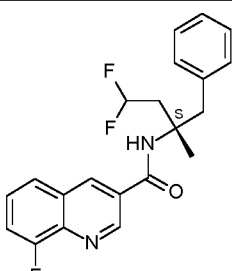
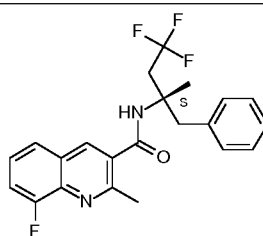
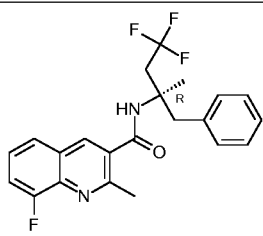
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-10	N-[(1R)-1-benzyl-1,3-dimethyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide		5.99	363		10cm Mobile phase: Hept/EtOH 80/20 Flow rate: 1.0 ml/min Detection: 235 nm Sample concentration: 1 mg/mL in ACN/Hept 50/50 Injection: 2μL
F-11	N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide		1.70	391	-109.9°	SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® ID, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: iPr gradient: 15% B in 2.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 235 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-12	N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide		2.16	391	+111.9°	
F-13	N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-7-fluoro-quinoline-3-carboxamide		1.53	365		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IA, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 20-40 % B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection:
F-14	N-[(1S)-1-benzyl-1,3-dimethyl-butyl]-7-fluoro-quinoline-3-carboxamide		1.15	365		

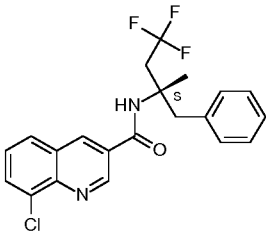
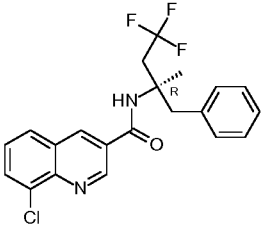
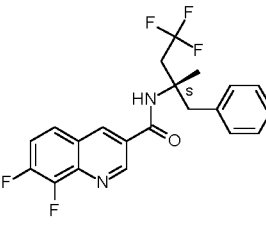
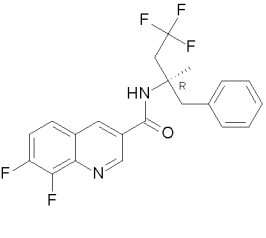
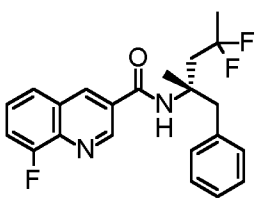
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
						230 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μ L
F-15	N-[(1S)-1-benzyl-1-methyl-but-3-enyl]-8-fluoroquinoline-3-carboxamide		2.17	349		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IA, 3 μ m, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 25% B in 4.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 235 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μ L
F-16	N-[(1R)-1-benzyl-1-methyl-but-3-enyl]-8-fluoroquinoline-3-carboxamide		1.58	349		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IA, 3 μ m, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 25% B in 4.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 235 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μ L
F-17	N-[(1R)-1-benzyl-1,3,3-trimethyl-butyl]-8-fluoroquinoline-3-carboxamide		1.45	379		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK®
F-18	N-[(1S)-1-benzyl-1,3,3-trimethyl-butyl]-8-fluoroquinoline-3-carboxamide		0.94	379		IA, 3 μ m, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 25% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 235 nm Sample concentration: 1

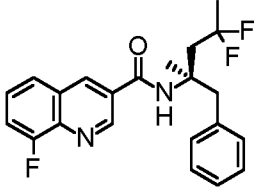
No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
						mg/mL in ACN/iPr 50/50 Injection: 1 μ L
F-19	N-[(1S)-1-benzyl-1,3-dimethyl-but-3-enyl]-7,8-difluoroquinoline-3-carboxamide		4.96	381		Column: Daicel SFC CHIRALPAK® IA, 3 μ m, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: iPr gradient: 15% B in 5.8 min
F-20	N-[(1R)-1-benzyl-1,3-dimethyl-but-3-enyl]-7,8-difluoroquinoline-3-carboxamide		4.11	381		ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 233 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μ L
F-21	N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-7,8-difluoroquinoline-3-carboxamide		1.50	383		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IA, 3 μ m, 0.3cm x 10cm, 40°C
F-22	N-[(1S)-1-benzyl-1,3-dimethyl-butyl]-7,8-difluoroquinoline-3-carboxamide		1.09	383		Mobile phase: A: CO ₂ B: MeOH gradient: 25% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 233 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μ L

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-23	N-[(1 <i>R</i>)-1-benzyl-3-fluoro-1,3-dimethylbutyl]-8-fluoroquinoline-3-carboxamide		0.88	383		SFC: IA, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 30% B in 1.8 min ABPR:
F-24	N-[(1 <i>S</i>)-1-benzyl-3-fluoro-1,3-dimethylbutyl]-8-fluoroquinoline-3-carboxamide		1.51	383		1800 psi Flow rate: 2.0 ml/min Detection: 230 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-25	N-[(1 <i>S</i>)-1-benzyl-3,3-difluoro-1-methylbutyl]quinoline-3-carboxamide		1.81	369		SFC: Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IA,
F-26	N-[(1 <i>R</i>)-1-benzyl-3,3-difluoro-1-methylbutyl]quinoline-3-carboxamide		1.30	369		3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 30% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 230 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-27	N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-methyl-quinoline-3-carboxamide		0.45	387		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® AY, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: EtOH gradient: 30% B in 1.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 2338 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-28	N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-methyl-quinoline-3-carboxamide		1.37	387		
F-29	N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-4-methyl-quinoline-3-carboxamide		1.97	405		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® OZ, 3μm, 0.3cm x 10cm, 40°C Mobile phase:
F-30	N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-4-methyl-quinoline-3-carboxamide		1.03	405		A: CO ₂ B: iPr gradient: 15% B in 1.8min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 220 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-31	N-[(1 <i>R</i>)-1-benzyl-3,3-difluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide		1.84	373		SFC: Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK®
F-32	N-[(1 <i>S</i>)-1-benzyl-3,3-difluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide		1.03	373		IF, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: MeOH gradient: 30% B in 4.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 220 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-33	N-[(1 <i>S</i>)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-2-methyl-quinoline-3-carboxamide		3.05	405		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® IC, 3μm, 0.3cm x 10cm, 40°C Mobile phase:
F-34	N-[(1 <i>R</i>)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-2-methyl-quinoline-3-carboxamide		3.67	405		A: CO ₂ B: iPR gradient: 10% B in 4.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 220 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
F-35	N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-chloro-quinoline-3-carboxamide		4.99	407		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® OZ, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: iPr gradient: 15% B in 2.8min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 237nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-36	N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-chloro-quinoline-3-carboxamide		1.16	407		
F-37	N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-7,8-difluoro-quinoline-3-carboxamide		1.05	409		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column: Daicel SFC CHIRALPAK® OZ, 3μm, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: iPr gradient: 10% B in 2.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 233 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μL
F-38	N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-7,8-difluoro-quinoline-3-carboxamide		1.51	409		
F-39	N-[(1S)-1-benzyl-3,3-difluoro-1-methyl-butyl]-8-fluoro-		3.30	387		SFC:Waters Acquity UPC ² /QDa PDA Detector Waters Acquity UPC ² Column:

No.	IUPAC name	STRUCTURE	RT (min)	[M+H] measured	$[\alpha]_D^{20}$	method
	quinoline-3-carboxamide					Daicel SFC CHIRALPAK® OZ, 3 μ m, 0.3cm x 10cm, 40°C Mobile phase: A: CO ₂ B: iPr gradient: 12% B in 4.8 min ABPR: 1800 psi Flow rate: 2.0 ml/min Detection: 234 nm Sample concentration: 1 mg/mL in ACN/iPr 50/50 Injection: 1 μ L
F-40	N-[(1R)-1-benzyl-3,3-difluoro-1-methyl-butyl]-8-fluoro-quinoline-3-carboxamide		2.10	387		

Biological examples

Botryotinia fuckeliana (*Botrytis cinerea*) / liquid culture (Gray mould)

- 5 Conidia of the fungus from cryogenic storage are directly mixed into nutrient broth (Vogels broth). After placing a (DMSO) solution of test compound into a microtiter plate (96-well format), the nutrient broth containing the fungal spores is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 3-4 days after application.
- 10 The following compounds of Tables E and F gave at least 80% control of *Botryotinia fuckeliana* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:
- E-1, E-2, E-3, E-5, E-6, E-7, E-8, E-10, E-11, E-12, E-13, E-14, E-15, E-16, E-17, E-18, E-19, E-20, E-21, E-22, E-23, E-24, E-25, E-26, E-27, E-28, E-29, E-30, E-31, E-32, E-33, E-34, E-35, E-36, E-37, E-38, E-39, E-40, E-41, E-42, E-43, E-44, E-45, E-46, E-47, E-48, E-49, E-50, E-51, E-52, E-53, E-54, E-55, E-56, E-57, E-58, E-59, E-60, E-61, E-62, E-63, E-64, E-65, E-66, E-67, E-69, E-70, E-71, E-72, E-73, E-74, E-75, E-76, E-77, E-79, E-80, E-81, E-82, E-84, E-85, E-86, E-87, E-88, E-89, E-90, E-91, E-92, E-93, E-94, E-95, E-96, E-97, E-98, E-99, E-100, E-101, E-102, E-103, E-104, E-106, E-107, E-109, E-110, E-111, E-112, E-113, E-114, E-115, E-116, E-117, E-118, E-119, E-121, E-123, E-124, E-125, F-1, F-2, F-3, F-4, F-5, F-6, F-7, F-8, F-9, F-10, F-11, F-12, F-13, F-14, F-16, F-17, F-18, F-19, F-20, F-21,

F-22, F-23, F-24, F-25, F-26, F-27, F-28, F-29, F-30, F-31, F-32, F-33, F-34, F-35, F-36, F-37, F-38, F-39, F-40

Fusarium culmorum / liquid culture (Head blight)

5 Conidia of the fungus from cryogenic storage 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 spores is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 3-4 days after application.

10 The following compounds of Tables E and F gave at least 80% control of *Fusarium culmorum* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

E-1, E-2, E-4, E-5, E-6, E-7, E-8, E-10, E-11, E-12, E-13, E-14, E-15, E-16, E-17, E-18, E-19, E-20, E-21, E-22, E-23, E-24, E-25, E-26, E-27, E-28, E-29, E-30, E-31, E-32, E-33, E-34, E-35, E-36, E-37, E-38, E-39, E-40, E-41, E-42, E-43, E-44, E-45, E-46, E-47, E-48, E-49, E-50, E-51, E-52, E-53, E-54, E-55, E-56, E-57, E-58, E-59, E-60, E-61, E-62, E-64, E-65, E-66, E-67, E-68, E-69, E-70, E-71, E-72, E-73, E-74, E-75, E-76, E-77, E-78, E-79, E-80, E-81, E-82, E-84, E-85, E-86, E-87, E-88, E-89, E-90, E-91, E-92, E-93, E-94, E-95, E-96, E-97, E-98, E-99, E-100, E-101, E-102, E-103, E-104, E-105, E-106, E-107, E-109, E-110, E-111, E-112, E-113, E-114, E-115, E-116, E-117, E-118, E-119, E-120, E-121, E-123, E-124, E-125, F-1, F-2, F-3, F-4, F-5, F-6, F-7, F-8, F-9, F-10, F-11, F-12, F-13, F-14, F-16, F-17, F-18, F-19, F-20, F-21, F-22, F-23, F-24, F-25, F-26, F-27, F-28, F-29, F-30, F-31, F-32, F-33, F-34, F-35, F-36, F-37, F-38, F-39, F-40

25 *Fusarium culmorum* / wheat / spikelet preventative (Head blight)

Wheat spikelets cv. Monsun are placed on agar in multiwell plates (24-well format) and sprayed with the formulated test compound diluted in water. The spikelets are inoculated with a spore suspension of the fungus 1 day after application. The inoculated spikelets are incubated at 20 °C and 60% rh under a light regime of 72 h semi darkness followed by 12 h light / 12 h darkness in a climate chamber and the activity of a compound is assessed as percent disease control compared to untreated when an appropriate level of disease damage appears on untreated check spikelets (6 - 8 days after application).

35 The following compounds of Tables E and F gave at least 80% control of *Fusarium culmorum* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

E-1, E-5, E-6, E-10, E-11, E-12, E-13, E-15, E-16, E-17, E-19, E-20, E-21, E-22, E-23, E-24, E-25, E-26, E-28, E-29, E-30, E-35, E-36, E-38, E-39, E-42, E-43, E-44, E-48, E-49, E-50, E-

51, E-52, E-55, E-56, E-57, E-58, E-59, E-60, E-61, E-62, E-66, E-67, E-69, E-70, E-71, E-72, E-74, E-75, E-76, E-77, E-79, E-80, E-81, E-82, E-84, E-85, E-86, E-88, E-89, E-90, E-91, E-92, E-93, E-94, E-95, E-96, E-97, E-98, E-99, E-100, E-101, E-102, E-103, E-104, E-105, E-106, E-107, E-109, E-113, E-114, E-125, F-1, F-2, F-3, F-4, F-5, F-9, F-10, F-11, F-12, F-13, F-14, F-16, F-17, F-18, F-19, F-20, F-21, F-23, F-24, F-25, F-26, F-27, F-28, F-29, F-31, F-32, F-33, F-35, F-36, F-37, F-39, F-40

Glomerella lagenarium (Colletotrichum lagenarium) / liquid culture (Anthracnose)

Conidia of the fungus from cryogenic storage 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 spores is added. The test plates are incubated at 24 °C and the inhibition of growth is measured photometrically 3-4 days after application.

The following compounds of Tables E and F gave at least 80% control of *Glomerella lagenarium* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

E-1, E-2, E-5, E-6, E-12, E-13, E-14, E-15, E-20, E-21, E-22, E-23, E-24, E-25, E-26, E-27, E-28, E-29, E-30, E-31, E-32, E-33, E-34, E-35, E-36, E-37, E-38, E-39, E-40, E-42, E-43, E-44, E-45, E-46, E-47, E-48, E-49, E-50, E-51, E-52, E-53, E-54, E-55, E-56, E-57, E-58, E-60, E-61, E-62, E-66, E-69, E-79, E-86, E-87, E-89, E-90, E-91, E-92, E-93, E-94, E-95, E-96, E-97, E-98, E-99, E-100, E-101, E-102, E-103, E-104, E-106, E-111, E-112, E-113, E-114, E-115, E-118, E-125, F-1, F-2, F-3, F-4, F-5, F-6, F-7, F-8, F-9, F-10, F-11, F-12, F-13, F-14, F-16, F-17, F-18, F-19, F-20, F-21, F-22, F-23, F-24, F-25, F-26, F-27, F-28, F-29, F-30, F-31, F-32, F-33, F-34, F-35, F-36, F-37, F-38, F-39, F-40

25

Gaeumannomyces graminis / liquid culture (Take-all of cereals)

Mycelial fragments of the fungus from cryogenic storage were 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 spores is

added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 4-5 days after application.

The following compounds of Tables E and F gave at least 80% control of *Gaeumannomyces graminis* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:
E-1, E-2, E-6, E-7, E-8, E-10, E-13, E-14, E-17, E-19, E-20, E-21, E-22, E-23, E-24, E-25, E-26, E-27, E-28, E-35, E-37, E-38, E-39, E-40, E-42, E-43, E-45, E-46, E-47, E-48, E-53, F-1, F-2, F-3, F-4, F-5, F-6, F-7, F-8, F-10, F-16, F-17, F-18

10 *Monographella nivalis* (*Microdochium nivale*) / liquid culture (foot rot cereals)

Conidia of the fungus from cryogenic storage 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 spores is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 4-5 days after application.

The following compounds of Tables E and F gave at least 80% control of *Monographella nivalis* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:
E-1, E-2, E-5, E-6, E-12, E-13, E-14, E-20, E-21, E-22, E-23, E-24, E-26, E-27, E-28, E-30, E-31, E-33, E-34, E-35, E-36, E-37, E-38, E-42, E-43, E-45, E-48, E-49, E-53, E-54, E-55, E-56, E-57, E-58, E-59, E-60, E-61, E-88, E-92, E-97, E-99, E-103, E-112, E-114, E-116, E-117, E-118, E-121, E-122, E-123, F-1, F-2, F-4, F-5, F-8, F-9, F-10, F-18, F-20, F-23, F-24, F-25, F-26, F-27, F-29, F-30, F-32, F-39

25 *Mycosphaerella arachidis* (*Cercospora arachidicola*) / liquid culture (early leaf spot)

Conidia of the fungus from cryogenic storage 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 spores is added. The

test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 4-5 days after application.

The following compounds of Tables E and F gave at least 80% control of *Mycosphaerella arachidis* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:
E-2, E-35, E-55, F-26

Magnaporthe grisea (Pyricularia oryzae) / liquid culture (Rice Blast)

Conidia of the fungus from cryogenic storage 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 spores is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 3-4 days after application.

The following compounds of Tables E and F gave at least 80% control of *Magnaporthe grisea* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

E-5, E-6, E-12, E-14, E-15, E-16, E-17, E-19, E-20, E-21, E-22, E-23, E-24, E-25, E-26, E-27, E-28, E-29, E-30, E-31, E-32, E-33, E-34, E-35, E-36, E-37, E-38, E-39, E-40, E-42, E-43, E-44, E-45, E-46, E-47, E-48, E-49, E-50, E-51, E-52, E-53, E-54, E-55, E-56, E-57, E-58, E-59, E-60, E-61, E-62, E-65, E-66, E-69, E-114, F-1, F-37, F-38, F-39, F-40.

Pyrenophora teres / barley / leaf disc preventative (Net blotch)

Barley leaf segments cv. Hasso are placed on agar in a multiwell plate (24-well format) and sprayed with the formulated test compound diluted in water. The leaf segments are inoculated with a spore suspension of the fungus 2 days after application. The inoculated leaf segments are incubated at 20 °C and 65% 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 disease control compared to untreated when an appropriate level of disease damage appears in untreated check leaf segments (5 - 7 days after application).

The following compounds of Tables E and F gave at least 80% control of *Pyrenophora teres* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:
E-14, E-26, E-55, E-114

Mycosphaerella graminicola (Septoria tritici) / liquid culture (Septoria blotch)

Conidia of the fungus from cryogenic storage 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 spores is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 4-5 days after application.

The following compounds of Tables E and F gave at least 80% control of

- 5 *Mycosphaerella graminicola* at 200 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

E-2, E-6, E-55, E-58, E-61, F-2, F-3, F-6, F-24, F-26

Sclerotinia sclerotiorum / liquid culture (cottony rot)

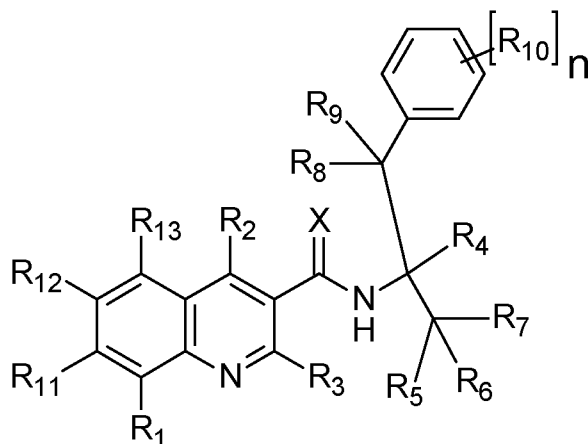
- 10 Mycelia fragments of a newly grown liquid culture of the fungus are directly mixed into nutrient broth (Vogels broth). After placing a (DMSO) solution of test compound into a microtiter plate (96-well format) the nutrient broth containing the fungal material is added. The test plates are incubated at 24 °C and the inhibition of growth is determined photometrically 3-4 days after application.

- 15 The following compounds of Tables E and F gave at least 80% control of *Sclerotinia sclerotiorum* at 20 ppm when compared to untreated control under the same conditions, which showed extensive disease development:

E-6, E-14, E-15, E-20, E-24, E-25, E-26, E-28, E-29, E-34, E-35, E-36, E-39, E-47, E-114, F-1, F-2, F-3, F-10

CLAIMS

1. A compound of formula (I):



(I)

wherein

X is O or S;

R₁ is hydrogen, halogen, methyl, methoxy or cyano;

R₂ and R₃ are each independently hydrogen, halogen or methyl;

R₄ is hydrogen, cyano, C₁-C₄ alkyl, or C₃-C₄ cycloalkyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, C₁-C₃ alkyl, C₁-C₃ alkoxy and C₁-C₃ alkylthio;

R₅ and R₆ are each independently selected from hydrogen, halogen, C₁-C₄ alkyl, C₁-C₄ alkoxy and C₁-C₄ alkylthio; or

R₅ and R₆ together with the carbon atom to which they are attached represent C=O, C=NOR_c, C₃-C₅ cycloalkyl or C₂-C₅ alkenyl, wherein the cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, C₁-C₃ alkyl, C₁-C₃ alkoxy and C₁-C₃ alkylthio;

R₇ is hydrogen, C₁-C₅ alkyl, C₃-C₅ cycloalkyl, C₂-C₅ alkenyl, C₃-C₅ cycloalkenyl, or C₂-C₅ alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, cycloalkenyl may be optionally substituted with 1 to 4 substituents independently selected from halogen, cyano, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl and C₁-C₃ alkylthio;

R₈ and R₉ are each independently selected from hydrogen, halogen, C₁-C₄ alkyl and C₁-C₄ alkoxy; or

R₈ and R₉ together with the carbon atom to which they are attached represent C₃-C₅ cycloalkyl, wherein the cycloalkyl may be optionally substituted with 1 to 3 substituents independently selected from halogen, cyano, C₁-C₃ alkyl, C₁-C₃ alkoxy and C₁-C₃ alkylthio;

each R_{10} independently represents halogen, nitro, cyano, formyl, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, C_3 - C_6 cycloalkyl, C_1 - C_5 alkoxy, C_3 - C_5 alkenyloxy, C_3 - C_5 alkynyloxy, C_1 - C_5 alkylthio, $-C(=NOR_c)C_1$ - C_5 alkyl, or C_1 - C_5 alkylcarbonyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy and alkylthio may be optionally substituted with 1 to 5 substituents independently selected from halogen, C_1 - C_3 alkyl, C_1 - C_3 alkoxy, cyano and C_1 - C_3 alkylthio; n is 0, 1, 2, 3, 4 or 5;

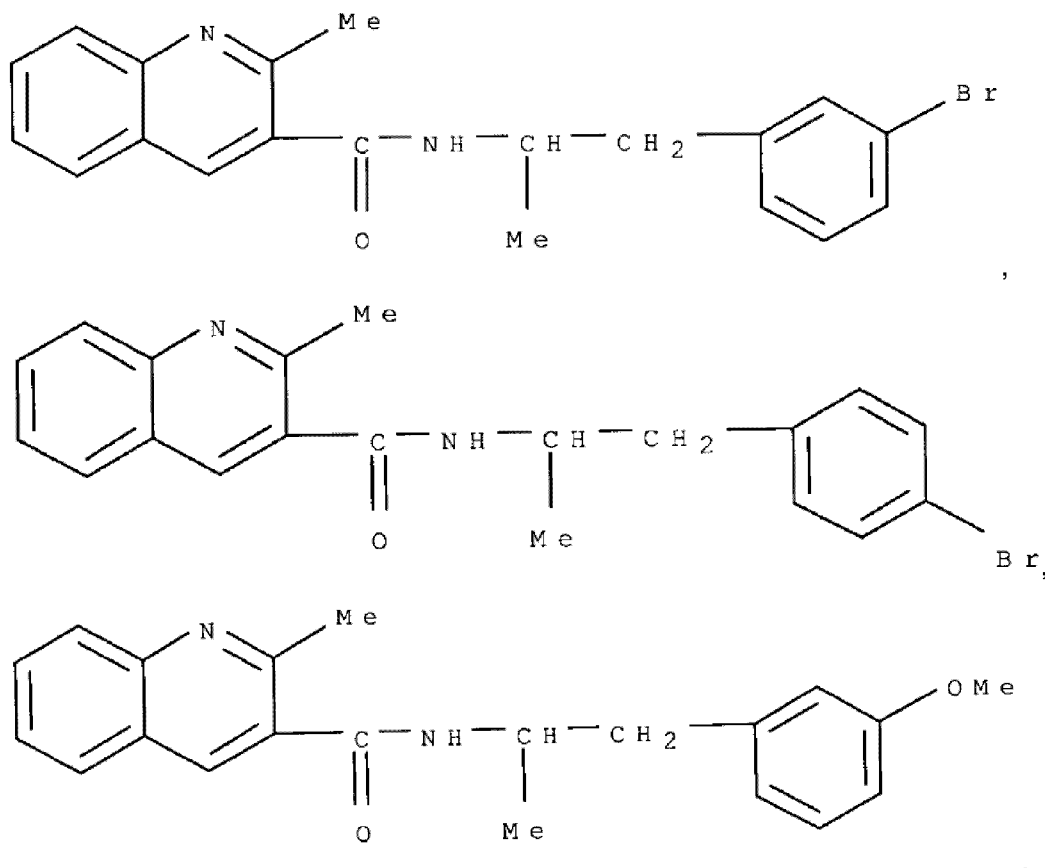
each R_c is independently selected from hydrogen, C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_3 - C_4 alkynyl, C_3 - C_4 cycloalkyl(C_1 - C_2)alkyl and C_3 - C_4 cycloalkyl, wherein the alkyl, cycloalkyl, alkenyl and alkynyl groups may be optionally substituted with 1 to 3 substituents independently selected from halogen and cyano;

R_{11} is hydrogen, halogen, methyl, methoxy or cyano;

R_{12} and R_{13} are each independently selected from hydrogen, halogen, methyl, methoxy or hydroxyl;

and salts and/or N-oxides thereof;

provided that the compound is not one of the following compounds:



2. A compound according to claim 1 wherein R_1 is hydrogen, fluoro, chloro, methyl, or cyano.

3. A compound according to claim 1 or 2 wherein R₂ and R₃ are each independently hydrogen or methyl.
4. A compound according to any one of claims 1, 2 or 3 wherein R₄ is hydrogen, cyano,
5 C₁-C₃ alkyl, or cyclopropyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, methoxy and methylthio.
5. A compound according to any one of claims 1, 2, 3 or 4 wherein R₅ and R₆ are each
10 independently selected from hydrogen, fluoro, C₁-C₂ alkyl, C₁-C₂ alkoxy and C₁-C₂ alkylthio; or R₅ and R₆ together with the carbon atom to which they are attached represent C=O or cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, methyl and cyano.
- 15 6. A compound according to any one of claims 1, 2, 3, 4, or 5 wherein R₇ is C₁-C₄ alkyl, C₃-C₄ cycloalkyl, C₂-C₄ alkenyl, or C₂-C₃ alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, hydroxyl and methylthio.
- 20 7. A compound according to any one of claims 1, 2, 3, 4, 5 or 6 wherein R₈ and R₉ are each independently selected from hydrogen, fluoro, C₁-C₂ alkyl and C₁-C₂ alkoxy; or R₈ and R₉ together with the carbon atom to which they are attached represent cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, cyano, and methyl.
- 25 8. A compound according to any one of claims 1, 2, 3, 4, 5, 6 or 7 wherein each R₁₀ independently represents halogen, cyano, C₁-C₃ alkyl, C₂-C₃ alkenyl, C₂-C₃ alkynyl, cyclopropyl, methoxy, allyloxy, propargyloxy, or C₁-C₂ alkylthio, wherein the alkyl, cyclopropyl, alkenyl, alkynyl, methoxy, allyloxy, propargyloxy and alkylthio may be
30 optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, methyl, and cyano; n is 0, 1, 2 or 3.
9. A compound according to any one of claims 1, 2, 3, 4, 5, 6, 7 or 8 wherein R₁₁ is
35 hydrogen, fluoro, chloro, methyl or cyano; and R₁₂ and R₁₃ are each independently selected from hydrogen, fluoro, methyl and hydroxyl.

10. A compound according to claim 1 wherein X is O or S; R₁ is hydrogen, fluoro, chloro, methyl, or cyano; R₂ and R₃ are each independently hydrogen or methyl; R₄ is hydrogen, cyano, C₁-C₃ alkyl, or cyclopropyl, wherein the alkyl and cycloalkyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, methoxy, and methylthio; R₅ and R₆ are each independently selected from hydrogen, fluoro, C₁-C₂ alkyl, C₁-C₂ alkoxy and C₁-C₂ alkylthio; or R₅ and R₆ together with the carbon atom to which they are attached represent C=O or cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, methyl and cyano; R₇ is C₁-C₄ alkyl, C₃-C₄ cycloalkyl, C₂-C₄ alkenyl, or C₂-C₃ alkynyl, wherein the alkyl, cycloalkyl, alkenyl, alkynyl, may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, cyano, methyl, hydroxyl and methylthio; R₈ and R₉ are each independently selected from hydrogen, fluoro, C₁-C₂ alkyl and C₁-C₂ alkoxy; or R₈ and R₉ together with the carbon atom to which they are attached represent cyclopropyl, wherein the cyclopropyl may be optionally substituted with 1 to 2 substituents independently selected from fluoro, cyano, and methyl; each R₁₀ independently represents halogen, cyano, C₁-C₃ alkyl, C₂-C₃ alkenyl, C₂-C₃ alkynyl, cyclopropyl, methoxy, allyloxy, propargyloxy, or C₁-C₂ alkylthio, wherein the alkyl, cyclopropyl, alkenyl, alkynyl, methoxy, allyloxy, propargyloxy and alkylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, methyl, and cyano; n is 0, 1, 2 or 3; R₁₁ is hydrogen, fluoro, chloro, methyl or cyano; and R₁₂ and R₁₃ are each independently selected from hydrogen, fluoro, methyl and hydroxyl; or a salt or N-oxide thereof.
11. A compound according to claim 1 wherein X is O or S; R₁ is hydrogen, fluoro, methyl, or cyano; R₂ is hydrogen and R₃ is hydrogen or methyl; or R₂ is hydrogen or methyl and R₃ is hydrogen; R₄ is hydrogen, cyano, methyl or ethyl, wherein the methyl and ethyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro and methoxy; R₅ and R₆ are each independently selected from hydrogen, fluoro, methyl, methoxy and methylthio; or R₅ and R₆ together with the carbon atom to which they are attached represent cyclopropyl; R₇ is C₁-C₄ alkyl, C₃-C₄ cycloalkyl, or C₂-C₄ alkenyl, wherein the alkyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro, hydroxyl, cyano and methyl; R₈ and R₉ are each independently selected from hydrogen, fluoro and methyl; or R₈ and R₉ together with the carbon atom to which they are attached represent cyclopropyl; each R₁₀ independently represents fluoro, chloro, cyano, methyl, cyclopropyl, methoxy or methylthio, wherein the methyl, cyclopropyl, methoxy

and methylthio may be optionally substituted with 1 to 3 substituents independently selected from fluoro and chloro; n is 0, 1 or 2; R₁₁ is hydrogen, fluoro, methyl or chloro; and R₁₂ and R₁₃ are each independently selected from hydrogen, fluoro and methyl; or a salt or N-oxide thereof.

5

12. A compound according to claim 1 wherein X is O or S; R₁ is hydrogen or fluoro; R₂ and R₃ are both hydrogen; R₄ is methyl or ethyl (wherein the methyl and ethyl may be optionally substituted with 1 to 3 fluoro substituents); R₅ and R₆ are each independently selected from hydrogen and fluoro; R₇ is methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, C₃-C₄ cycloalkyl, or C₂-C₄ alkenyl, wherein the methyl, ethyl, n-propyl, iso-propyl, sec-butyl, tert-butyl, cycloalkyl and alkenyl may be optionally substituted with 1 to 3 substituents independently selected from fluoro, chloro and methyl; R₈ and R₉ are each independently selected from hydrogen or fluoro; each R₁₀ independently represents fluoro, chloro, cyano or methyl, wherein the methyl may be optionally substituted with 1 to 3 fluoro substituents; n is 0, 1 or 2; and R₁₁ is hydrogen or fluoro; R₁₂ and R₁₃ are both hydrogen; or a salt or N-oxide thereof.
13. A compound according to to any one of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 wherein X is O.
14. A composition comprising a fungicidally effective amount of a compound of formula (I) as defined in any of claims 1 – 13.
15. A composition according to claim 14, wherein the composition further comprises at least one additional active ingredient and/or a diluent.
16. A method of combating, preventing or controlling phytopathogenic diseases which comprises applying to a phytopathogen, to the locus of a phytopathogen, or to a plant susceptible to attack by a phytopathogen, or to propagation material thereof, a fungicidally effective amount of a compound of formula (I) as defined in any of claims 1 – 13 or a composition comprising a fungicidally effective amount of a compound of formula (I) as defined in any of claims 1 – 13.

35

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2017/055273

A. CLASSIFICATION OF SUBJECT MATTER

INV. A01N43/42 C07D215/54
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)

A01N C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE REGISTRY CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 16 December 2009 (2009-12-16), XP002769886, Database accession no. 1197511-46-8 abstract	1-5,7-9, 13
X	----- WO 2006/016708 A1 (ISHIHARA SANGYO KAISHA [JP]; NAKAMURA YUJI [JP]; MITANI SHIGERU [JP];) 16 February 2006 (2006-02-16) page 114; claims 1,12-16; compounds 1-195	1-16
A	----- EP 1 669 348 A1 (EISAI CO LTD [JP]) 14 June 2006 (2006-06-14) page 212; claims; examples	1-16



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

5 May 2017

Date of mailing of the international search report

29/05/2017

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

Bedel, Christian

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2017/055273

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006016708	A1	16-02-2006	AR 050520 A1 01-11-2006
		AT 549927 T 15-04-2012	
		AU 2005272370 A1 16-02-2006	
		BR PI0514221 A 03-06-2008	
		CA 2575073 A1 16-02-2006	
		CY 1112603 T1 10-02-2016	
		DK 1776011 T3 23-04-2012	
		EP 1776011 A1 25-04-2007	
		ES 2383308 T3 20-06-2012	
		HR P20120285 T1 30-04-2012	
		JP 5391257 B2 15-01-2014	
		JP 2012102101 A 31-05-2012	
		KR 20070047778 A 07-05-2007	
		NZ 552838 A 30-07-2010	
		PT 1776011 E 25-05-2012	
		RS 52319 B 31-12-2012	
		SI 1776011 T1 29-06-2012	
		TW 200621156 A 01-07-2006	
		US 2008318779 A1 25-12-2008	
		US 2010261675 A1 14-10-2010	
		US 2010261735 A1 14-10-2010	
		WO 2006016708 A1 16-02-2006	
EP 1669348	A1	14-06-2006	EP 1669348 A1 14-06-2006
			JP 4795022 B2 19-10-2011
			US 2007105943 A1 10-05-2007
			US 2011195999 A1 11-08-2011
			WO 2005033079 A1 14-04-2005

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 80999-WO-ORG-P1	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2017/055273	International filing date (<i>day/month/year</i>) 7 March 2017 (07-03-2017)	(Earliest) Priority Date (<i>day/month/year</i>) 10 March 2016 (10-03-2016)
Applicant SYNGENTA PARTICIPATIONS AG		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6**bis**(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____
☐ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention
 b. ☐ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2017/055273

A. CLASSIFICATION OF SUBJECT MATTER

INV. A01N43/42 C07D215/54
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)

A01N C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE REGISTRY CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 16 December 2009 (2009-12-16), XP002769886, Database accession no. 1197511-46-8 abstract	1-5,7-9, 13
X	----- WO 2006/016708 A1 (ISHIHARA SANGYO KAISHA [JP]; NAKAMURA YUJI [JP]; MITANI SHIGERU [JP];) 16 February 2006 (2006-02-16) page 114; claims 1,12-16; compounds 1-195	1-16
A	----- EP 1 669 348 A1 (EISAI CO LTD [JP]) 14 June 2006 (2006-06-14) page 212; claims; examples -----	1-16



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

5 May 2017

Date of mailing of the international search report

29/05/2017

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

Bedel, Christian

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2017/055273

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006016708	A1	16-02-2006	AR 050520 A1 01-11-2006
			AT 549927 T 15-04-2012
			AU 2005272370 A1 16-02-2006
			BR PI0514221 A 03-06-2008
			CA 2575073 A1 16-02-2006
			CY 1112603 T1 10-02-2016
			DK 1776011 T3 23-04-2012
			EP 1776011 A1 25-04-2007
			ES 2383308 T3 20-06-2012
			HR P20120285 T1 30-04-2012
			JP 5391257 B2 15-01-2014
			JP 2012102101 A 31-05-2012
			KR 20070047778 A 07-05-2007
			NZ 552838 A 30-07-2010
			PT 1776011 E 25-05-2012
			RS 52319 B 31-12-2012
			SI 1776011 T1 29-06-2012
			TW 200621156 A 01-07-2006
			US 2008318779 A1 25-12-2008
			US 2010261675 A1 14-10-2010
			US 2010261735 A1 14-10-2010
			WO 2006016708 A1 16-02-2006
EP 1669348	A1	14-06-2006	EP 1669348 A1 14-06-2006
			JP 4795022 B2 19-10-2011
			US 2007105943 A1 10-05-2007
			US 2011195999 A1 11-08-2011
			WO 2005033079 A1 14-04-2005