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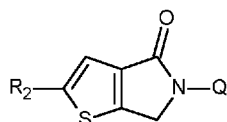
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(54) Title: PESTICIDALLY ACTIVE HETEROCYCLIC DERIVATIVES WITH SULFUR CONTAINING SUBSTITUENTS



- (57) Abstract: Compounds of the formula (I) wherein the substituents are as defined in claim 1. Furthermore, the present invention relates to agrochemical compositions which comprise compounds of formula (I), to preparation of these compositions, and to the use of the compounds or compositions in agriculture or horticulture for combating, preventing or controlling animal pests, including arthropods and in particular insects, molluscs, nematodes or representatives of the order Acarina.
- (I)

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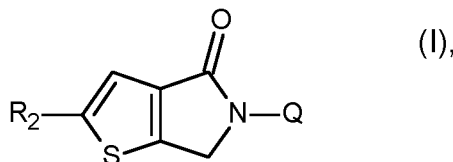
Pesticidally active heterocyclic derivatives with sulfur containing substituents

The present invention relates to pesticidally active, in particular insecticidally active heterocyclic derivatives containing sulfur substituents, to processes for their preparation, to compositions comprising those compounds, and to their use for controlling animal pests, including arthropods and in particular insects or representatives of the order Acarina.

Heterocyclic benzannulated dihydropyrrolone and phthalimide derivatives with sulfur-containing substituents have been described in the literature, for example in *J. Org. Chem.* **2003**, 62, 8240 and *Bull. Chem Soc. Chim. Belg.* **1997**, 106, 151. However, none of these references have described to have a pesticidal effect. Structurally different pesticidally active heterocyclic derivatives with sulfur-containing substituents have been described, for example in WO2012/012086848, WO2013/018928 and WO2019/131575.

It has now surprisingly been found that certain novel pesticidally active derivatives with sulfur containing substituents have favorable properties as pesticides.

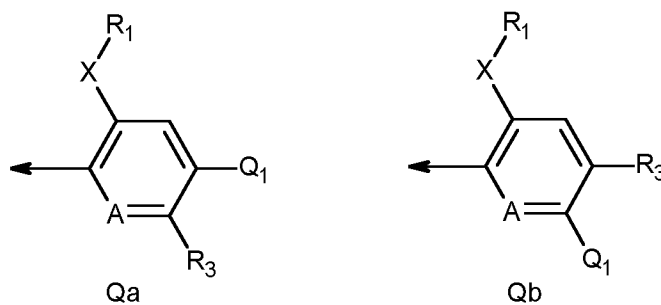
The present invention therefore provides compounds of formula I,



wherein

R₂ is C₁-C₆haloalkyl;

Q is a radical selected from the group consisting of formula Qa and Qb



wherein the arrow denotes the point of attachment to the nitrogen atom of the bicyclic ring;

and wherein A represents CH or N;

X is S, SO, or SO₂;

R₁ is C₁-C₄alkyl, or C₃-C₆cycloalkyl-C₁-C₄alkyl;

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Q₁ is hydrogen, halogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano, C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)₂, -N(R₄)C(=O)R₅, -N(R₄)CON(R₄)₂, (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or

Q₁ is a five- to six-membered aromatic ring system, linked via a ring carbon atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkoxy, C₁-C₄haloalkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl and C₁-C₄alkylsulfonyl; and said ring system can contain 1, 2 or 3 ring heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, where said ring system may not contain more than one ring oxygen atom and may not contain more than one ring sulfur atom; or

Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkoxy, C₁-C₄haloalkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl and C₁-C₄alkylsulfonyl; and said ring system contains 1, 2 or 3 ring heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, where said ring system contains at least one ring nitrogen atom and may not contain more than one ring oxygen atom and may not contain more than one ring sulfur atom;

R₃ is hydrogen, halogen or C₁-C₄alkyl;

each R₄ independently is hydrogen, C₁-C₄alkyl or C₃-C₆cycloalkyl; and

R₅ is C₁-C₆alkyl, C₁-C₆haloalkyl or C₃-C₆cycloalkyl.

The present invention also provides agrochemically acceptable salts, stereoisomers, enantiomers, tautomers and N-oxides of the compounds of formula I.

Compounds of formula I which have at least one basic centre can form, for example, acid addition salts, for example with strong inorganic acids such as mineral acids, for example perchloric acid, sulfuric acid, nitric acid, nitrous acid, a phosphorus acid or a hydrohalic acid, with strong organic carboxylic acids, such as C₁-C₄alkanecarboxylic acids which are unsubstituted or substituted, for example by halogen, for example acetic acid, such as saturated or unsaturated dicarboxylic acids, for example oxalic acid, malonic acid, succinic acid, maleic acid, fumaric acid or phthalic acid, such as hydroxycarboxylic acids, for example ascorbic acid, lactic acid, malic acid, tartaric acid or citric acid, or such as benzoic acid, or with organic sulfonic acids, such as C₁-C₄alkane- or arylsulfonic acids which are unsubstituted or substituted, for example by halogen, for example methane- or p-toluenesulfonic acid. Compounds of formula I which have at least one acidic group can form, for example, salts with bases, for example mineral salts such as alkali metal or alkaline earth metal salts, for example sodium, potassium or magnesium salts, or salts with ammonia or an organic amine, such as morpholine, piperidine, pyrrolidine, a mono-, di- or tri-lower-alkylamine, for example ethyl-, diethyl-, triethyl- or dimethylpropylamine, or a mono-, di- or trihydroxy-lower-alkylamine, for example mono-, di- or triethanolamine.

In each case, the compounds of formula (I) according to the invention are in free 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. Albin and S. Pietra, CRC Press, Boca Raton 1991.

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

Where substituents are indicated as being itself further substituted, this means that they carry one or more identical or different substituents, e.g. one to four substituents. Normally not more than three such optional substituents are present at the same time. Preferably not more than two such substituents are present at the same time (i.e. the group is substituted by one or two of the substituents indicated). Where the additional substituent group is a larger group, such as cycloalkyl or phenyl, it is most preferred that only one such optional substituent is present. 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 "C₁-C_nalkyl" as used herein refers to a saturated straight-chain or branched hydrocarbon radical attached via any of the carbon atoms having 1 to n carbon atoms, for example, any one of the radicals methyl, ethyl, n-propyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 2, 2-dimethylpropyl, 1-ethylpropyl, n-hexyl, n-pentyl, 1, 1-dimethylpropyl, 1, 2-dimethylpropyl, 1- methylpentyl, 2- methylpentyl, 3-methylpentyl, 4-methylpentyl, 1, 1-dimethylbutyl, 1,2- dimethylbutyl, 1, 3- dimethylbutyl, 2, 2-dimethylbutyl, 2, 3-dimethylbutyl, 3, 3-dimethylbutyl, 1-ethylbutyl, 2-ethylbutyl, 1,1, 2-trimethylpropyl, 1,2, 2-trimethylpropyl, 1-ethyl-1- methylpropyl, or 1-ethyl-2-methylpropyl.

The term "C₁-C_nhaloalkyl" as used herein refers to a straight-chain or branched saturated alkyl radical attached via any of the carbon atoms having 1 to n carbon atoms (as mentioned above), where some or all of the hydrogen atoms in these radicals may be replaced by fluorine, chlorine, bromine and/or iodine, i.e., for example, any one of chloromethyl, dichloromethyl, trichloromethyl, fluoromethyl, difluoromethyl, trifluoromethyl, chlorofluoromethyl, dichlorofluoromethyl, chlorodifluoromethyl, 2- fluoroethyl, 2-chloroethyl, 2-bromoethyl, 2-iodoethyl, 2, 2-difluoroethyl, 2,2, 2-trifluoroethyl, 2-chloro-2- fluoroethyl, 2-chloro-2, 2-difluoroethyl, 2, 2-dichloro-2-fluoroethyl, 2,2, 2-trichloroethyl, pentafluoroethyl, 2-fluoropropyl, 3-fluoropropyl, 2,2- difluoropropyl, 2, 3-difluoropropyl, 2-chloropropyl, 3-chloropropyl, 2, 3-dichloropropyl, 2- bromopropyl, 3-bromopropyl, 3,3, 3-trifluoropropyl, 3,3, 3- trichloropropyl, 2,2, 3,3, 3- pentafluoropropyl, heptafluoropropyl, 1-(fluoromethyl)-2-fluoroethyl, 1- (chloromethyl)-2-chloroethyl, 1-(bromomethyl)-2-bromoethyl, 4-fluorobutyl, 4-chlorobutyl, 4-bromobutyl or nonafluorobutyl. According a term "C₁-C₂-fluoroalkyl" would refer to a C₁-C₂-alkyl radical which

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carries 1,2, 3,4, or 5 fluorine atoms, for example, any one of difluoromethyl, trifluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 2, 2-difluoroethyl, 2,2, 2-trifluoroethyl, 1,1, 2, 2-tetrafluoroethyl or pentafluoroethyl.

- 5 The term "C₁-C_nalkoxy" as used herein refers to a straight-chain or branched saturated alkyl radical having 1 to n carbon atoms (as mentioned above) which is attached via an oxygen atom, i.e., for example, any one of methoxy, ethoxy, n-propoxy, 1-methylethoxy, n-butoxy, 1-methylpropoxy, 2-methylpropoxy or 1, 1-dimethylethoxy.
- 10 The term "C₁-C_nhaloalkoxy" as used herein refers to a C₁-C_nalkoxy radical as mentioned above which is partially or fully substituted by fluorine, chlorine, bromine and/or iodine, i.e., for example, any one of chloromethoxy, dichloromethoxy, trichloromethoxy, fluoromethoxy, difluoromethoxy, trifluoromethoxy, chlorofluoromethoxy, dichlorofluoromethoxy, chlorodifluoromethoxy, 2-
- 15 trifluoroethoxy, 2-chloroethoxy, 2-bromoethoxy, 2-iodoethoxy, 2, 2-difluoroethoxy, 2,2, 2-trifluoroethoxy, 2-chloro-2-fluoroethoxy, 2-chloro-2, 2-difluoroethoxy, 2, 2-dichloro-2-fluoroethoxy, 2,2, 2-trichloroethoxy, pentafluoroethoxy, 2-fluoropropoxy, 3-fluoropropoxy, 2, 2-difluoropropoxy, 2, 3-difluoropropoxy, 2-chloropropoxy, 3-chloropropoxy, 2, 3-dichloropropoxy, 2-bromopropoxy, 3-bromopropoxy, 3,3, 3-trifluoropropoxy, 3,3, 3-trichloropropoxy, 2,2, 3,3, 3-pentafluoropropoxy, heptafluoropropoxy, 1- (fluoromethyl)-2-fluoroethoxy, 1- (chloromethyl)-2-chloroethoxy, 1-
- 20 (bromomethyl)-2-bromoethoxy, 4-fluorobutoxy, 4-chlorobutoxy, or 4-bromobutoxy.

- The term "C₁-C_n-alkylsulfanyl" as used herein refers to a straight chain or branched saturated alkyl radical having 1 to n carbon atoms (as mentioned above) which is attached via a sulfur atom, i.e., for example, any one of methylthio, ethylthio, n-propylthio, 1-methylethylthio, butylthio, 1-
- 25 methylpropylthio, 2-methylpropylthio or 1, 1-dimethylethylthio.

- The term "C₁-C_nalkylsulfinyl" as used herein refers to a straight chain or branched saturated alkyl radical having 1 to n carbon atoms (as mentioned above) which is attached *via* the sulfur atom of the sulfinyl group, i.e., for example, any one of methylsulfinyl, ethylsulfinyl, n-propylsulfinyl, 1-methylethyl-sulfinyl, n-butylsulfinyl, 1-methylpropylsulfinyl, 2-methylpropylsulfinyl, 1, 1-dimethyl-
- 30 ethylsulfinyl, n-pentylsulfinyl, 1-methylbutylsulfinyl, 2-methylbutylsulfinyl, 3-methyl-butylsulfinyl, 1, 1-dimethylpropylsulfinyl, 1, 2-dimethylpropylsulfinyl, 2,2- dimethylpropylsulfinyl or 1-ethylpropylsulfinyl.

- 35 The term "C₁-C_nalkylsulfonyl" as used herein refers to a straight chain or branched saturated alkyl radical having 1 to n carbon atoms (as mentioned above) which is attached *via* the sulfur atom of the sulfonyl group, i.e., for example, any one of methylsulfonyl, ethylsulfonyl, n-propylsulfonyl, isopropylsulfonyl, n-butylsulfonyl, 1-methylpropylsulfonyl, 2-methylpropylsulfonyl or t-butylsulphonyl.

The term "C₁-C_ncyanoalkyl" as used herein refers to a straight chain or branched saturated alkyl radicals having 1 to n carbon atoms (as mentioned above) which is substituted by a cyano group, for example cyanomethylene, cyanoethylene, 1,1-dimethylcyanomethyl, cyanomethyl, cyanoethyl, and 1-dimethylcyanomethyl.

5

The suffix "-C₁-C_nalkyl" after terms such as "C₃-C_ncycloalkyl", wherein n is an integer from 1-6, as used herein refers to a straight chain or branched saturated alkyl radicals which is substituted by C₃-C_ncycloalkyl. An example of C₃-C_ncycloalkyl-C₁-C_nalkyl is for example, cyclopropylmethyl.

10 Similarly, the suffix "-C₁-C_nalkoxy" after terms such as "C₃-C_mcyanocycloalkyl", wherein n is an integer from 1-4 and m is an integer from 3-6, as used herein refers to a a straight-chain or branched saturated alkoxy radicals which is substituted by C₃-C_mcyanocycloalkyl. An example of C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy is for example, (1-cyanocyclopropyl)methoxy.

15 The term "C₁-C_nalkoxy" as used herein refers to a straight-chain or branched saturated alkyl radical having 1 to n carbon atoms (as mentioned above) which is attached via an oxygen atom, i.e., for example, any one of methoxy, ethoxy, n-propoxy, 1-methylethoxy, n-butoxy, 1-methylpropoxy, 2-methylpropoxy or 1, 1-dimethylethoxy.

20 The term "C₃-C₆cycloalkyl" as used herein refers to 3-6 membered cycloalkyl groups such as cyclopropane, cyclobutane, cyclopentane and cyclohexane.

Halogen is generally fluorine, chlorine, bromine or iodine. This also applies, correspondingly, to halogen in combination with other meanings, such as haloalkyl.

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In the context of this invention "mono- or polysubstituted" in the definition of the Q₁ substituents, means typically, depending on the chemical structure of the substituents, monosubstituted to five-times substituted, more preferably mono-, double- or triple-substituted.

30 In the context of the this invention, the phrase "Q₁ is a five- to six-membered aromatic ring system, linked via a ring carbon atom to the ring which contains the substituent A ..." and the phrase "Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A ...", as the case may be, refer to the manner of attachment of particular embodiments of the substituent Q₁ to the radical Q as represented by either formula Qa or formula Qb, as the case
35 may be.

In the context of this invention, examples of "Q₁ is a five- to six-membered aromatic ring system, linked via a ring carbon atom to the ring which contains the substituent A, ... ; and said ring system can contain 1, 2 or 3 ring heteroatoms ..." are, but not limited to, phenyl, pyrazolyl, triazolyl, pyridinyl and

pyrimidinyl; preferably phenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidin-2-yl, pyrimidin-4-yl, and pyrimidin-5-yl.

In the context of this invention, examples of "Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, ... ; and said ring system contains 1, 2 or 3 ring heteroatoms ..." are, but not limited to, pyrazolyl, pyrrolyl, imidazolyl and triazolyl; preferably pyrrol-1-yl, pyrazol-1-yl, triazol-2-yl, 1,2,4-triazol-1-yl, triazol-1-yl, and imidazol-1-yl.

Certain embodiments according to the invention are provided as set out below.

Embodiment 1 provides compounds of formula I, or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, as defined above.

Embodiment 2 provides compounds, or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, according to embodiment 1 wherein Q is Q_a and preferred values of R₂, A, X, R₁, Q₁, R₃, R₄ and R₅ are, in any combination thereof, as set out below:

Preferably R₂ is C₁-C₄haloalkyl;

More preferably R₂ is C₁-C₂haloalkyl;

Most preferably R₂ is CF₂CF₃ or CF₃;

Preferably A is N or CH;

Most preferably A is N;

Preferably X is S or SO₂;

Most preferably X is SO₂;

Preferably R₁ is C₁-C₄alkyl or cyclopropyl-C₁-C₄alkyl;

More preferably R₁ is ethyl or cyclopropylmethyl;

Most preferably R₁ is ethyl;

Preferably Q₁ is hydrogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano, C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy;

Also preferred is when Q₁ is a five- to six-membered aromatic ring system linked via a ring carbon atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said ring system can contain 1 or 2 ring nitrogen atoms;

Also preferred is when Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said ring system contains 2 or 3 ring nitrogen atoms.

More preferably Q₁ is hydrogen, trifluoromethyl, difluoroethyl, cyclopropyl, cyanocyclopropyl, cyanoisopropyl, cyanoisopropoxy, cyanocyclopropylmethoxy, trifluoroethoxy, difluoropropoxy,

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(oxazolidin-2-one)-3-yl, 2-pyridyloxy, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl;

Most preferably Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-

- 5 cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 2-pyridyloxy, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl;

Preferably each R₄ independently is hydrogen or C₁-C₄alkyl;

More preferably each R₄ independently is hydrogen or methyl;

- 10 Most preferably each R₄ is methyl;

Preferably R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl;

More preferably R₅ is methyl, ethyl or cyclopropyl;

Most preferably R₅ is methyl;

Preferably R₃ is hydrogen or C₁-C₄alkyl;

- 15 More preferably R₃ is hydrogen or methyl; and

Most preferably R₃ is hydrogen.

Embodiment 3 provides compounds, or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, according to embodiment 1 wherein Q is Q_b and preferred values of R₂,

- 20 R₁, X, Q₁, A, R₄, R₅ and R₃ are, in any combination thereof, as set out below:

Preferably R₂ is C₁-C₄haloalkyl;

More preferably R₂ is C₁-C₂haloalkyl;

Most preferably R₂ is CF₂CF₃ or CF₃;

Preferably A is N or CH;

- 25 Most preferably A is N;

Preferably X is S or SO₂;

Most preferably X is SO₂;

Preferably R₁ is C₁-C₄alkyl or cyclopropyl-C₁-C₄alkyl;

More preferably R₁ is ethyl or cyclopropylmethyl;

- 30 Most preferably R₁ is ethyl;

Preferably Q₁ is C₃-C₆cycloalkyl, -N(R₄)COR₅, or (oxazolidin-2-one)-3-yl;

Also preferred is when Q₁ is a five- to six-membered aromatic ring system linked via a ring carbon atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-

substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said

- 35 ring system can contain 1 or 2 ring nitrogen atoms;

Also preferred is when Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said ring system contains 2 or 3 ring nitrogen atoms.

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More preferably Q₁ is cyclopropyl, (oxazolidin-2-one)-3-yl, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl;

Most preferably Q₁ is cyclopropyl, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl),
 5 (oxazolidin-2-one)-3-yl, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl;

Preferably each R₄ independently is hydrogen or C₁-C₄alkyl;

More preferably each R₄ independently is hydrogen or methyl;

Most preferably each R₄ is methyl;

10 Preferably R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl;

More preferably R₅ is methyl, ethyl or cyclopropyl;

Most preferably R₅ is methyl;

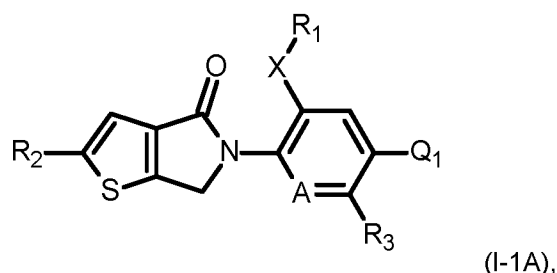
Preferably R₃ is hydrogen or C₁-C₄alkyl;

More preferably R₃ is hydrogen or methyl; and

15 Most preferably R₃ is hydrogen.

Further embodiments according to the invention are provided as set forth below.

20 A preferred group of compounds of formula I is represented by the compounds of formula I-1A



wherein A, R₁, R₂, R₃, X, Q₁, R₄ and R₅ are as defined under formula I above; or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-1A.

25 In one preferred group of compounds of formula I-1A,

A is CH or N;

R₁ is C₁-C₄alkyl or cyclopropyl-C₁-C₄alkyl;

R₂ is C₁-C₂haloalkyl;

R₃ is hydrogen or C₁-C₄alkyl;

30 X is S or SO₂;

Q₁ is hydrogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano,

C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -

N(R₄)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy; in which each R₄ independently is hydrogen or C₁-C₄alkyl; and R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl.

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In another preferred group of compounds of formula I-1A,

A is CH or N;

R₁ is ethyl or cyclopropylmethyl;

R₂ is CF₂CF₃ or CF₃;

5 R₃ is hydrogen or methyl;

X is S or SO₂; and

Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, or 2-pyridyloxy.

10

In another further preferred group of compounds of formula I-1A, Q₁ is a five- to six-membered aromatic ring system linked via a ring carbon atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said ring system can contain 1 or 2 ring nitrogen atoms. In this
15 embodiment, more preferably Q₁ is C-linked pyrimidinyl.

Also preferred compounds of formula I-1A are those wherein Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and
20 C₁-C₄haloalkyl; and said ring system contains 2 or 3 ring nitrogen atoms. In this embodiment, more preferably Q₁ is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; or Q₁ is N-linked triazolyl.

In another preferred group of compounds of formula I-1A,

25 A is CH or N;

R₁ is ethyl or cyclopropylmethyl;

R₂ is CF₂CF₃ or CF₃;

R₃ is hydrogen or methyl;

X is S or SO₂; and

30 Q₁ is 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

In compounds of formula I-1A and all of the preferred embodiments of compounds of formula I-1A mentioned above, unless otherwise specified, A, R₁, R₂, R₃, X, Q₁, R₄ and R₅ are as defined under formula I above;

35 preferably A is CH or N, most preferably A is N;

preferably R₁ is ethyl or cyclopropylmethyl; most preferably R₁ is ethyl;

preferably R₂ is C₁-C₂haloalkyl; most preferably R₂ is CF₂CF₃ or CF₃;

preferably X is S or SO₂; most preferably X is SO₂;

preferably R₃ is hydrogen;

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preferably Q₁ is hydrogen, trifluoromethyl, difluoroethyl, cyclopropyl, cyanocyclopropyl, cyanoisopropyl, cyanoisopropoxy, cyanocyclopropylmethoxy, trifluoroethoxy, difluoropropoxy, (oxazolidin-2-one)-3-yl, 2-pyridyloxy, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently

either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl;

more preferably Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 2-pyridyloxy, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

One further preferred group of compounds according to this embodiment are compounds of formula (I-1A-1) which are compounds of formula (I-1A) wherein

preferably A is N;

preferably R₁ is C₁-C₂alkyl; most preferably R₁ is ethyl;

preferably R₂ is C₁-C₂fluoroalkyl; most preferably R₂ is CF₂CF₃ or CF₃;

preferably X is S or SO₂; most preferably X is SO₂;

preferably R₃ is hydrogen;

preferably Q₁ is hydrogen, trifluoromethyl, cyclopropyl, difluoroethyl, cyanocyclopropyl, cyanoisopropyl, cyanoisopropoxy, cyanocyclopropylmethoxy, trifluoroethoxy, difluoropropoxy,

(oxazolidin-2-one)-3-yl, 2-pyridyloxy, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl;

more preferably Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy,

2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 2-pyridyloxy, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

One further preferred group of compounds according to this embodiment are compounds of formula (I-1A-2) which are compounds of formula (I-1A-1) wherein

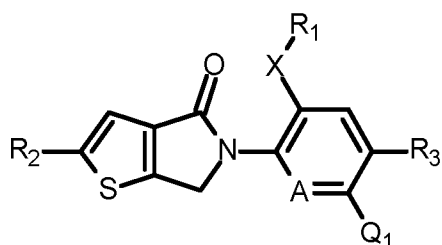
preferably R₁ is ethyl; preferably R₂ is CF₂CF₃ or CF₃; and preferably X is SO₂.

One further preferred group of compounds according to this embodiment are compounds of formula (I-1A-3) which are compounds of formula (I-1A-2) wherein

preferably A is CH.

Another preferred group of compounds of formula I is represented by the compounds of formula I-2A

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(I-2A),

wherein A, R₁, R₂, R₃, X, Q₁, R₄ and R₅ are as defined under formula I above; or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-2A.

5 In one preferred group of compounds of formula I-2A,

A is CH or N;

R₁ is C₁-C₄alkyl or cyclopropyl-C₁-C₄alkyl;

R₂ is C₁-C₂haloalkyl;

R₃ is hydrogen or C₁-C₄alkyl;

10 X is S or SO₂;

Q₁ is C₃-C₆cycloalkyl, -N(R₄)COR₅, or (oxazolidin-2-one)-3-yl; in which each R₄ independently is hydrogen or C₁-C₄alkyl; and R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl.

In another preferred group of compounds of formula I-2A,

15 A is CH or N;

R₁ is ethyl or cyclopropylmethyl;

R₂ is CF₂CF₃ or CF₃;

R₃ is hydrogen or methyl;

X is S or SO₂; and

20 Q₁ is cyclopropyl, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), or (oxazolidin-2-one)-3-yl.

In another further preferred group of compounds of formula I-2A, Q₁ is a five- to six-membered aromatic ring system linked via a ring carbon atom to the ring which contains the substituent A, said
25 ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said ring system can contain 1 or 2 ring nitrogen atoms. In this embodiment, more preferably Q₁ is C-linked pyrimidinyl.

Also preferred compounds of formula I-2A are those wherein Q₁ is a five-membered aromatic ring
30 system linked via a ring nitrogen atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono-substituted by substituents selected from the group consisting of halogen and C₁-C₄haloalkyl; and said ring system contains 2 or 3 ring nitrogen atoms. In this embodiment, more preferably Q₁ is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; or Q₁ is N-linked triazolyl.

In another preferred group of compounds of formula I-2A,

A is CH or N;

R₁ is ethyl or cyclopropylmethyl;

5 R₂ is CF₂CF₃ or CF₃;

R₃ is hydrogen or methyl;

X is S or SO₂; and

Q₁ is 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

10 In compounds of formula I-2A and all of the preferred embodiments of compounds of formula I-2A mentioned above, unless otherwise specified, A, R₁, R₂, R₃, X, Q₁, R₄ and R₅ are as defined under formula I above;

preferably A is CH or N, more preferably A is N;

preferably R₁ is ethyl or cyclopropylmethyl; most preferably R₁ is ethyl;

15 preferably R₂ is C₁-C₂haloalkyl; most preferably R₂ is CF₂CF₃ or CF₃;

preferably X is S or SO₂; most preferably X is SO₂;

preferably R₃ is hydrogen;

preferably Q₁ is cyclopropyl, (oxazolidin-2-one)-3-yl, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is

20 independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl;

more preferably Q₁ is cyclopropyl, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

25 One further preferred group of compounds according to this embodiment are compounds of formula (I-2A-1) which are compounds of formula (I-2A) wherein

preferably A is N;

preferably R₁ is C₁-C₂alkyl; most preferably R₁ is ethyl;

preferably R₂ is C₁-C₂fluoroalkyl; most preferably R₂ is CF₂CF₃ or CF₃;

30 preferably X is S or SO₂; most preferably X is SO₂;

preferably R₃ is hydrogen;

preferably Q₁ is cyclopropyl, (oxazolidin-2-one)-3-yl, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl;

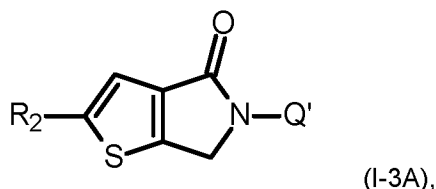
35 more preferably Q₁ is cyclopropyl, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

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One further preferred group of compounds according to this embodiment are compounds of formula (I-2A-2) which are compounds of formula (I-2A-1) wherein preferably R_1 is ethyl; preferably R_2 is CF_2CF_3 or CF_3 ; and preferably X is SO_2 .

- 5 One further preferred group of compounds according to this embodiment are compounds of formula (I-2A-3) which are compounds of formula (I-2A-2) wherein preferably A is CH.

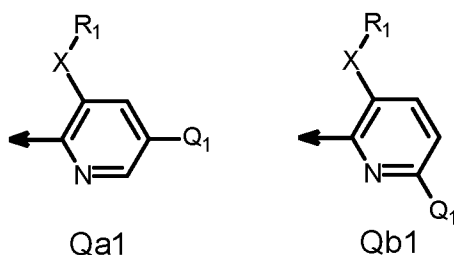
An outstanding group of compounds according to the invention are those of formula I-3A



wherein

R_2 is C_1 - C_4 haloalkyl, preferably CF_3 or CF_2CF_3 ;

Q' is a radical selected from the group consisting of formula Qa1 and Qb1



- 15 wherein the arrow denotes the point of attachment to the nitrogen atom of the bicyclic ring; and wherein
- X is S, SO , or SO_2 , preferably S or SO_2 , even more preferably SO_2 ;
- R_1 is C_1 - C_4 alkyl, preferably ethyl;
- Q_1 is hydrogen, C_1 - C_6 haloalkyl, C_3 - C_6 cycloalkyl, C_3 - C_6 cycloalkyl monosubstituted by cyano, C_1 - C_6 cyanoalkyl, C_1 - C_6 cyanoalkoxy, C_3 - C_6 cyanocycloalkyl- C_1 - C_4 alkoxy, C_1 - C_6 haloalkoxy, - $N(R_4)COR_5$, (oxazolidin-2-one)-3-yl or 2-pyridyloxy;
- 20 preferably Q_1 is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, $-N(CH_3)COCH_3$, $-N(CH_3)COCH_2CH_3$, $-N(CH_3)CO(cyclopropyl)$, (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or
- 25 Q_1 is unsubstituted pyrimidinyl, preferably pyrimidin-2-yl; or
- Q_1 is unsubstituted N-linked triazolyl, preferably 1,2,4-triazol-1-yl; or
- Q_1 is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; preferably Q_1 is 3-chloro-pyrazol-1-yl or 3-trifluoromethyl-pyrazol-1-yl;
- 30 R_4 is C_1 - C_4 alkyl, preferably methyl; and

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R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl, preferably methyl, ethyl or cyclopropyl; or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-3A.

One further outstanding group of compounds according to this embodiment are compounds of formula (I-3A-1) which are compounds of formula (I-3A) wherein

R₂ is C₁-C₂fluoroalkyl, preferably CF₃ or CF₂CF₃;

Q' is a radical selected from the group consisting of formula Qa1 and Qb1, wherein

X is SO₂;

R₁ is C₁-C₂alkyl, preferably ethyl;

Q₁ is hydrogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano, C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy;

preferably Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or

Q₁ is unsubstituted pyrimidinyl, preferably pyrimidin-2-yl; or

Q₁ is unsubstituted N-linked triazolyl, preferably 1,2,4-triazol-1-yl; or

Q₁ is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; preferably Q₁ is 3-chloro-pyrazol-1-yl or 3-trifluoromethyl-pyrazol-1-yl;

R₄ is C₁-C₄alkyl, preferably methyl; and

R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl, preferably methyl, ethyl or cyclopropyl.

One further outstanding group of compounds according to this embodiment are compounds of formula (I-3A-2) which are compounds of formula (I-3A) wherein

R₂ is CF₃ or CF₂CF₃;

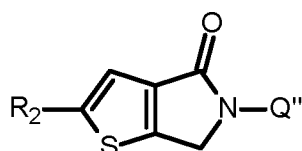
Q' is a radical selected from the group consisting of formula Qa1 and Qb1, wherein

X is SO₂;

R₁ is ethyl; and

Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 2-pyridyloxy, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

Another outstanding group of compounds according to the invention are those of formula I-4A



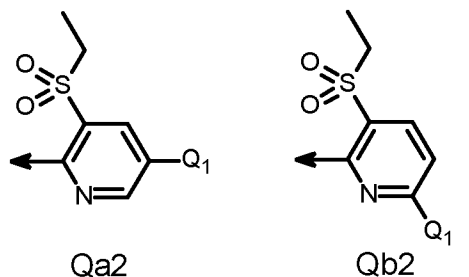
(I-4A),

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wherein

R₂ is C₁-C₄haloalkyl, preferably CF₃ or CF₂CF₃;

Q" is a radical selected from the group consisting of formula Qa2 and Qb2



- 5 wherein the arrow denotes the point of attachment to the nitrogen atom of the bicyclic ring;
and wherein

Q₁ is hydrogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano, C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy;

- 10 preferably Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or

Q₁ is unsubstituted pyrimidinyl, preferably pyrimidin-2-yl; or

- 15 Q₁ is unsubstituted N-linked triazolyl, preferably 1,2,4-triazol-1-yl; or

Q₁ is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; preferably Q₁ is 3-chloro-pyrazol-1-yl or 3-trifluoromethyl-pyrazol-1-yl;

R₄ is C₁-C₄alkyl, preferably methyl; and

R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl, preferably methyl, ethyl or cyclopropyl; or an agrochemically

- 20 acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-4A.

One further outstanding group of compounds according to this embodiment are compounds of formula (I-4A-1) which are compounds of formula (I-4A) wherein

R₂ is C₁-C₂fluoroalkyl, preferably CF₃ or CF₂CF₃.

25

One further outstanding group of compounds according to this embodiment are compounds of formula (I-4A-2) which are compounds of formula (I-4A-1) wherein

Q" is a radical selected from the group consisting of formula Qa2 and Qb2, wherein

- 30 Q₁ is hydrogen, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, -N(CH₃)COCH₃, 2-pyridyloxy, 3-chloro-pyrazol-1-yl, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

One further outstanding group of compounds according to this embodiment are compounds of formula (I-4A-3) which are compounds of formula (I-4A-1) wherein

Q" is a radical selected from the group consisting of formula Qa2 and Qb2, wherein

Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, 1,2,4-triazol-1-yl or pyrimidin-2-yl.

5

Compounds according to the invention may possess any number of benefits including, inter alia, advantageous levels of biological activity for protecting plants against insects 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 or environmental profile). In particular, it has been surprisingly found that certain compounds of formula (I) may show an advantageous safety profile with respect to non-target arthropods, in particular pollinators such as honey bees, solitary bees, and bumble bees. Most particularly, *Apis mellifera*.

10

15 In another aspect the present invention provides a composition comprising an insecticidally, acaricidally, nematocidally or molluscicidally effective amount of a compound of formula (I), or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, as defined in any of the embodiments under compounds of formula (I-1A), (I-1A-1), (I-1A-2), (I-1A-3), (I-2A), (I-2A-1), (I-2A-2), (I-2A-3), (I-3A), (I-3A-1), (I-3A-2), (I-4A), (I-4A-1), (I-4A-2), and (I-4A-3) and, optionally, an auxiliary or diluent.

20

In a further aspect the present invention provides a method of combating and controlling insects, acarines, nematodes or molluscs which comprises applying to a pest, to a locus of a pest, or to a plant susceptible to attack by a pest an insecticidally, acaricidally, nematocidally or molluscicidally effective amount of a compound of formula (I), or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, as defined in any of the embodiments under compounds of formula (I-1A), (I-1A-1), (I-1A-2), (I-1A-3), (I-2A), (I-2A-1), (I-2A-2), (I-2A-3), (I-3A), (I-3A-1), (I-3A-2), (I-4A), (I-4A-1), (I-4A-2), and (I-4A-3) (above) or a composition as defined above.

25

30 In a yet further aspect, the present invention provides a method for the protection of plant propagation material from the attack by insects, acarines, nematodes or molluscs, which comprises treating the propagation material or the site, where the propagation material is planted, with a composition as defined above.

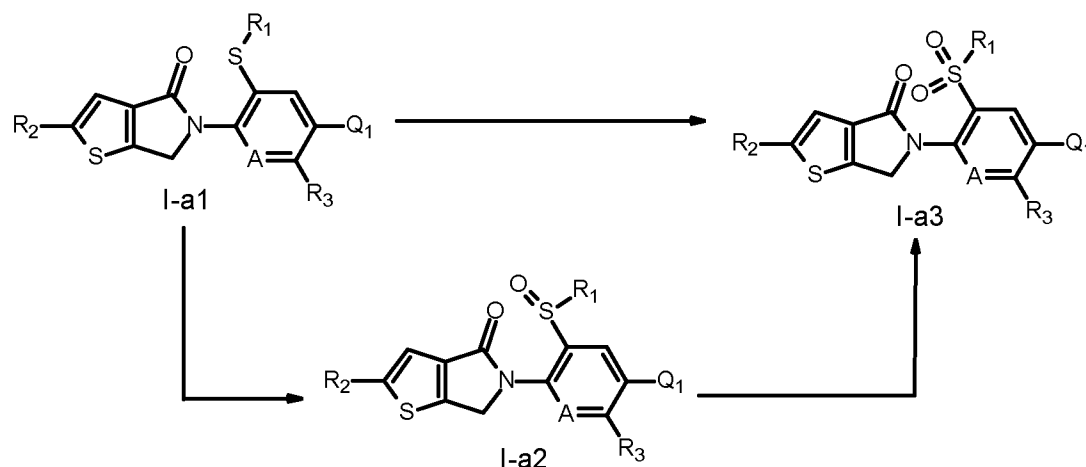
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35 The process according to the invention for preparing compounds of formula I is carried out by methods known to those skilled in the art. Compounds of formula I-a3, wherein X is SO₂ and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above, may be prepared by oxidation of compounds of formula I-a2, wherein X is SO and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above. The reaction can be performed with reagents such as a peracid, for example peracetic acid or m-chloroperbenzoic acid, or

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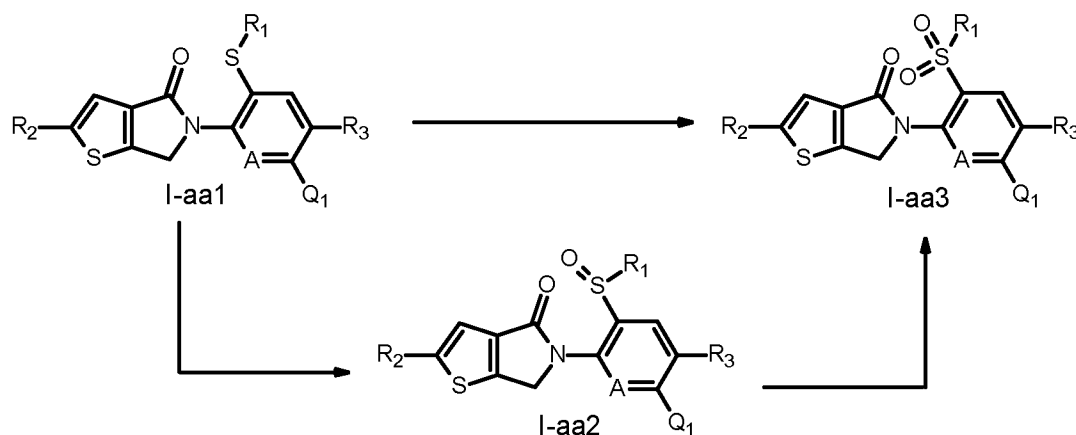
a hydroperoxide, as for example, hydrogen peroxide or tert-butylhydroperoxide, or an inorganic oxidant, such as a monoperoxo-disulfate salt or potassium permanganate. In a similar way, compounds of formula I-a2, wherein X is SO and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above, may be prepared by oxidation of compounds of formula I-a1, wherein X is S and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above, under analogous conditions described above. Similarly, compounds of formula I-a3, wherein X is SO₂ and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above, can be prepared by oxidation of compounds of formula I-a1, wherein X is S and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above, under analogous conditions described above. These reactions can be performed in various organic or aqueous solvents compatible to these conditions, by temperatures from below 0°C up to the boiling point of the solvent system. The transformation of compounds of the formula I-a1 into compounds of the formula I-a2 and I-a3 is represented in Scheme 1.

Scheme 1:



Compounds of formula I-aa2 and I-aa3 (scheme 2), wherein X is SO and SO₂ respectively, and A, R₁, R₂, R₃, and Q₁ are defined as under formula I above, may be prepared by analogous procedure as described in scheme 1 for the synthesis of compounds of formula I-a2 and I-a3.

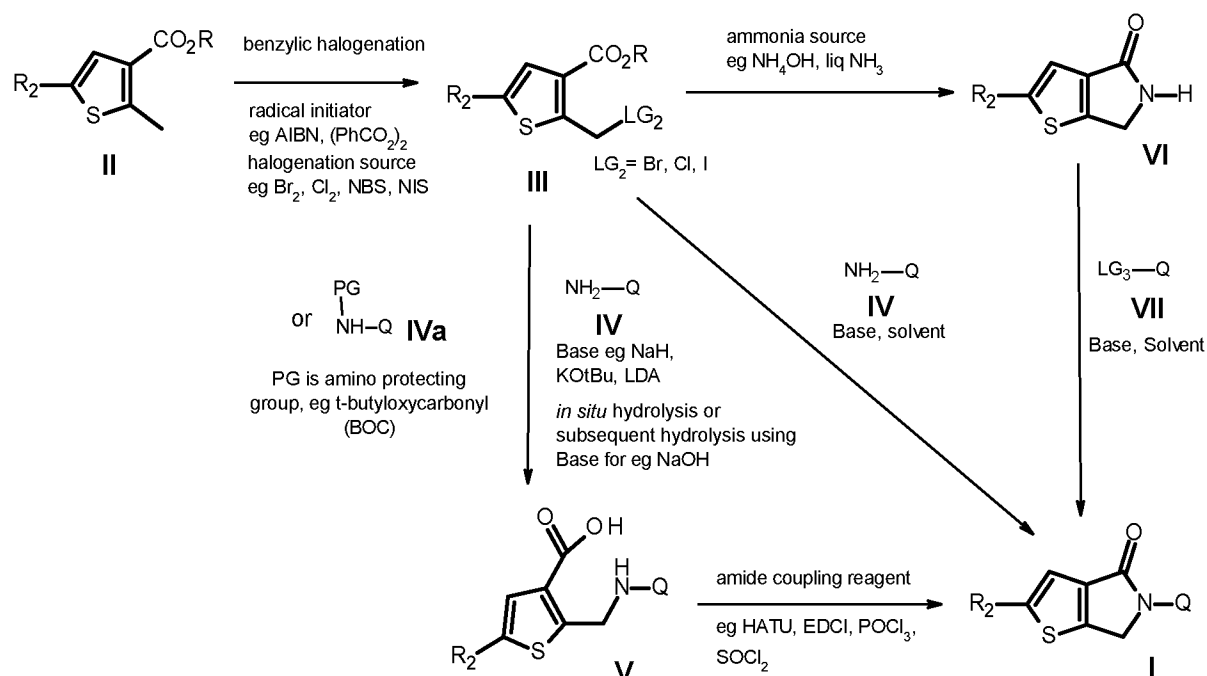
Scheme 2:



Compounds of formula I wherein R₂ and Q are defined as under formula I above,

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Scheme 3:



may be prepared (scheme 3) by reacting compounds of formula VI, wherein R₂ is as defined in

formula I above, with compounds of formula VII, wherein Q is as defined in formula I above and in

5 which LG₃ is a halogen (or a pseudo-halogen leaving group, such as a triflate), in the presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium hydride, in an appropriate solvent such as for example tetrahydrofuran, dioxane, N,N-dimethylformamide, N,N-

dimethylacetamide or acetonitrile, at temperatures between 0 and 150°C, optionally under microwave

10 irradiation. Alternatively, compounds of formula I wherein R₂ and Q are defined as under formula I above may be prepared by reacting compounds of formula VI, wherein R₂ is as defined in formula I

above, with compounds of formula VII, wherein Q is as defined in formula I above and in which LG₃ is a halogen, preferably bromo or iodo (or a pseudo-halogen leaving group, such as a triflate), in the

15 presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or potassium *tert*-butoxide, in the presence of a metal catalyst, either a copper catalyst, for example copper(I) iodide, optionally in the presence of a ligand, for example diamine ligands (e.g. N,N'-

dimethylethylenediamine or *trans*-cyclohexyldiamine), or dibenzylideneacetone (dba), or 1,10-phenanthroline, at temperatures between 30-180°C, optionally under microwave irradiation, or a

palladium catalyst, for example palladium(II)acetate, bis(dibenzylideneacetone)palladium(0) (Pd(dba)₂) or tris(dibenzylideneacetone)dipalladium(0) (Pd₂(dba)₃), optionally in form of a chloroform adduct, or a

20 palladium pre-catalyst, such as for example *tert*-BuBrettPhos Pd G3 [(2-Di-*tert*-butylphosphino-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl)-2-(2'-amino-1,1'-biphenyl)]palladium(II) methanesulfonate or BrettPhos Pd G3 [(2-di-cyclohexylphosphino-3,6-dimethoxy-2',4',6'- triisopropyl-1,1'-biphenyl)-2-(2'-

amino-1,1'-biphenyl)]palladium(II) methanesulfonate, and optionally in the presence of a ligand, for example SPhos, *t*-BuBrettPhos or Xantphos, at temperatures between 60-120°C, optionally under

25 microwave irradiation. The above alternative reactions may be carried out in the presence of a solvent

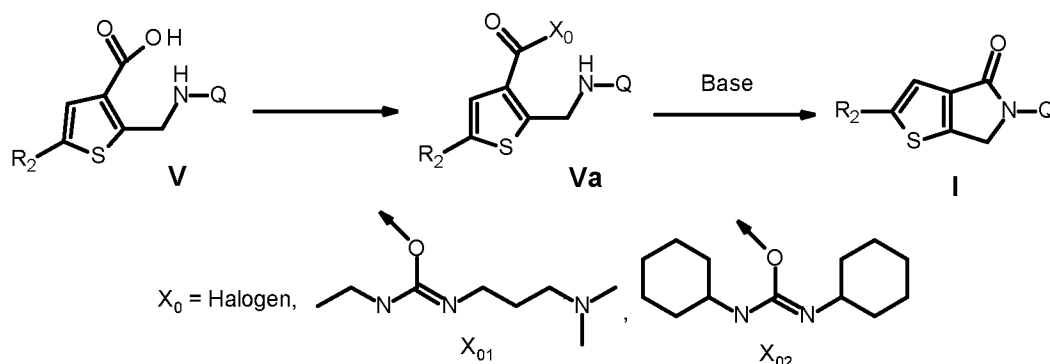
such as toluene, dimethylformamide DMF, N-methyl pyrrolidine NMP, dimethyl sulfoxide DMSO, dioxane, or tetrahydrofuran THF, and are described in the literature, for example in WO2012031004, WO2009042907 and Synthetic Communications, 41: 67–72, 2011.

Alternatively, compounds of formula I wherein R₂ and Q are defined as under formula I above, may be prepared by reacting compounds of formula III, wherein R₂ is as defined in formula I above and LG₂ is a leaving group, for example Br, Cl or I, preferably bromo, and R is C₁–C₈alkyl, benzyl or a phenyl group, with compounds of formula IV, wherein Q is as defined in formula I above, in the presence of a base such as sodium carbonate, potassium carbonate or cesium carbonate, sodium hydride, N,N-diisopropylethylamine or KOtBu, and in the presence of a solvent such as ethanol, methanol, dioxane, toluene, acetonitrile, DMF, DMA, DMSO, or THF, at temperatures between 0 and 150°C, optionally under microwave irradiation. Such reactions proceeds *via* nucleophilic substitution and subsequent cyclization and are reported in the literature, for example in WO2009042907.

Alternatively, compounds of formula I wherein R₂ and Q are defined as under formula I above, can be prepared by cyclizing compounds of formula V, wherein R₂ and Q are as defined in formula I, for example in the presence of phosphorus oxychloride (other amide coupling reagent may also be used, such as thionyl chloride SOCl₂, HATU or EDCI), optionally in the presence of a base, such as triethylamine, pyridine or Hünig's base, optionally in the presence of a solvent or diluent, such as toluene or xylene, at temperatures between 0 and 180°C, preferably between 20 and 120°C.

Compounds of formula I wherein R₂ and Q are defined as under formula I above,

Scheme 4:



can also be prepared (scheme 4) by cyclization of the formula Va, wherein R₂ and Q are defined as under formula I above, and in which X₀ is halogen, preferably chlorine, or X₀ is either X₀₁ or X₀₂, in the presence of a base, such as triethylamine, N,N-diisopropylethylamine or pyridine, optionally in the presence of a catalyst (such as 4-dimethylaminopyridine DMAP), in an inert solvents such as dichloromethane, tetrahydrofuran, dioxane, N,N-dimethyl-formamide, N,N-dimethylacetamide, acetonitrile, ethyl acetate or toluene, at temperatures between 0 and 50°C. Certain bases, such as pyridine and triethylamine, may be employed successfully as both base and solvent.

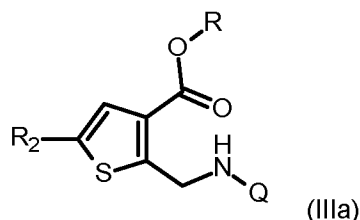
Compounds of formula Va, wherein R₂ and Q are defined as under formula I above, and in which X₀ is halogen, preferably chlorine, or X₀ is either X₀₁ or X₀₂, can be prepared by activation of compound of formula V, wherein R₂ and Q are defined as under formula I above, by methods known to those skilled

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in the art and described in, for example, Tetrahedron, 2005, 61 (46), 10827-10852. Preferred is the formation of an activated species Va, wherein R₂ and Q are defined as under formula I above, and in which X₀ is halogen, preferably chlorine. For example, compounds Va where X₀ is halogen, preferably chlorine, are formed by treatment of V with, for example, oxalyl chloride (COCl)₂ or thionyl chloride SOCl₂ in the presence of catalytic quantities of N,N-dimethylformamide DMF in inert solvents such as methylene chloride CH₂Cl₂ or tetrahydrofuran THF at temperatures between 20 to 100°C, preferably 25°C. Alternatively, treatment of compounds of formula V with, for example, 1-ethyl-3-(3-dimethylaminopropyl)carbo-diimide EDC or dicyclohexyl carbodiimide DCC will generate an activated species Va, wherein X₀ is X₀₁ or X₀₂ respectively, in an inert solvent, such as pyridine or tetrahydrofuran THF, optionally in the presence of a base, such as triethylamine, at temperatures between 50-180°C.

Compounds of formula VI, wherein R₂ is as defined in formula I above, can be prepared (scheme 3) by reacting compounds of formula III, wherein R₂ is as defined in formula I above and LG₂ is a leaving group, for example Br, Cl or I, preferably bromo, and R is C₁-C₆alkyl, benzyl or a phenyl group, with ammonia or surrogates of ammonia, for example NH₄OH, in the presence of a solvent such as ethanol, methanol, dioxane, toluene, DMF, DMA, DMSO, or THF, at temperatures between 0 and 150°C, optionally under microwave irradiation.

Compounds of formula V, wherein R₂ and Q are defined as under formula I above, can be prepared by a nucleophilic substitution reaction of compounds of formula III, wherein R₂ is as defined in formula I above and LG₂ is a leaving group, for example Br, Cl or I, preferably bromo, and R is C₁-C₆alkyl, benzyl or a phenyl group, with an amino compound of formula IV, wherein Q is as defined in formula I above, under conditions described above, followed by *in situ* hydrolysis of the formed intermediate ester of formula IIIa,



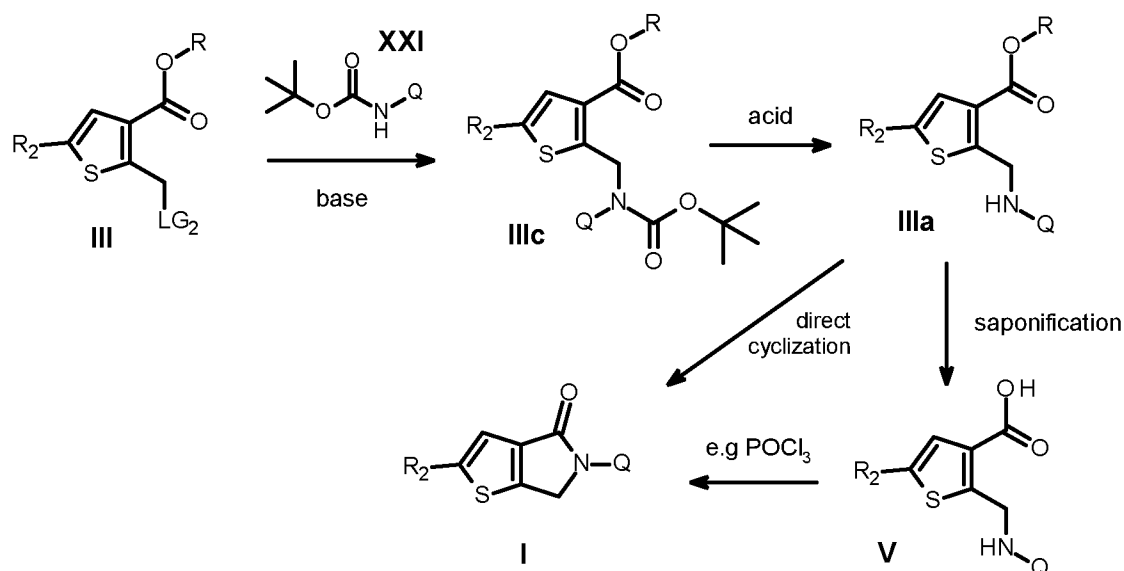
wherein R₂ and Q are defined as under formula I above, and in which R is C₁-C₆alkyl, benzyl or a phenyl group.

The *in situ* generated unhydrolyzed ester compound of formula IIIa may be isolated and can also be converted *via* a saponification reaction into the carboxylic acid of formula V, under conditions known to a person skilled in the art, for example in the presence of suitable base, such as sodium hydroxide NaOH, lithium hydroxide LiOH, or barium hydroxide Ba(OH)₂ (optionally in form of a hydrate), in the presence of a solvent such as ethanol, methanol, dioxane, tetrahydrofuran or water (or mixtures thereof). Alternatively, Krapcho-type conditions (e.g. heating the substrate IIIa in the presence of sodium or lithium chloride in N-methyl pyrrolidone or aqueous dimethylsulfoxide DMSO, optionally under microwave irradiation) can also be used to convert compounds of formula IIIa into compounds of formula V.

The direct conversion of compound of formula III to compound of formula IIIa can be carried out in the presence of base, such as sodium hydride, KOtBu, butyllithium, or lithium diisopropylamide amongst others, and in the presence of a solvent, such as dioxane, DMF, DMA, DMSO, or THF, at temperatures between -30 and 150°C.

- 5 The above reaction for the preparation of compounds of formula V can also be carried out by reacting compounds of formula III, with compounds of formula IVa, wherein Q is as defined in formula I above, and PG is an amino protecting group, for example tert-butyloxycarbonyl (BOC), under similar conditions as described above (as for the preparation of compounds of formula V by reacting compounds of formula III and compounds of formula IV), followed by deprotection of the amino protecting group PG. The deprotection of the amino protecting groups is well known to those skilled in the art, for example BOC protecting groups can be removed in the presence of acids, such as hydrochloric acid, or trifluoroacetic acid, optionally in the presence of an inert solvent, such as dichloromethane, tetrahydrofuran, dioxane or benzonitrile, at temperatures between 0 and 70°C. This process of forming compounds of formula V (and I) from compounds of formula III and IVa is detailed in scheme 4a and reflecting the particular situation wherein the group PG of IVa is tert-butyloxycarbonyl (BOC), defining compounds of formula XXI, wherein Q is as defined in formula I above.

Scheme 4a (substituent definitions mentioned previously remain valid):



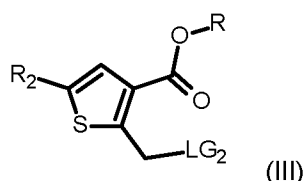
- 20 Compounds of formula III and compounds of formula XXI react to compounds of formula IIIc, in the presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium hydride, or N,N-diisopropylethylamine or potassium *tert*-butoxide KOtBu, in the presence of a solvent such as ethanol, methanol, dioxane, toluene, acetonitrile, DMF, N,N-dimethylacetamide DMA, DMSO, or THF, at temperatures between 0 and 150°C, optionally under microwave irradiation.
- 25 *tert*-Butyloxycarbonyl (BOC) group removal in compounds of formula IIIc, mediated by acids, such as hydrochloric acid, or trifluoroacetic acid, optionally in the presence of an inert solvent, such as dichloromethane, tetrahydrofuran, dioxane or benzonitrile, at temperatures between 0 and 70°C,

generates compounds of formula IIIa. Saponification of compounds of formula IIIa in the presence of a suitable base, for example sodium hydroxide NaOH, lithium hydroxide LiOH or barium hydroxide Ba(OH)₂, in the presence of a solvent such as ethanol, methanol, dioxane, tetrahydrofuran or water (or mixtures thereof), forms the carboxylic acids of formula V (alternatively, Krapcho-type conditions as described above may be used). Cyclization of compounds of formula V to compounds of formula I is achieved, for example, in the presence of phosphorus oxychloride (other amide coupling reagent may also be used, such as thionyl chloride SOCl₂, HATU or EDCI), optionally in the presence of a base, such as triethylamine, pyridine or Hünig's base, optionally in the presence of a solvent or diluent, such as toluene or xylene, at temperatures between 0 and 180°C, preferably between 20 and 120°C.

Alternatively, a direct cyclization of compounds of formula IIIa into compounds of formula I may be achieved under conditions mentioned below in scheme 9.

Compounds of formula III, wherein R₂ is as defined in formula I above and LG₂ is a leaving group, for example Br, Cl or I, preferably bromo, and R is C₁-C₆alkyl, benzyl or a phenyl group, can be prepared (scheme 3) by a radical induced benzylic halogenation of compounds of formula II, wherein R₂ is as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group. Such reaction are well known to those skilled in the art and may be carried out in the presence of electrophilic halogenating reagents such as bromine Br₂, N-bromosuccinimide NBS, chlorine Cl₂, N-chlorosuccinimide NCS or N-iodosuccinimide NIS amongst others, and in the presence of radical initiator, for example AIBN (azobisisobutyronitrile) or benzoyl peroxide, or under photochemical conditions, in the presence of solvents such as toluene, xylene, acetonitrile, hexane, dichloroethane, or carbon tetrachloride, and at temperatures ranging from 20°C to the boiling point of the reaction mixture. Such reactions are known, for example by the name of Wohl-Ziegler bromination, and are reported in literature, such as in *Synthesis*, 2015, 47, 1280-1290 and *J. Am. Chem. Soc.*, 1963, 85 (3), pp 354-355.

The compounds of formula III,

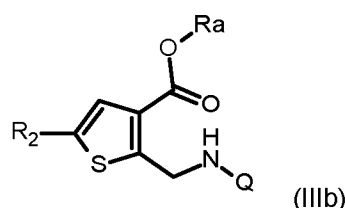


wherein

R₂ is as defined under formula I above, and in which LG₂ is a leaving group, for example bromo Br, chloro Cl or iodo I, and R is C₁-C₆alkyl, benzyl or a phenyl group, are novel, especially developed for the preparation of the compounds of formula I according to the invention and therefore represent a further object of the invention. The preferences and preferred embodiments of the substituents of the compounds of formula I are also valid for the compounds of formula III. Preferably, LG₂ is bromo or chloro; even more preferably LG₂ is bromo. Preferably R is C₁-C₆alkyl; even more preferably R is methyl or ethyl.

The compounds of formula IIIb, encompassing compounds of formula IIIa and compounds of formula V,

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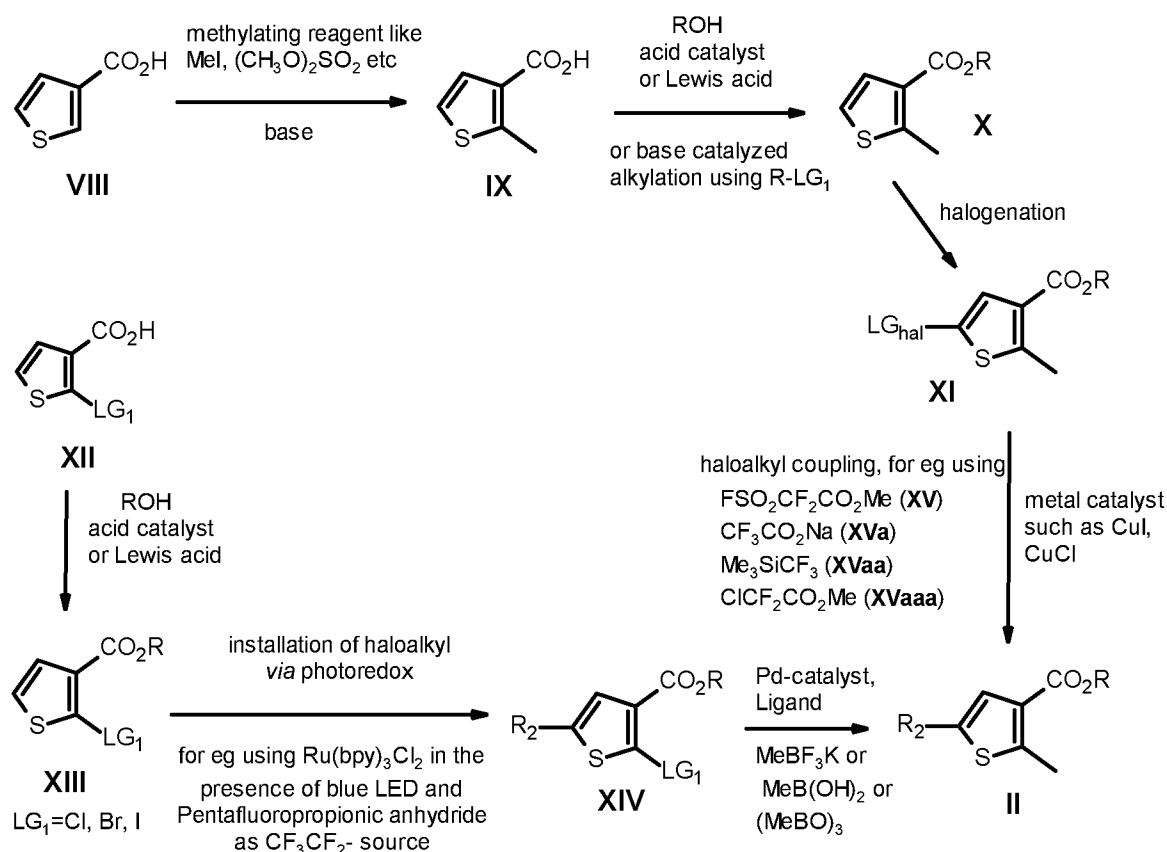
wherein

R₂ and Q are as defined under formula I above, and in which Ra is hydrogen, C₁-C₆alkyl, benzyl or a phenyl group, are novel, especially developed for the preparation of the compounds of formula I

- 5 according to the invention and therefore represent a further object of the invention. The preferences and preferred embodiments of the substituents of the compounds of formula I are also valid for the compounds of formula IIIb. Preferably, Ra is hydrogen or C₁-C₆alkyl; even more preferably, Ra is hydrogen, methyl or ethyl; most preferably Ra is hydrogen.

- 10 Compounds of formula II, wherein R₂ is as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group,

Scheme 5:



may be prepared (scheme 5) by a Suzuki reaction, which involves for example, reacting compounds of formula XIV, wherein R₂ is as defined in formula I above, LG₁ is a halogen Br, Cl, or I, preferably Cl, and in which R is C₁-C₆alkyl, benzyl or a phenyl group, with trimethylboroxine (MeBO)₃ or potassium methyltrifluoroborate MeBF₃K, amongst other methyl boronic acid equivalents. The reaction may be

catalyzed by a palladium based catalyst, for example tetrakis(triphenyl-phosphine)palladium(0), (1,1'-bis(diphenylphosphino)ferrocene)dichloro-palladium-dichloromethane (1:1 complex) or chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (XPhos palladacycle), in presence of a base, like sodium carbonate, tripotassium phosphate or cesium fluoride, in a solvent or a solvent mixture, like, for example dioxane, acetonitrile, N,N-dimethyl-formamide, a mixture of 1,2-dimethoxyethane and water or of dioxane/water, or of toluene/water, preferably under inert atmosphere. The reaction temperature can preferentially range from room temperature to the boiling point of the reaction mixture, or the reaction may be performed under microwave irradiation. Such Suzuki reactions are well known to those skilled in the art and have been reviewed, for example, in *J. Organomet. Chem.* 576, 1999, 147–168.

Compounds of formula XIV, wherein R_2 is as defined in formula I above, LG_1 is a halogen Br, Cl, or I, preferably Cl, and in which R is C_1 - C_6 alkyl, benzyl or a phenyl group, can be prepared by reacting compounds of formula XIII, wherein LG_1 is a halogen Br, Cl, or I, preferably Cl, and in which R is C_1 - C_6 alkyl, benzyl or a phenyl group, with a R_2 haloalkyl radical source (R_2 is as defined in formula I above) under visible light photoredox conditions, and in the presence of a photocatalyst. Examples of photocatalyst include tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate, tris(2,2'-bipyrimide)ruthenium(II) dichloride, dichlorotris(1,10-phenanthroline)ruthenium(II) chloride, $[Ir\{dFCF_3ppy\}_2(bpy)]PF_6$, or $Ir(dFppy)_3$, amongst other ruthenium or iridium based catalysts. Examples of a R_2 haloalkyl radical source include trifluoromethanesulfonyl chloride, trifluoromethanesulfonic anhydride, trifluoroacetic anhydride, pentafluoropropionic anhydride amongst others. Such a reaction in the presence of trifluoroacetic anhydride or pentafluoropropionic anhydride, and similar others, can be carried out optionally in the presence of a pyridine N-oxide derivative, for example 4-phenylpyridine-N-oxide or pyridine N-oxide, which facilitates the formation of haloalkyl radical. The photoredox reaction can be carried out in the presence of a suitable solvent, such as acetonitrile, tetrahydrofuran, toluene, or trifluorotoluene amongst others, at temperature in the range of 0°C to the boiling point of the reaction mixture, preferably between 25 to 40°C. Such reactions are reported, for example, in WO 19/168140 and *Nature Commun.* 6, 7919 (2015).

Compounds of formula XIII, wherein LG_1 is a halogen Br, Cl, or I, preferably Cl, and in which R is C_1 - C_6 alkyl, benzyl or a phenyl group, can be prepared by reacting compounds of formula XII, wherein LG_1 is a halogen Br, Cl, or I, preferably Cl, and in which R is C_1 - C_6 alkyl, benzyl or a phenyl group, with a compound of formula ROH, wherein R is C_1 - C_6 alkyl, benzyl or a phenyl group, in the presence of an acid catalyst, for example, sulfuric acid or a Lewis acid such as $Sc(OTf)_3$ or $FeCl_3$. Such esterification reactions are well known to those skilled in the state of art, and known, for example, by the name of Fischer Esterification reaction, and are reported in literature, for example, in *J. Org. Chem.*, 2006, 71, 3332-3334, *Chem. Commun.*, 1997, 351-352 and *Synthesis*, 2008, 3407-3410. Such esterification reaction can also be carried out by reacting compounds of formula XII with trimethylsilyldiazomethane $TMSCHN_2$ to form compounds of formula XIII, wherein LG_1 is a halogen Br, Cl, or I, preferably Cl, and in which R is methyl, and are reported in *Angew. Chem. Int. Ed.* 2007, 46, 7075.

Alternatively, compounds of formula II, wherein R₂ is as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group, can be prepared (scheme 5) from compounds of formula XI, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, and in which LG_{hal} is a halogen, for example chloro, bromo or iodo, by a metal catalyzed coupling with haloalkyl reagents, such as methyl difluoro(fluoro-sulfonyl)acetate (XV), sodium trifluoroacetate(XVa), trifluoromethyltrimethylsilane (XVaa) or methyl chlorodifluoroacetate (XVaaa), amongst other nucleophilic (metal)-haloalkyl reagents. The reaction is carried out in the presence of a metal catalyst, for example copper catalysts, such as copper chloride CuCl, copper iodide CuI, or [Cu(MeCN)₄]BF₄, amongst others, optionally in the presence of a ligand, such as tetramethylethylenediamine, 1,10-phenanthroline, amongst other amino ligands. The reaction is generally carried out in the presence of a solvent such as dimethylacetamide, N,N-dimethylformamide, toluene, N-methyl-2-pyrrolidone, N,N'-dimethylpropyleneurea, or hexamethylphosphoramide, at temperatures between 20°C to the boiling point of the reaction mixture. Such reactions are described, for example, in Journal of Fluorine Chemistry, 61(3), 279-84; 1993, WO 2018/064119 A1, Bioorg. Med. Chem. 24 (2016) 2504–2518, *Org. Lett.*, **2015**, 17, 532-535, *J. Org. Chem.*, **2013**, 78, 11126-11146, *Org. Lett.*, **2014**, 16, 4268-4271.

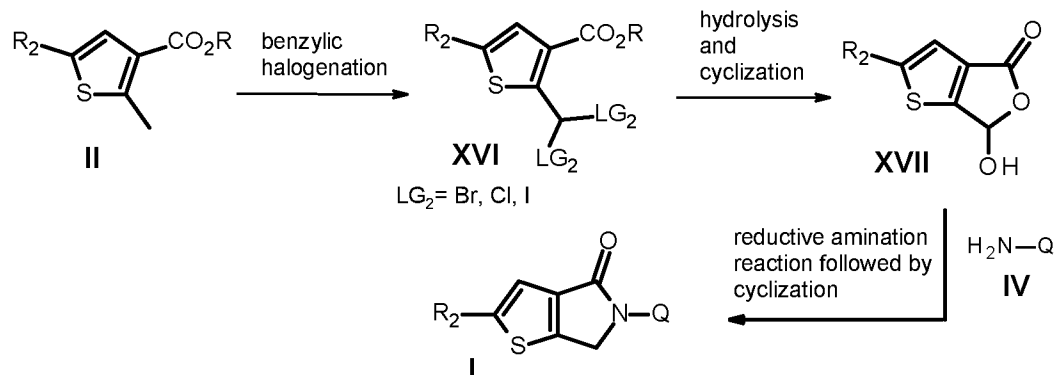
Compounds of formula XI, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, and in which LG_{hal} is a halogen, for example chloro, bromo or iodo, can be prepared by halogenation of compounds of formula X, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, with a halogenating reagent such as pyridinium bromide perbromide, bromine, or N-bromosuccinimide, amongst others, optionally in the presence of a base, such as butyl lithium, lithium diisopropylamide, or potassium tert-butoxide, amongst others. Such reactions are known and described, for example, in *Org. Process Res. Dev.* 2019, 23, 69–77 and *European Journal of Medicinal Chemistry* 2018, 156, 269-294.

Compounds of formula X, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, can be prepared by reacting compounds of formula IX with a compound of formula ROH, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, in the presence of an acid catalyst, for example, sulfuric acid or a Lewis acid such as Sc(OTf)₃ or FeCl₃. Such esterification reactions are well known to those skilled in the state of art, and known, for example, by the name of Fischer Esterification reaction, and are reported in literature, for example, in *J. Org. Chem.*, 2006, 71, 3332-3334, *Chem. Commun.*, 1997, 351-352 and *Synthesis*, 2008, 3407-3410. Such esterification reaction can also be carried out by reacting compounds of formula IX with trimethylsilyldiazomethane TMSCHN₂ to form compounds of formula X, wherein R is methyl, and are reported in *Angew. Chem. Int. Ed.* 2007, 46, 7075. Compounds of formula X, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, can also be prepared by reacting compounds of formula IX with compounds of formula R-LG₁, wherein R is C₁-C₆alkyl, benzyl or a phenyl group, and LG₁ is a leaving group such as, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, in the presence of base such as potassium carbonate, sodium carbonate, cesium carbonate, sodium hydride, amongst other bases.

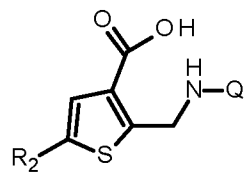
Compounds of formula IX are known in the literature and have been prepared from compounds of formula VIII under conditions described, for example, in Organic Process Research & Development, 23(1), 69-77; 2019, and Bioorganic & Medicinal Chemistry Letters, 21(18), 5417-5422; 2011.

- 5 Alternatively compounds of formula I, wherein R_2 and Q are defined as under formula I above, may be prepared following scheme 6.

Scheme 6:

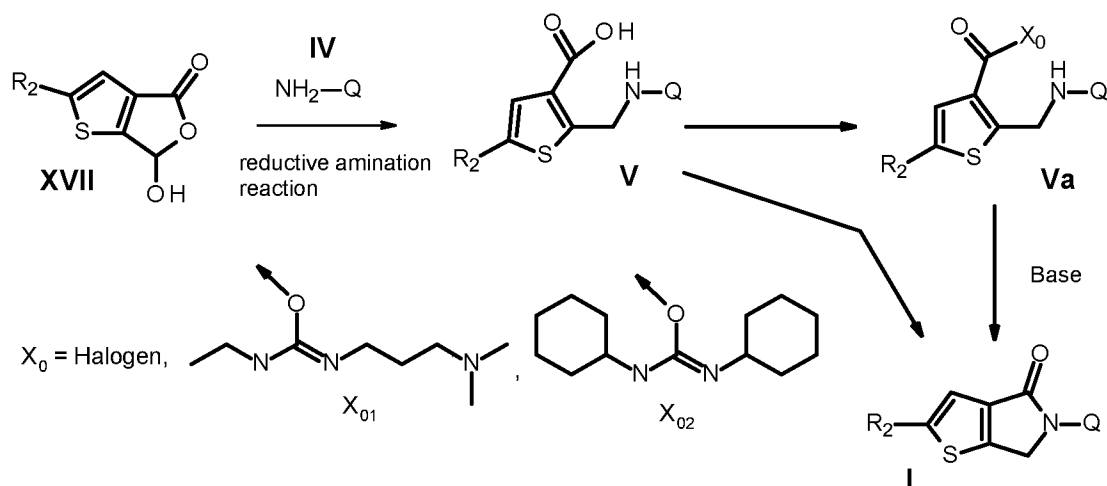


- 10 Compounds of formula I, wherein R_2 and Q are defined as under formula I above, may be prepared from compounds of formula XVII, wherein R_2 is defined as under formula I above, by a reductive amination reaction with amino compounds of formula IV, wherein Q is as defined in formula I above, to form compounds of formula V



- 15 wherein R_2 and Q are defined as under formula I above. Such compounds of formula V can be further cyclized to form compounds of formula I, as described in schemes 3 and 4 above. This process is illustrated in more details within scheme 7.

Scheme 7:



The reductive amination reaction to convert compounds of formula XVII to compounds of formula V can be carried out in the presence of a reducing agent, for example sodium cyanoborohydride or sodium triacetoxyborohydride, amongst others, and optionally in the presence of an acid such as trifluoroacetic acid, formic acid, or acetic acid (and the like), at temperatures ranging from 0°C to the boiling point of the reaction mixture. The reaction can be carried out in the presence of inert solvents, such as ethanol, methanol, dioxane or tetrahydrofuran.

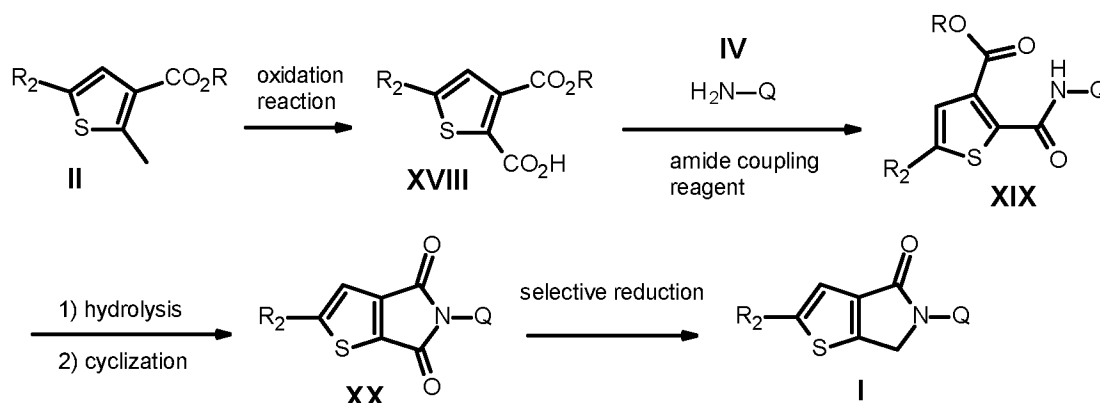
The direct transformation of compounds of formula V into compounds of formula I, or alternatively via compounds of formula Va, is outlined above in schemes 3 and 4. Conditions involving a (multi)-step conversion of compounds of formula XVII into compounds of formula I have also been described in, for example, Bioorganic & Medicinal Chemistry Letters 26 (2016) 5947–5950.

Compounds of formula XVII, wherein R₂ is as defined in formula I above, may be prepared (scheme 6) from compound of formula XVI, wherein R₂ is as defined in formula I above, and in which LG₂ is chloro, bromo or iodo, preferably bromo, and R is C₁–C₆alkyl, benzyl or a phenyl group, by a hydrolysis and intramolecular cyclization reaction. The reaction can be carried out either under basic conditions using metal hydroxides, such as aqueous sodium or potassium hydroxide, in the presence of a solvent such as dioxane, tetrahydrofuran or water, and at temperatures ranging from 20 to 150°C, as reported in, for example, Synlett 1992, (6), 531–533, or under aqueous acidic conditions, for example using acetic acid, hydrochloric acid or sulfuric acid, in the presence of a solvent such as water, dioxane, or a halogenated solvent such as dichloroethane, as reported in, for example, Tetrahedron 62 (2006) 9589–9602.

Compounds of formula XVI, wherein R₂ is as defined in formula I above, and in which LG₂ is chloro, bromo or iodo, preferably bromo, and R is C₁–C₆alkyl, benzyl or a phenyl group, may be prepared from compounds of formula II, wherein R₂ is as defined in formula I above, and R is C₁–C₆alkyl, benzyl or a phenyl group, by means of a benzylic dihalogenation reaction analogous to conditions described in scheme 3 for the conversion of compounds of formula II into compounds of formula III, and in the presence of preferably at least two equivalents of the halogenating source.

Alternatively compounds of formula I, wherein R₂ and Q are defined as under formula I above,

Scheme 8:



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may be prepared (scheme 8) from compounds of formula XX, wherein R_2 and Q are defined as under formula I above, *via* a selective reduction of one of the carbonyl functional group. The reaction can be carried out in the presence of a reducing agent, for example sodium borohydride NaBH_4 , lithium aluminum hydride LiAlH_4 , or hydrogen in the presence of palladium on carbon, or a combination of two reducing agents, for example NaBH_4 followed by triethylsilane. Such reactions have been described in, for example, US20100160303.

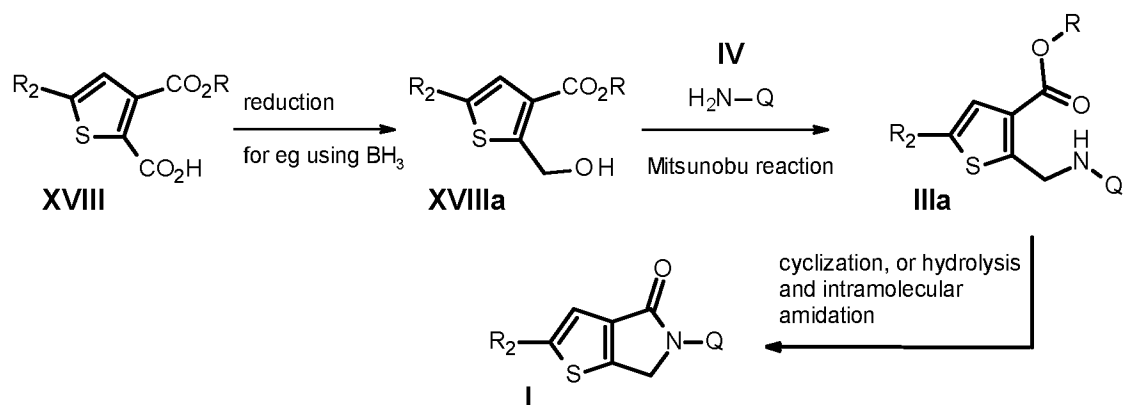
Compounds of formula XX, wherein R_2 and Q are defined as under formula I above, may be prepared from compounds of formula XIX, wherein R_2 and Q are defined as under formula I above, and R is C_1 - C_6 alkyl, benzyl or a phenyl group, by a hydrolysis reaction and a subsequent cyclization reaction, under similar conditions described in scheme 3 and 4, and schemes 6 and 7.

Compounds of formula XIX, wherein R_2 and Q are defined as under formula I above, and R is C_1 - C_6 alkyl, benzyl or a phenyl group, may be prepared by reacting compounds of formula XVIII, wherein R_2 is defined as under formula I above, and R is C_1 - C_6 alkyl, benzyl or a phenyl group, with amino compounds of formula IV, wherein Q is as defined in formula I above, using similar amidation conditions as described in scheme 4.

Compounds of formula XVIII, wherein R_2 is defined as under formula I above, and R is C_1 - C_6 alkyl, benzyl or a phenyl group, may be prepared by benzylic oxidation of compounds of formula II, wherein R_2 is as described in formula I above, and R is C_1 - C_6 alkyl, benzyl or a phenyl group. The reaction can be carried out in the presence of oxidative reagents, such as potassium permanganate KMnO_4 , tetrabutylammonium permanganate NBu_4MnO_4 , potassium persulfate $\text{K}_2\text{S}_2\text{O}_8$ (also known as potassium peroxydisulfate) in the presence of oxygen, or under photochemical conditions in the presence of oxygen, and at temperatures ranging from 20°C to the boiling point of the reaction mixture. The reaction is carried out in the presence of inert solvent, such as acetonitrile, ethyl acetate, DMSO, or dichloroethane. Such reactions are known in the literature, for example in *Synthesis* 2017, 49, 4007-4016, *Synthesis* 2006, 1757-1759 and *IOSR Journal of Applied Chemistry* 2014, 7, 16-27.

Alternatively compounds of formula I, wherein R_2 and Q are as defined in formula I above,

Scheme 9:



may be prepared (scheme 9) by a direct cyclization reaction of compounds of formula IIIa, wherein R₂ and Q are as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group. Such a cyclization reaction can be carried out in the presence of a base, for example potassium *tert*-butoxide, lithium diisopropylamide, or sodium hydride, amongst others, at temperature ranging from -20°C to the boiling point of the reaction mixture, and in the presence of an inert solvent, such as tetrahydrofuran, dioxane, or DMF. Such reactions have been reported in, for example, Synlett 2006(4): 591-594.

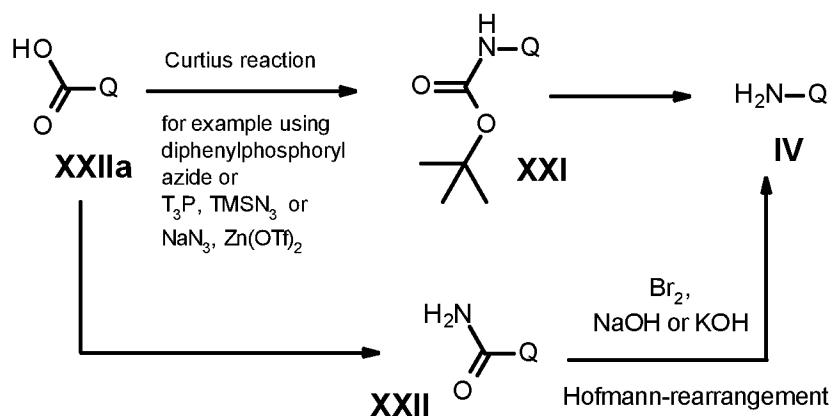
The conversion of compounds IIIa into compounds of formula I may also be conducted by means of a hydrolysis/intramolecular amidation sequence as described in schemes 3 and 4.

Compounds of formula IIIa, wherein R₂ and Q are as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group, may be prepared by reacting compounds of formula XVIIIa, wherein R₂ is as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group, with compounds of formula IV, wherein Q is as defined in formula I above, under Mitsunobu conditions. Such reactions known to those skilled in art can be carried out in the presence of phosphine reagent, such as triphenylphosphine, tributylphosphine, or polymer supported triphenyl phosphine, amongst others, in the presence of an azodicarboxylate reagent, such as diethyl azodicarboxylate or diisopropyl azodicarboxylate, at temperature ranging from 0°C to 100°C, and in the presence of an inert solvent, such as acetonitrile, dichloromethane, tetrahydrofuran, or toluene. Such reactions have been reported in, for example, Synthesis, 1981(1), 1-28.

Compounds of formula XVIIIa, wherein R₂ is as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group, can be prepared by reacting compounds of formula XVIII, wherein R₂ is as defined in formula I above, and R is C₁-C₆alkyl, benzyl or a phenyl group, with reducing agents such as, for example, metal hydrides (like lithium aluminumhydride), DIBAL-H, or boranes (like diborane, borane dimethyl sulfide or borane tetrahydrofuran complex), amongst others, at temperatures ranging from 0°C to 150°C, and in the presence of an inert solvent, such as tetrahydrofuran or dioxane. Such reactions have been reported in, for example, Tetrahedron Letters, 1982, 23, 2475-2478.

Compounds of formula IV, wherein Q is as defined in formula I above, can be prepared by the deprotection reaction of the *tert*-butyl group of compounds of formula XXI, wherein Q is as defined in formula I above (scheme 10).

Scheme 10:



The reaction can be carried out in the presence of an acid, such as trifluoroacetic acid, hydrochloric acid or sulfuric acid, amongst others, and under conditions known to those skilled in the art and already described above.

Compounds of formula XXI, wherein Q is as defined in formula I above, may be prepared by the

- 5 reaction of compounds of formula XXIIa, wherein Q is as defined in formula I above, with an organo-azide, in the presence of a suitable base, and tert-butanol *t*-BuOH, optionally in the presence of a coupling agent, optionally in the presence of Lewis acid, and in the presence of an inert solvent, at temperatures between 50°C and boiling point of the reaction mixture. The reaction can be carried out in the presence of coupling agent such as T₃P or *via* activation of the carboxylic acid with thionyl chloride SOCl₂ or oxalyl chloride, or other coupling agents as described in scheme 4 for the conversion of compounds of formula V into compounds of formula Va. Examples of organo-azide compounds include trimethylsilyl azide TMSN₃, sodium azide, or tosyl azide, and suitable solvents may be toluene, xylene, THF or acetonitrile. Examples of suitable Lewis acids may include zinc triflate Zn(OTf)₂, Sc(OTf)₂, or Cu(OTf)₂, amongst others. Compounds of formula XXI can also be prepared by
- 10 reacting compounds of formula XXIIa with diphenylphosphorylazide in the presence of an organic base such as triethylamine or diisopropylethylamine, amongst others, in the presence of *tert*-butanol *t*-BuOH and an inert solvent, for example halogenated solvents such as dichloromethane or dichloroethane, or cyclic ethers such as tetrahydrofuran, amongst others, and at temperatures ranging from 50°C to the boiling point of the reaction mixture. Such reactions of converting carboxylic acids
- 20 into BOC protected amines are well known to those skilled in the state of art by the name of the Curtius reaction, and are reported in, for example, *Org. Lett.*, 2005, 7, 4107-4110; *Journal of Medicinal Chemistry*, 49(12), 3614-3627; 2006, and *J. Am. Chem. Soc.*, 1972, 94 (17), pp 6203-6205.

The following compounds of formula XXI are known in the literature and are described below:

- tert-butyl N-[3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)-2-pyridyl]carbamate (CAS 2641574-60-7, described in
- 25 WO2021085370); tert-Butyl N-[5-(1-cyano-1-methylethyl)-3-ethylsulfonyl-2-pyridyl]carbamate (CAS 2484397-79-5, described in WO2020174094); tert-Butyl N-[3-(ethylsulfonyl)-2-pyridyl]carbamate (CAS 2484398-04-9, described in WO2020174094).

- Compounds of formula IV, wherein Q is as defined in formula I above, may also be prepared from
- 30 compounds of formula XXII, wherein Q is as defined in formula I above, by a Hofmann-rearrangement reaction. The reaction can be carried out in the presence of a base, for example metal hydroxides such as aqueous sodium or potassium hydroxide, or organic bases such as DBU (1,8-diaza-bicyclo(5.4.0)undec-7-ene), in the presence of electrophilic halogenating reagents such as chlorine, bromine or N-bromo-succinimide, and at temperatures ranging from 20°C to the boiling point of the
- 35 reaction mixture. Such reactions are known by the name of Hofmann-rearrangement, and are reported in, for example, *Chem. Ber.* 1881, 14, 2725.

The following compounds of formula IV are known in the literature and are described below:

2-(6-amino-5-ethylsulfonyl-3-pyridyl)-2-methyl-propanenitrile (CAS 2484397-83-1, described in WO2020174094); 1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropanecarbonitrile (CAS 2484397-84-2,

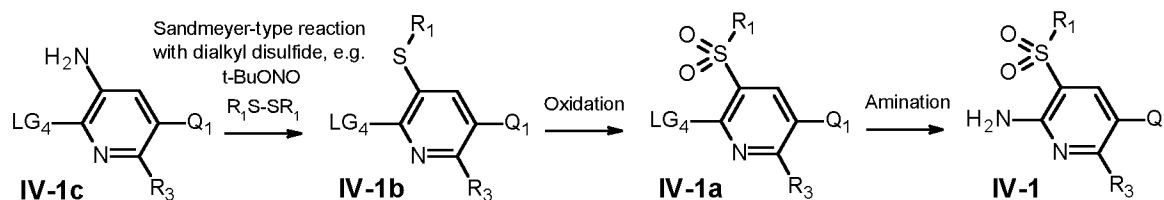
described in WO2020174094); 3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)pyridin-2-amine (CAS 2641574-57-2, described in WO2021085370).

Compounds of formula XXII, wherein Q is as defined in formula I above, may be prepared by the reaction of compounds of formula XXIIa, wherein Q is as defined in formula I above, with ammonia NH₃, or ammonia surrogates, such as, for example, NH₄OH, in the presence of carboxylic acid activating agents as described in scheme 4.

Compounds of formula XXIIa, wherein Q is as defined in formula I above, are either known, commercially available or may be prepared by those skilled in the art. In particular the following compounds of formula XXIIa are known in the literature and are described below:

5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 2417036-66-7, described in WO2020141136); 5-(1-cyano-1-methyl-ethyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 2225113-81-3, described in WO2018077565); 5-(1-cyano-1-methyl-ethyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 2243224-65-7, described in WO2018153778); 5-(1-cyanocyclopropyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 2225113-77-7, described in WO2019234158); 5-(1-cyanocyclopropyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 1879106-82-7, described in WO2016087265); 3-ethylsulfonyl-5-(trifluoromethyl)pyridine-2-carboxylic acid (CAS 1421952-02-4, described in WO2016107831); 3-ethylsulfonyl-5-(trifluoromethyl)pyridine-2-carboxylic acid (CAS 1421953-19-6, described in CN110606828); 3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)pyridine-2-carboxylic acid (CAS 2016034-28-7, described in WO2019008115); 5-[acetyl(methyl)amino]-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 2632239-16-6, described in WO2021053110); 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 1970134-21-4, described in WO2016116338); 3-ethylsulfonyl-6-pyrimidin-2-yl-pyridine-2-carboxylic acid (CAS 1970134-19-0, described in WO2016116338).

The subgroup of compounds of formula IV, wherein Q is defined as Q_a, in which X is SO₂, A is N, and R₁, R₃ and Q₁ are as defined in formula I, can be defined as compounds of formula IV-1 (scheme 10a).
Scheme 10a:



Compounds of formula IV-1 can be prepared by an amination reaction, which involves for example, reacting compounds of formula IV-1a, wherein R₁, R₃ and Q₁ are as defined in formula I, and LG₄ is a halogen, preferably F, Br or Cl, with ammonia, or a salt thereof (such as a hydrohalide salt, preferably a hydrochloride or a hydrobromide salt, or any other equivalent salt). The source of nitrogen may be ammonia NH₃ itself or an ammonia equivalent such as for example ammonium hydroxide NH₄OH,

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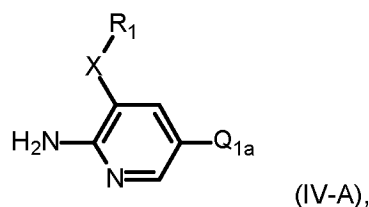
ammonium chloride NH_4Cl , ammonium acetate NH_4OAc , ammonium carbonate $(\text{NH}_4)_2\text{CO}_3$, and other NH_3 surrogates. This transformation is preferably performed in suitable solvents (or diluents) such as alcohols, amides, esters, ethers, nitriles and water, particularly preferred are methanol, ethanol, 2,2,2-trifluoroethanol, propanol, iso-propanol, N,N-dimethylformamide, N,N-dimethylacetamide, dioxane, tetrahydrofuran, dimethoxyethane, acetonitrile, ethyl acetate, water or mixtures thereof, optionally in presence of a base, at temperatures between 0-150°C, preferably at temperatures ranging from room temperature to the boiling point of the reaction mixture, optionally under microwave irradiation.

Compounds of formula IV-1a, wherein R_1 , R_3 and Q_1 are as defined in formula I, and LG_4 is halogen, preferably F, Br or Cl, can be prepared by oxidizing compounds of formula IV-1b, wherein R_1 , R_3 and Q_1 are as defined in formula I, and LG_4 is halogen, preferably F, Br or Cl, under conditions already described above (sulfide to sulfone oxidation).

Compounds of formula IV-1b, wherein R_1 , R_3 and Q_1 are as defined in formula I, and LG_4 is halogen, preferably F, Br or Cl, can be prepared by reacting compounds of formula IV-1c, wherein R_3 and Q_1 are as defined in formula I, and LG_4 is halogen, preferably F, Br or Cl, with a disulfide $\text{R}_1\text{S-SR}_1$ or alternatively a thiol R_1SH , wherein R_1 is as defined in formula I above, in the presence of a nitrite, such as tert-butyl nitrite t-BuONO, isoamyl nitrite, or sodium nitrite, and in presence of a hydrohalic acid (preferably HBr or HCl), under Sandmeyer-type reaction conditions. This transformation is preferably performed in an inert solvent, such as acetonitrile or a halogenated solvent, like 1,2-dichloroethane, at temperatures between 0-150°C, preferably at temperatures ranging from room temperature to the boiling point of the reaction mixture, optionally in the presence of copper salts.

Certain compounds of formula IV-1c, wherein R_3 and Q_1 are as defined in formula I, and LG_4 is halogen, preferably F, Br or Cl, are either known, commercially available or may be prepared by those skilled in the art.

The compounds of formula IV-A

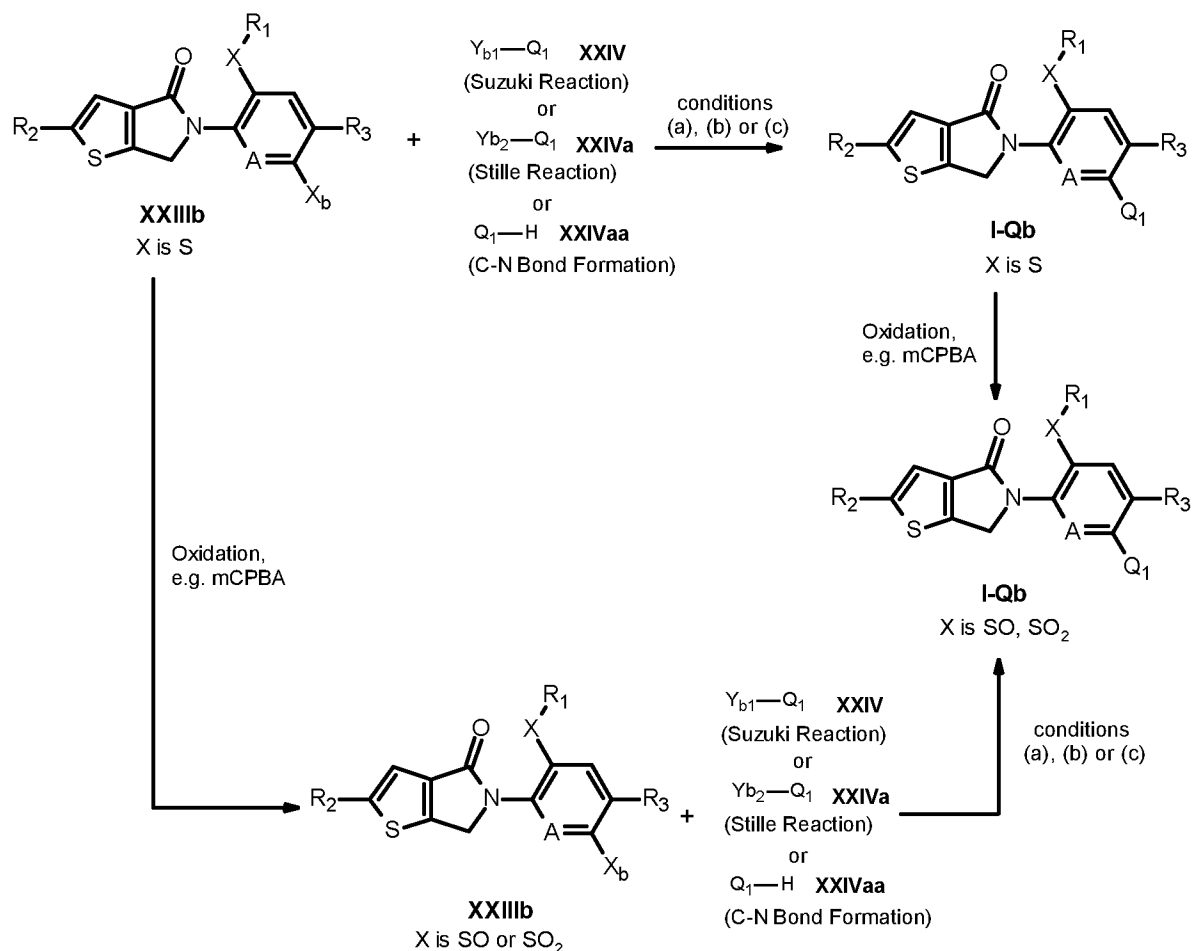


wherein

R_1 and X are as defined under formula I above, and Q_{1a} is 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl or 2-pyridyloxy, are novel, especially developed for the preparation of the compounds of formula I according to the invention and therefore represent a further object of the invention. The preferences and preferred embodiments of the substituents of the compounds of formula I are also valid for the compounds of formula IV-A.

The subgroup of compounds of formula I, wherein R_2 is as defined in formula I above, and wherein Q is defined as Q_b , in which A, Q_1 , R_3 , X and R_1 are as defined in formula I, may be defined as compounds of formula I- Q_b (scheme 11).

Scheme 11:



(a) Suzuki reaction: Pd cat. (e.g. Pd(PPh₃)₄ or Pd(dppf)Cl₂), base (e.g. Na₂CO₃), solvent (e.g. 1,2-dimethoxyethane/water), 25-180°C.

(b) Stille reaction: Pd cat. (e.g. $\text{Pd}(\text{PPh}_3)_4$ or $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$), solvent (e.g. toluene), 25-180°C.

(c) C-N bond formation: Optional base (e.g. K_2CO_3 or Cs_2CO_3), optional presence of copper or palladium catalyst, optional additive (such as N,N'-dimethylethylenediamine), optional ligand (such as Xantphos), solvent (e.g. dioxane, pyridine or N,N-dimethylformamide DMF), 25-180°C.

In the particular situation within scheme 11 when Q₁ is an optionally substituted triazole linked via a ring nitrogen atom to the ring which contains the group A, then compounds of formula I-Qb, wherein X is SO or SO₂, may be prepared from compounds of formula XXIIIb, wherein A, R₃, R₁ and R₂ are as defined in formula I above, and in which X is SO or SO₂, and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, by reaction (C-N bond formation) with an optionally substituted triazole Q₁-H (which contains an appropriate NH functionality) (XXIVaa), wherein Q₁ is N-linked triazolyl, in solvents such as alcohols (eg. methanol, ethanol, isopropanol, or higher boiling linear or branched alcohols), pyridine or acetic acid, optionally in the presence of an additional base, such as potassium carbonate K₂CO₃ or cesium carbonate Cs₂CO₃, optionally in the presence of a copper catalyst, for example copper(I) iodide, at temperatures between 30-180°C, optionally under microwave irradiation.

In the particular situation within scheme 11 when Q_1 is $-N(R_4)COR_5$, wherein R_4 and R_5 are as defined in formula I, then compounds of formula I-Qb, wherein X is SO or SO_2 , may be prepared from compounds of formula XXIIIb, wherein A, R_1 , R_2 and R_3 are as defined in formula I, and in which X is SO or SO_2 , and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, by reaction (C-N bond formation) with a reagent Q_1-H (XXIVaa) equivalent to $HN(R_4)COR_5$, wherein R_4 and R_5 are as defined in formula I. Such a reaction is performed in the presence of a base, such as potassium carbonate, cesium carbonate, sodium hydroxide, in an inert solvent, such as toluene, dimethylformamide DMF, N-methyl pyrrolidine NMP, dimethyl sulfoxide DMSO, dioxane, tetrahydrofuran THF, and the like, optionally in the presence of a catalyst, for example palladium(II)acetate, bis(dibenzylideneacetone)palladium(0) ($Pd(dba)_2$) or tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$, optionally in form of a chloroform adduct), or a palladium pre-catalyst such as for example *tert*-BuBrettPhos Pd G3 [(2-Di-*tert*-butylphosphino-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl)-2-(2'-amino-1,1'-biphenyl)]palladium(II) methanesulfonate or BrettPhos Pd G3 [(2-di-cyclohexylphosphino-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl)-2-(2'-amino-1,1'-biphenyl)]palladium(II) methanesulfonate, and optionally in the presence of a ligand, for example SPhos, *t*-BuBrettPhos or Xantphos, at temperatures between 60-120 °C, optionally under microwave irradiation.

In the particular situation within scheme 11 when Q_1 is $-N(R_4)_2$, wherein R_4 is as defined in formula I, then compounds of formula I-Qb, wherein X is SO or SO_2 , may be prepared from compounds of formula XXIIIb, wherein A, R_1 , R_2 and R_3 are as defined in formula I, and in which X is SO or SO_2 , and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, by reaction (C-N bond formation) with a reagent Q_1-H (XXIVaa) equivalent to $HN(R_4)_2$, or a salt thereof (such as a hydrohalide salt, preferably a hydrochloride or a hydrobromide salt, or a trifluoroacetic acid salt, or any other equivalent salt), wherein R_4 is as defined in formula I. Such a reaction is commonly performed in an inert solvent such as alcohols, amides, esters, ethers, nitriles and water, particularly preferred are methanol, ethanol, 2,2,2-trifluoroethanol, propanol, isopropanol, N,N-dimethylformamide, N,N-dimethylacetamide, dioxane, tetrahydrofuran, dimethoxyethane, acetonitrile, ethyl acetate, toluene, water or mixtures thereof, at temperatures between 0-150 °C, optionally under microwave irradiation or pressurized conditions using an autoclave, optionally in the presence of a copper catalyst, such as copper powder, copper(I) iodide or copper sulfate (optionally in form of a hydrate), or mixtures thereof, optionally in presence a ligand, for example diamine ligands (e.g. N,N'-dimethylethylenediamine or *trans*-cyclohexyldiamine) or dibenzylideneacetone (dba), or 1,10-phenanthroline, and optionally in presence of a base such as potassium phosphate.

Reagents $HN(R_4)_2$, or $HN(R_4)COR_5$, wherein R_4 and R_5 are as defined in formula I, are either known, commercially available or may be prepared by methods known to a person skilled in the art.

Alternatively, compounds of formula I-Qb, wherein X is SO or SO₂, may be prepared by a Suzuki reaction, which involves for example, reacting compounds of formula XXIIIb, wherein A, R₁, R₂ and R₃ are as defined in formula I, and in which X is SO or SO₂, and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, with compounds of formula (XXIV), wherein Q₁ is as defined in formula I, and wherein Y_{b1} can be a boron-derived functional group, such as for example B(OH)₂ or B(OR_{b1})₂ wherein R_{b1} can be a C₁-C₄alkyl group or the two groups OR_{b1} can form together with the boron atom a five membered ring, as for example a pinacol boronic ester. The reaction may be catalyzed by a palladium based catalyst, for example tetrakis(triphenyl-phosphine)palladium(0), (1,1'-bis(diphenylphosphino)ferrocene)dichloro-palladium-dichloromethane (1:1 complex) or chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-biphenyl)]palladium(II) (XPhos palladacycle), in presence of a base, like sodium carbonate, tripotassium phosphate or cesium fluoride, in a solvent or a solvent mixture, like, for example dioxane, acetonitrile, N,N-dimethylformamide, a mixture of 1,2-dimethoxyethane and water or of dioxane/water, or of toluene/water, preferably under inert atmosphere. The reaction temperature can preferentially range from room temperature to the boiling point of the reaction mixture, or the reaction may be performed under microwave irradiation. Such Suzuki reactions are well known to those skilled in the art and have been reviewed, for example, in J.Organomet. Chem. 576, 1999, 147-168.

Alternatively compounds of formula I-Qb, wherein X is SO or SO₂, may be prepared by a Stille reaction between compounds of formula (XXIVa), wherein Q₁ is as defined above, and wherein Y_{b2} is a trialkyltin derivative, preferably tri-n-butyl tin or tri-methyl-tin, and compounds of formula XXIIIb, wherein A, R₁, R₂ and R₃ are as defined in formula I, and in which X is SO or SO₂, and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate. Such Stille reactions are usually carried out in the presence of a palladium catalyst, for example tetrakis(triphenylphosphine)palladium(0), or bis(triphenylphosphine)palladium(II) dichloride, in an inert solvent such as N,N-dimethylformamide, acetonitrile, toluene or dioxane, optionally in the presence of an additive, such as cesium fluoride, or lithium chloride, and optionally in the presence of a further catalyst, for example copper(I)iodide. Such Stille couplings are also well known to those skilled in the art, and have been described in for example J. Org. Chem., 2005, 70, 8601-8604, J. Org. Chem., 2009, 74, 5599-5602, and Angew. Chem. Int. Ed., 2004, 43, 1132-1136.

When Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, then compounds of formula I-Qb, wherein X is SO or SO₂, may be prepared from compounds of formula XXIIIb, wherein A, R₁, R₂ and R₃ are as defined in formula I, and in which X is SO or SO₂, and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, by reaction with a heterocycle Q₁-H (which contains an appropriate NH functionality) (XXIVaa), wherein Q₁ is as defined above, in the presence of a base, such as potassium carbonate K₂CO₃ or cesium carbonate Cs₂CO₃, optionally in the presence of a copper catalyst, for example copper(I)

iodide, with or without an additive such as L-proline, N,N'-dimethylcyclohexane-1,2-diamine or N,N'-dimethyl-ethylene-diamine, in an inert solvent such as N-methylpyrrolidone NMP or N,N-dimethylformamide DMF at temperatures between 30-150 °C, optionally under microwave irradiation. Oxidation of compounds of formula XXIIIb, wherein A, R₁, R₂ and R₃ are as defined in formula I, and in which X is S, and wherein X_b is a leaving group like, for example, chlorine, bromine or iodine (preferably chlorine or bromine), or an aryl- or alkylsulfonate such as trifluoromethanesulfonate, with a suitable oxidizing agent, into compounds of formula XXIIIb, wherein X is SO or SO₂ may be achieved under conditions already described above.

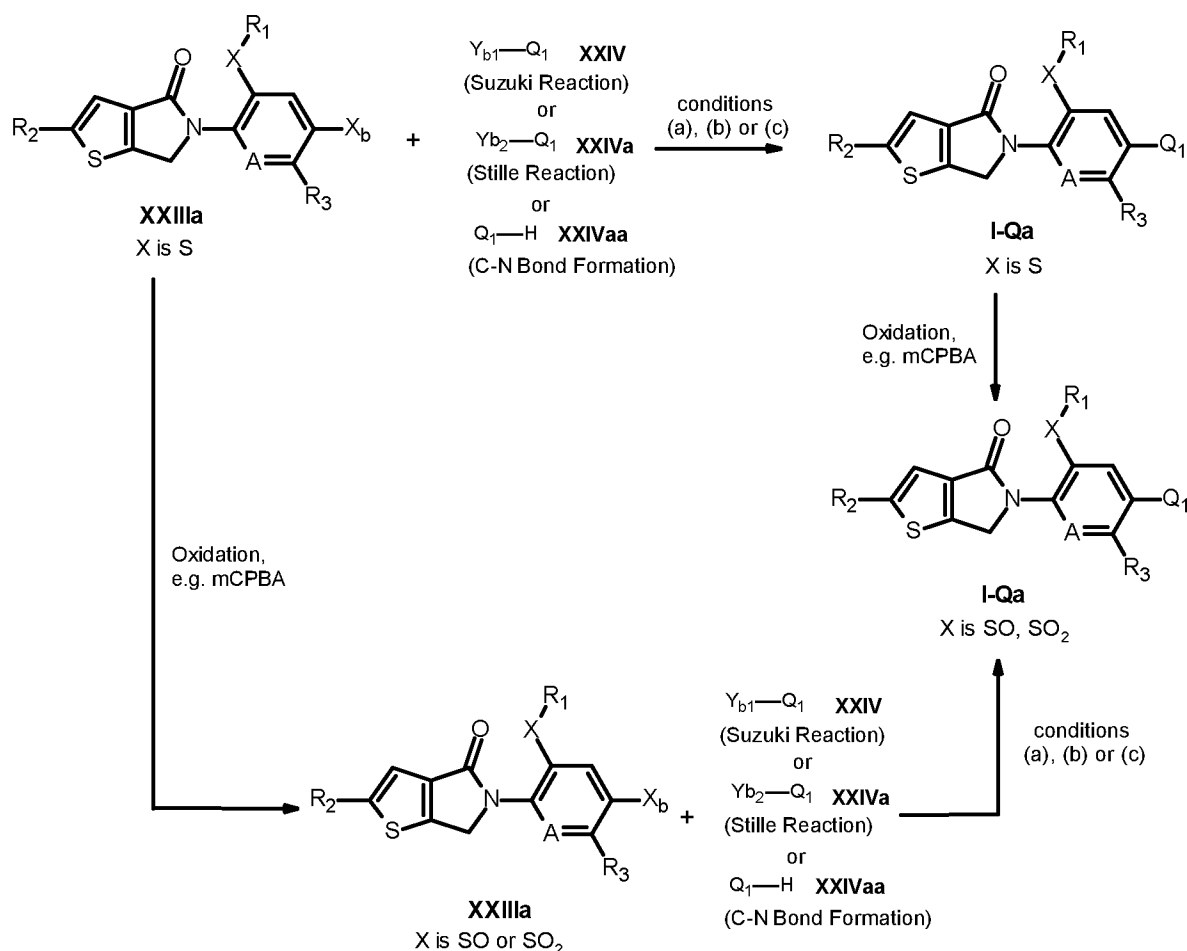
A large number of compounds of the formula (XXIV), (XXIVa) and (XXIVaa) are commercially available or can be prepared by those skilled in the art.

Alternatively, compounds of formula I-Qb, wherein X is SO or SO₂, may be prepared from compounds of formula XXIIIb, wherein X is S (sulfide) by involving the same chemistry as described above, but by changing the order of the steps (i.e. by running the sequence XXIIIb (X is S) to I-Qb (X is S) via Suzuki, Stille or C-N bond formation, followed by an oxidation step to form I-Qb (X is SO or SO₂).

The subgroup of compounds of formula I, wherein R₂ is as defined above, and wherein Q is defined as Qa, in which A, Q₁, R₃, X and R₁ are as defined in formula I, may be defined as compounds of formula I-Qa (scheme 12). The chemistry described previously in scheme 11 to access compounds of formula I-Qb from compounds of formula XXIIIb, can be applied analogously (scheme 12) for the preparation of compounds of formula I-Qa from compounds of formula XXIIIa, wherein all substituent definitions mentioned previously remain valid.

Scheme 12:

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(a) Suzuki reaction: Pd cat. (e.g. Pd(PPh₃)₄ or Pd(dppf)Cl₂), base (e.g. Na₂CO₃), solvent (e.g. 1,2-dimethoxyethane/water), 25-180°C.

(b) Stille reaction: Pd cat. (e.g. Pd(PPh₃)₄ or Pd(PPh₃)Cl₂), solvent (e.g. toluene), 25-180°C.

(c) C-N bond formation: Optional base (e.g. K₂CO₃ or Cs₂CO₃), optional presence of copper or palladium catalyst, optional additive (such as N,N'-dimethylethylenediamine), optional ligand (such as Xantphos), solvent (e.g. dioxane, pyridine or N,N-dimethylformamide DMF), 25-180°C.

The reactants can be reacted in the presence of a base. Examples of suitable bases are alkali metal or alkaline earth metal hydroxides, alkali metal or alkaline earth metal hydrides, alkali metal or alkaline earth metal amides, alkali metal or alkaline earth metal alkoxides, alkali metal or alkaline earth metal acetates, alkali metal or alkaline earth metal carbonates, alkali metal or alkaline earth metal dialkylamides or alkali metal or alkaline earth metal alkylsilylamides, alkylamines, alkylenediamines, free or N-alkylated saturated or unsaturated cycloalkylamines, basic heterocycles, ammonium hydroxides and carbocyclic amines. Examples which may be mentioned are sodium hydroxide, sodium hydride, sodium amide, sodium methoxide, sodium acetate, sodium carbonate, potassium tert-butoxide, potassium hydroxide, potassium carbonate, potassium hydride, lithium diisopropylamide, potassium bis(trimethylsilyl)amide, calcium hydride, triethylamine, diisopropylethylamine, triethylenediamine, cyclohexylamine, N-cyclohexyl-N,N-dimethylamine, N,N-diethylaniline, pyridine, 4-(N,N-dimethylamino)pyridine, quinuclidine, N-methylmorpholine, benzyltrimethylammonium hydroxide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

The reactants can be reacted with each other as such, i.e. without adding a solvent or diluent. In most cases, however, it is advantageous to add an inert solvent or diluent or a mixture of these. If the reaction is carried out in the presence of a base, bases which are employed in excess, such as triethylamine, pyridine, N-methylmorpholine or N,N-diethylaniline, may also act as solvents or diluents.

The reactions are advantageously carried out in a temperature range from approximately -80°C to approximately +140°C, preferably from approximately -30°C to approximately +100°C, in many cases in the range between ambient temperature and approximately +80°C.

A compound of formula I can be converted in a manner known per se into another compound of formula I by replacing one or more substituents of the starting compound of formula I in the customary manner by (an) other substituent(s) according to the invention, and by post modification of compounds of with reactions such as oxidation, alkylation, reduction, acylation and other methods known by those skilled in the art.

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

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

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

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

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

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

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

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

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

N-oxides can be prepared by reacting a compound of the formula I with a suitable oxidizing agent, for example the H_2O_2 /urea adduct in the presence of an acid anhydride, e.g. trifluoroacetic anhydride.

Such oxidations are known from the literature, for example from *J. Med. Chem.*, 32 (12), 2561-73, 1989 or WO 2000/15615.

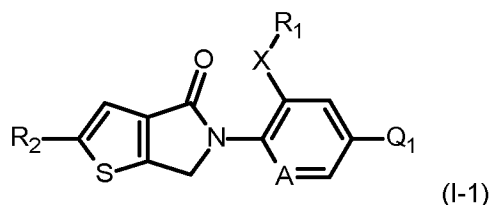
It is advantageous to isolate or synthesize in each case the biologically more effective isomer, for example enantiomer or diastereomer, or isomer mixture, for example enantiomer mixture or diastereomer mixture, if the individual components have a different biological activity.

The compounds of formula I and, where appropriate, the tautomers thereof, in each case in free form or in salt form, can, if appropriate, also be obtained in the form of hydrates and/or include other solvents, for example those which may have been used for the crystallization of compounds which are present in solid form.

The compounds of formula I according to the following Tables A-1 to A-12 and Tables C-1 to C-12 can be prepared according to the methods described above. The examples which follow are intended to illustrate the invention and show preferred compounds of formula I, in the form of a compound of formula I-1 to I-2.

The tables below illustrate specific compounds of the invention.

Table A-1 provides 18 compounds A-1.001 to A-1.018 of formula I-1 wherein R₂ is CF₃, A is N, X is S, R₁ is ethyl and Q₁ are as defined in table B.



For example, compound A-1.009 is

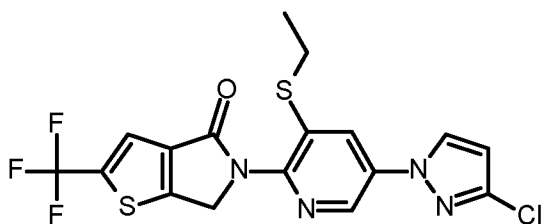
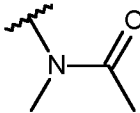
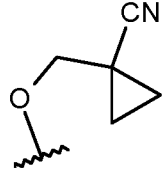
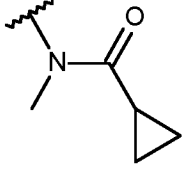
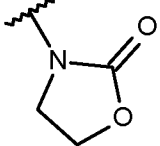
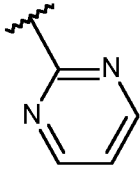
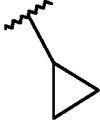
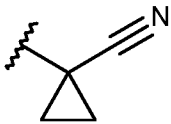
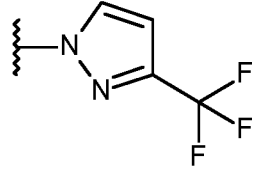
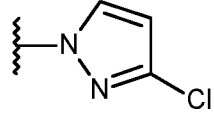


Table B: Substituent definitions of Q₁

Index	Q ₁
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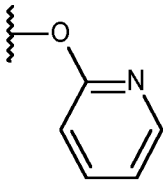
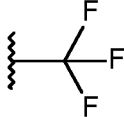
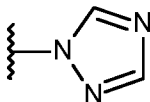
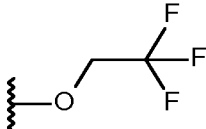
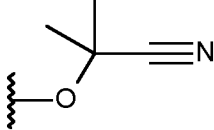
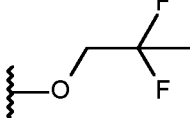
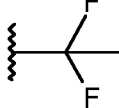
Index	Q ₁
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Table A-2 provides 18 compounds A-2.001 to A-2.018 of formula I-1 wherein R₂ is CF₃, A is N, X is SO, R₁ is ethyl and Q₁ are as defined in table B.

-43-

Table A-3 provides 18 compounds A-3.001 to A-3.018 of formula I-1 wherein R_2 is CF_3 , A is N, X is SO_2 , R_1 is ethyl and Q_1 are as defined in table B.

Table A-4 provides 18 compounds A-4.001 to A-4.018 of formula I-1 wherein R_2 is CF_3 , A is CH, X is S, R_1 is ethyl and Q_1 are as defined in table B.

- 5 Table A-5 provides 18 compounds A-5.001 to A-5.018 of formula I-1 wherein R_2 is CF_3 , A is CH, X is SO, R_1 is ethyl and Q_1 are as defined in table B.

Table A-6 provides 18 compounds A-6.001 to A-6.018 of formula I-1 wherein R_2 is CF_3 , A is CH, X is SO_2 , R_1 is ethyl and Q_1 are as defined in table B.

- 10 Table A-7 provides 18 compounds A-7.001 to A-7.018 of formula I-1 wherein R_2 is CF_2CF_3 , A is N, X is S, R_1 is ethyl and Q_1 are as defined in table B.

Table A-8 provides 18 compounds A-8.001 to A-8.018 of formula I-1 wherein R_2 is CF_2CF_3 , A is N, X is SO, R_1 is ethyl and Q_1 are as defined in table B.

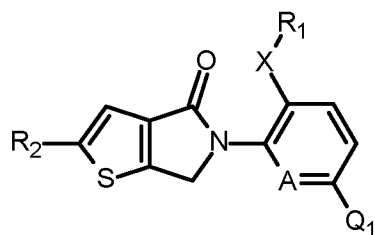
Table A-9 provides 18 compounds A-9.001 to A-9.018 of formula I-1 wherein R_2 is CF_2CF_3 , A is N, X is SO_2 , R_1 is ethyl and Q_1 are as defined in table B.

- 15 Table A-10 provides 18 compounds A-10.001 to A-10.018 of formula I-1 wherein R_2 is CF_2CF_3 , A is CH, X is S, R_1 is ethyl and Q_1 are as defined in table B.

Table A-11 provides 18 compounds A-11.001 to A-11.018 of formula I-1 wherein R_2 is CF_2CF_3 , A is CH, X is SO, R_1 is ethyl and Q_1 are as defined in table B.

- 20 Table A-12 provides 18 compounds A-12.001 to A-12.018 of formula I-1 wherein R_2 is CF_2CF_3 , A is CH, X is SO_2 , R_1 is ethyl and Q_1 are as defined in table B.

The tables below further illustrate specific compounds of the invention.



(I-2)

- 25 Table C-1 provides 9 compounds C-1.001 to C-1.009 of formula I-2 wherein R_2 is CF_3 , A is N, X is S, R_1 is ethyl and Q_1 are as defined in Table D.

Table D: Substituent definitions of Q_1

Index	Q ₁
1	
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Table C-2 provides 9 compounds C-2.001 to C-2.009 of formula I-2 wherein R_2 is CF_3 , A is N, X is SO, R_1 is ethyl and Q_1 are as defined in Table D.

Table C-3 provides 9 compounds C-3.001 to C-3.009 of formula I-2 wherein R_2 is CF_3 , A is N, X is SO_2 , R_1 is ethyl and Q_1 are as defined in Table D.

- 5 Table C-4 provides 9 compounds C-4.001 to C-4.009 of formula I-2 wherein R_2 is CF_3 , A is CH, X is S, R_1 is ethyl and Q_1 are as defined in Table D.

Table C-5 provides 9 compounds C-5.001 to C-5.009 of formula I-2 wherein R_2 is CF_3 , A is CH, X is SO, R_1 is ethyl and Q_1 are as defined in Table D.

- 10 Table C-6 provides 9 compounds C-6.001 to C-6.009 of formula I-2 wherein R_2 is CF_3 , A is CH, X is SO_2 , R_1 is ethyl and Q_1 are as defined in Table D.

Table C-7 provides 9 compounds C-7.001 to C-7.009 of formula I-2 wherein R_2 is CF_2CF_3 , A is N, X is S, R_1 is ethyl and Q_1 are as defined in Table D.

Table C-8 provides 9 compounds C-8.001 to C-8.009 of formula I-2 wherein R_2 is CF_2CF_3 , A is N, X is SO, R_1 is ethyl and Q_1 are as defined in Table D.

- 15 Table C-9 provides 9 compounds C-9.001 to C-9.009 of formula I-2 wherein R_2 is CF_2CF_3 , A is N, X is SO_2 , R_1 is ethyl and Q_1 are as defined in Table D.

Table C-10 provides 9 compounds C-10.001 to C-10.009 of formula I-2 wherein R_2 is CF_2CF_3 , A is CH, X is S, R_1 is ethyl and Q_1 are as defined in Table D.

- 20 Table C-11 provides 9 compounds C-11.001 to C-11.009 of formula I-2 wherein R_2 is CF_2CF_3 , A is CH, X is SO, R_1 is ethyl and Q_1 are as defined in Table D.

Table C-12 provides 9 compounds C-12.001 to C-12.009 of formula I-2 wherein R_2 is CF_2CF_3 , A is CH, X is SO_2 , R_1 is ethyl and Q_1 are as defined in Table D.

- 25 The compounds of formula I according to the invention are preventively and/or curatively valuable active ingredients in the field of pest control, even at low rates of application, which have a very favorable biocidal spectrum and are well tolerated by warm-blooded species, fish and plants. The active ingredients according to the invention act against all or individual developmental stages of normally sensitive, but also resistant, animal pests, such as insects or representatives of the order Acarina. The insecticidal or acaricidal activity of the active ingredients according to the invention can
30 manifest itself directly, i. e. in destruction of the pests, which takes place either immediately or only after some time has elapsed, for example during ecdysis, or indirectly, for example in a reduced oviposition and/or hatching rate, a good activity corresponding to a destruction rate (mortality) of at least 50 to 60%.

Examples of the above-mentioned animal pests are:

from the order *Acarina*, for example,

Acalitus spp, Aculus spp, Acaricalus spp, Aceria spp, Acarus siro, Amblyomma spp., Argas spp.,

- 5 Boophilus spp., Brevipalpus spp., Bryobia spp, Calipitimerus spp., Chorioptes spp., Dermanyssus gallinae, Dermatophagoides spp, Eotetranychus spp, Eriophyes spp., Hemitarsonemus spp, Hyalomma spp., Ixodes spp., Olygonychus spp, Ornithodoros spp., Polyphagotarsonus latus, Panonychus spp., Phyllocoptura oleivora, Phytionemus spp, Polyphagotarsonemus spp, Psoroptes spp., Rhipicephalus spp., Rhizoglyphus spp., Sarcoptes spp., Steneotarsonemus spp, Tarsonemus spp. and Tetranychus spp.;

from the order *Anoplura*, for example,

Haematopinus spp., Linognathus spp., Pediculus spp., Pemphigus spp. and Phylloxera spp.;

from the order *Coleoptera*, for example,

- 15 Agriotes spp., Amphimallon majale, Anomala orientalis, Anthonomus spp., Aphodius spp, Astylus atromaculatus, Ataenius spp, Atomaria linearis, Chaetocnema tibialis, Cerotoma spp, Conoderus spp, Cosmopolites spp., Cotinis nitida, Curculio spp., Cyclocephala spp, Dermestes spp., Diabrotica spp., Diloboderus abderus, Epilachna spp., Eremnus spp., Heteronychus arator, Hypothenemus hampei, Lagria vilosa, Leptinotarsa decemlineata, Lissorhoptrus spp., Liogenys spp, Maecolaspis spp, Maladera castanea, Megascelis spp, Meligethes aeneus, Melolontha spp., Myochrous armatus, 20 Oryzaephilus spp., Otiorhynchus spp., Phyllophaga spp, Phlyctinus spp., Popillia spp., Psylliodes spp., Rhyssomatus aubtilis, Rhizopertha spp., Scarabeidae, Sitophilus spp., Sitotroga spp., Somaticus spp, Sphenophorus spp, Sternechus subsignatus, Tenebrio spp., Tribolium spp. and Trogoderma spp.;

from the order *Diptera*, for example,

- 25 Aedes spp., Anopheles spp, Antherigona soccata, Bactrocea oleae, Bibio hortulanus, Bradysia spp, Calliphora erythrocephala, Ceratitis spp., Chrysomyia spp., Culex spp., Cuterebra spp., Dacus spp., Delia spp, Drosophila melanogaster, Fannia spp., Gastrophilus spp., Geomyza tripunctata, Glossina spp., Hypoderma spp., Hyppobosca spp., Liriomyza spp., Lucilia spp., Melanagromyza spp., Musca spp., Oestrus spp., Orseolia spp., Oscinella frit, Pegomyia hyoscyami, Phorbia spp., Rhagoletis spp, Rivelia quadrifasciata, Scatella spp, Sciara spp., Stomoxys spp., Tabanus spp., Tannia spp. and 30 Tipula spp.;

from the order *Hemiptera*, for example,

- Acanthocoris scabrator, Acrosternum spp, Adelphocoris lineolatus, Amblypelta nitida, Bathycoelia thalassina, Blissus spp, Cimex spp., Clavigralla tomentosicollis, Creontiades spp, Distantiella theobroma, Dichelops furcatus, Dysdercus spp., Edessa spp, Euschistus spp., Eurydema pulchrum, 35 Eurygaster spp., Halyomorpha halys, Horcias nobilellus, Leptocoris spp., Lygus spp, Margarodes spp, Murgantia histrionica, Neomegalotomus spp, Nesidiocoris tenuis, Nezara spp., Nysius simulans, Oebalus insularis, Piesma spp., Piezodorus spp, Rhodnius spp., Sahlbergella singularis, Scaptocoris castanea, Scotinophara spp. , Thyanta spp , Triatoma spp., Vatica illudens;

- Acyrtosium pisum, Adalges spp, Agalliana ensigera, Agonosцена targionii, Aleurodicus spp, Aleurocanthus spp, Aleurolobus barodensis, Aleurothrix floccosus, Aleyrodes brassicae, Amarasca biguttula, Amritodus atkinsoni, Aonidiella spp., Aphididae, Aphis spp., Aspidiotus spp., Aulacorthum solani, Bactericera cockerelli, Bemisia spp, Brachycaudus spp, Brevicoryne brassicae, Cacopsylla
- 5 spp, Cavariella aegopodii Scop., Ceroplaster spp., Chrysomphalus aonidium, Chrysomphalus dictyospermi, Cicadella spp, Cofana spectra, Cryptomyzus spp, Cicadulina spp, Coccus hesperidum, Dalbulus maidis, Dialeurodes spp, Diaphorina citri, Diuraphis noxia, Dysaphis spp, Empoasca spp., Eriosoma larigerum, Erythroneura spp., Gascardia spp., Glycaspis brimblecombei, Hyadaphis pseudobrassicae, Hyalopterus spp, Hyperomyzus pallidus, Idioscopus clypealis, Jacobiasca lybica,
- 10 Laodelphax spp., Lecanium corni, Lepidosaphes spp., Lopaphis erysimi, Lyogenys maidis, Macrosiphum spp., Mahanarva spp, Metcalfa pruinosa, Metopolophium dirhodum, Myndus crudus, Myzus spp., Neotoxoptera sp, Nephotettix spp., Nilaparvata spp., Nippolachnus piri Mats, Odonaspis ruthae, Oregma lanigera Zehnter, Parabemisia myricae, Paratrioza cockerelli, Parlatoria spp., Pemphigus spp., Peregrinus maidis, Perkinsiella spp, Phorodon humuli, Phylloxera spp, Planococcus
- 15 spp., Pseudaulacaspis spp., Pseudococcus spp., Pseudatomoscelis seriatus, Psylla spp., Pulvinaria aethiopica, Quadraspidiotus spp., Quesada gigas, Recilia dorsalis, Rhopalosiphum spp., Saissetia spp., Scaphoideus spp., Schizaphis spp., Sitobion spp., Sogatella furcifera, Spissistilus festinus, Tarophagus Proserpina, Toxoptera spp, Trialeurodes spp, Tridiscus sporoboli, Trionymus spp, Trioza erytrae , Unaspis citri, Zyginia flammigera, Zyginidia scutellaris, ;
- 20 from the order *Hymenoptera*, for example, Acromyrmex, Arge spp, Atta spp., Cephus spp., Diprion spp., Diprionidae, Gilpinia polytoma, Hoplocampa spp., Lasius spp., Monomorium pharaonis, Neodiprion spp., Pogonomymex spp, Slenopsis invicta, Solenopsis spp. and Vespa spp.;
- from the order *Isoptera*, for example,
- 25 Coptotermes spp, Cornitermes cumulans, Incisitermes spp, Macrotermes spp, Mastotermes spp, Microtermes spp, Reticulitermes spp.; Solenopsis geminate
- from the order *Lepidoptera*, for example,
- Acleris spp., Adoxophyes spp., Aegeria spp., Agrotis spp., Alabama argillaceae, Amylois spp., Anticarsia gemmatilis, Archips spp., Argyresthia spp, Argyrotaenia spp., Autographa spp., Bucculatrix
- 30 thurberiella, Busseola fusca, Cadra cautella, Carposina nipponensis, Chilo spp., Choristoneura spp., Chrysoteuchia topiaria, Clysia ambiguella, Cnaphalocrocis spp., Cnephasia spp., Cochylis spp., Coleophora spp., Colias lesbia, Cosmophila flava, Crambus spp, Crocidolomia binotalis, Cryptophlebia leucotreta, Cydalima perspectalis, Cydia spp., Diaphania perspectalis, Diatraea spp., Diparopsis castanea, Earias spp., Eldana saccharina, Ephestia spp., Epinotia spp, Estigmene acrea,
- 35 Etiella zinckinella, Eucosma spp., Eupoecilia ambiguella, Euproctis spp., Euxoa spp., Feltia jaculiferia, Grapholita spp., Hedyia nubiferana, Heliothis spp., Hellula undalis, Herpetogramma spp, Hyphantria cunea, Keiferia lycopersicella, Lasmopalpus lignosellus, Leucoptera scitella, Lithocollethis spp., Lobesia botrana, Loxostege bifidalis, Lymantria spp., Lyonetia spp., Malacosoma spp., Mamestra brassicae, Manduca sexta, Mythimna spp, Noctua spp, Operophtera spp., Orniodes indica, Ostrinia

nubilalis, Pammene spp., Pandemis spp., Panolis flammea, Papaipema nebris, Pectinophora gossypi-
 ela, Perileucoptera coffeella, Pseudaletia unipuncta, Phthorimaea operculella, Pieris rapae, Pieris
 spp., Plutella xylostella, Prays spp., Pseudoplusia spp, Rachiplusia nu, Richia albicosta, Scirpophaga
 spp., Sesamia spp., Sparganothis spp., Spodoptera spp., Sylepta derogate, Synanthedon spp.,

5 Thaumetopoea spp., Tortrix spp., Trichoplusia ni, Tuta absoluta, and Yponomeuta spp.;

from the order *Mallophaga*, for example,

Damalinea spp. and Trichodectes spp.;

from the order *Orthoptera*, for example,

Blatta spp., Blattella spp., Grylotalpa spp., Leucophaea maderae, Locusta spp., Neocurtilla

10 hexadactyla, Periplaneta spp. , Scapteriscus spp, and Schistocerca spp.;

from the order *Psocoptera*, for example,

Liposcelis spp.;

from the order *Siphonaptera*, for example,

Ceratophyllus spp., Ctenocephalides spp. and Xenopsylla cheopis;

15

from the order *Thysanoptera*, for example,

Calliothrips phaseoli, Frankliniella spp., Heliothrips spp, Hercinothrips spp., Parthenothrips spp,

Scirtothrips aurantii, Sericothrips variabilis, Taeniothrips spp., Thrips spp;

from the order *Thysanura*, for example, Lepisma saccharina.

20

The active ingredients according to the invention can be used for controlling, i. e. containing or
 destroying, pests of the abovementioned type which occur in particular on plants, especially on useful
 plants and ornamentals in agriculture, in horticulture and in forests, or on organs, such as fruits,
 flowers, foliage, stalks, tubers or roots, of such plants, and in some cases even plant organs which are
 25 formed at a later point in time remain protected against these pests.

Suitable target crops are, in particular, cereals, such as wheat, barley, rye, oats, rice, maize or
 sorghum; beet, such as sugar or fodder beet; fruit, for example pomaceous fruit, stone fruit or soft fruit,
 such as apples, pears, plums, peaches, almonds, cherries or berries, for example strawberries,
 30 raspberries or blackberries; leguminous crops, such as beans, lentils, peas or soya; oil crops, such as
 oilseed rape, mustard, poppies, olives, sunflowers, coconut, castor, cocoa or ground nuts; cucurbits,
 such as pumpkins, cucumbers or melons; fibre plants, such as cotton, flax, hemp or jute; citrus fruit,
 such as oranges, lemons, grapefruit or tangerines; vegetables, such as spinach, lettuce, asparagus,
 cabbages, carrots, onions, tomatoes, potatoes or bell peppers; Lauraceae, such as avocado,
 35 Cinnamomum or camphor; and also tobacco, nuts, coffee, eggplants, sugarcane, tea, pepper,
 grapevines, hops, the plantain family and latex plants.

The compositions and/or methods of the present invention may be also used on any ornamental
 and/or vegetable crops, including flowers, shrubs, broad-leaved trees and evergreens.

For example the invention may be used on any of the following ornamental species: *Ageratum* spp., *Alonsoa* spp., *Anemone* spp., *Anisodonteia capensis*, *Anthemis* spp., *Antirrhinum* spp., *Aster* spp., *Begonia* spp. (e.g. *B. elatior*, *B. semperflorens*, *B. tubéreaux*), *Bougainvillea* spp., *Brachycome* spp., *Brassica* spp. (ornamental), *Calceolaria* spp., *Capsicum annuum*, *Catharanthus roseus*, *Canna* spp.,

- 5 *Centaurea* spp., *Chrysanthemum* spp., *Cineraria* spp. (*C. maritime*), *Coreopsis* spp., *Crassula coccinea*, *Cuphea ignea*, *Dahlia* spp., *Delphinium* spp., *Dicentra spectabilis*, *Dorotheantus* spp., *Eustoma grandiflorum*, *Forsythia* spp., *Fuchsia* spp., *Geranium gnaphalium*, *Gerbera* spp., *Gomphrena globosa*, *Heliotropium* spp., *Helianthus* spp., *Hibiscus* spp., *Hortensia* spp., *Hydrangea* spp., *Hypoestes phyllostachya*, *Impatiens* spp. (*I. Walleriana*), *Iresines* spp., *Kalanchoe* spp., *Lantana* spp., *Lavatera trimestris*, *Leonotis leonurus*, *Lilium* spp., *Mesembryanthemum* spp., *Mimulus* spp.,
10 *Monarda* spp., *Nemesia* spp., *Tagetes* spp., *Dianthus* spp. (carnation), *Canna* spp., *Oxalis* spp., *Bellis* spp., *Pelargonium* spp. (*P. peltatum*, *P. Zonale*), *Viola* spp. (pansy), *Petunia* spp., *Phlox* spp., *Plectranthus* spp., *Poinsettia* spp., *Parthenocissus* spp. (*P. quinquefolia*, *P. tricuspidata*), *Primula* spp., *Ranunculus* spp., *Rhododendron* spp., *Rosa* spp. (rose), *Rudbeckia* spp., *Saintpaulia* spp.,
15 *Salvia* spp., *Scaevola aemola*, *Schizanthus wisetonensis*, *Sedum* spp., *Solanum* spp., *Surfinia* spp., *Tagetes* spp., *Nicotinia* spp., *Verbena* spp., *Zinnia* spp. and other bedding plants.

For example the invention may be used on any of the following vegetable species: *Allium* spp. (*A. sativum*, *A. cepa*, *A. oschaninii*, *A. Porrum*, *A. ascalonicum*, *A. fistulosum*), *Anthriscus cerefolium*, *Apium graveolus*, *Asparagus officinalis*, *Beta vulgaris*, *Brassica* spp. (*B. Oleracea*, *B. Pekinensis*, *B. rapa*), *Capsicum annuum*, *Cicer arietinum*, *Cichorium endivia*, *Cichorium* spp. (*C. intybus*, *C. endivia*),
20 *Citrillus lanatus*, *Cucumis* spp. (*C. sativus*, *C. melo*), *Cucurbita* spp. (*C. pepo*, *C. maxima*), *Cyanara* spp. (*C. scolymus*, *C. cardunculus*), *Daucus carota*, *Foeniculum vulgare*, *Hypericum* spp., *Lactuca sativa*, *Lycopersicon* spp. (*L. esculentum*, *L. lycopersicum*), *Mentha* spp., *Ocimum basilicum*, *Petroselinum crispum*, *Phaseolus* spp. (*P. vulgaris*, *P. coccineus*), *Pisum sativum*, *Raphanus sativus*,
25 *Rheum rhaponticum*, *Rosemarinus* spp., *Salvia* spp., *Scorzonera hispanica*, *Solanum melongena*, *Spinacea oleracea*, *Valerianella* spp. (*V. locusta*, *V. eriocarpa*) and *Vicia faba*.

Preferred ornamental species include African violet, *Begonia*, *Dahlia*, *Gerbera*, *Hydrangea*, *Verbena*, *Rosa*, *Kalanchoe*, *Poinsettia*, *Aster*, *Centaurea*, *Coreopsis*, *Delphinium*, *Monarda*, *Phlox*, *Rudbeckia*, *Sedum*, *Petunia*, *Viola*, *Impatiens*, *Geranium*, *Chrysanthemum*, *Ranunculus*, *Fuchsia*, *Salvia*,
30 *Hortensia*, rosemary, sage, St. Johnswort, mint, sweet pepper, tomato and cucumber.

The active ingredients according to the invention are especially suitable for controlling *Aphis craccivora*, *Diabrotica balteata*, *Heliothis virescens*, *Myzus persicae*, *Plutella xylostella* and *Spodoptera littoralis* in cotton, vegetable, maize, rice and soya crops. The active ingredients according to the invention are further especially suitable for controlling *Mamestra* (preferably in vegetables),
35 *Cydia pomonella* (preferably in apples), *Empoasca* (preferably in vegetables, vineyards), *Leptinotarsa* (preferably in potatoes) and *Chilo suppressalis* (preferably in rice).

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In a further aspect, the invention may also relate to a method of controlling damage to plant and parts thereof by plant parasitic nematodes (Endoparasitic-, Semiendoparasitic- and Ectoparasitic nematodes), especially plant parasitic nematodes such as root knot nematodes, Meloidogyne hapla, Meloidogyne incognita, Meloidogyne javanica, Meloidogyne arenaria and other Meloidogyne species; 10 cyst-forming nematodes, Globodera rostochiensis and other Globodera species; Heterodera avenae, Heterodera glycines, Heterodera schachtii, Heterodera trifolii, and other Heterodera species; Seed gall nematodes, Anguina species; Stem and foliar nematodes, Aphelenchoides species; Sting nematodes, Belonolaimus longicaudatus and other Belonolaimus species; Pine nematodes, Bursaphelenchus xylophilus and other Bursaphelenchus species; Ring nematodes, Criconema species, Criconemella 15 species, Criconemoides species, Mesocriconema species; Stem and bulb nematodes, Ditylenchus destructor, Ditylenchus dipsaci and other Ditylenchus species; Awl nematodes, Dolichodorus species; Spiral nematodes, Helicotylenchus multicinctus and other Helicotylenchus species; Sheath and sheathoid nematodes, Hemicycliophora species and Hemicriconemoides species; Hirshmanniella species; Lance nematodes, Hoploaimus species; false rootknot nematodes, Nacobbus species; 20 Needle nematodes, Longidorus elongatus and other Longidorus species; Pin nematodes, Pratylenchus species; Lesion nematodes, Pratylenchus neglectus, Pratylenchus penetrans, Pratylenchus curvatus, Pratylenchus goodeyi and other Pratylenchus species; Burrowing nematodes, Radopholus similis and other Radopholus species; Reniform nematodes, Rotylenchus robustus, Rotylenchus reniformis and other Rotylenchus species; Scutellonema species; Stubby root 25 nematodes, Trichodorus primitivus and other Trichodorus species, Paratrichodorus species; Stunt nematodes, Tylenchorhynchus claytoni, Tylenchorhynchus dubius and other Tylenchorhynchus species; Citrus nematodes, Tylenchulus species; Dagger nematodes, Xiphinema species; and other plant parasitic nematode species, such as Subanguina spp., Hypsoperine spp., Macroposthonia spp., Melinus spp., Punctodera spp., and Quinisulcius spp..

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The compounds of the invention may also have activity against the molluscs. Examples of which include, for example, Ampullariidae; Arion (A. ater, A. circumscriptus, A. hortensis, A. rufus); Bradybaenidae (Bradybaena fruticum); Cepaea (C. hortensis, C. Nemoralis); ochlodina; Deroceras (D. agrestis, D. empiricorum, D. laeve, D. reticulatum); Discus (D. rotundatus); Euomphalia; Galba (G. 35 trunculata); Helicella (H. itala, H. obvia); Helicidae Helicigona arbustorum); Helicodiscus; Helix (H. aperta); Limax (L. cinereoniger, L. flavus, L. marginatus, L. maximus, L. tenellus); Lymnaea; Milax (M. gagates, M. marginatus, M. sowerbyi); Opeas; Pomacea (P. canaticulata); Vallonia and Zonitoides.

The term "crops" is to be understood as including also crop plants which have been so transformed by the use of recombinant DNA techniques that they are capable of synthesising one or more selectively acting toxins, such as are known, for example, from toxin-producing bacteria, especially those of the genus *Bacillus*.

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Toxins that can be expressed by such transgenic plants include, for example, insecticidal proteins, 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

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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

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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

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synthase, chitinases and glucanases.

In the context of the present invention there are to be understood by δ -endotoxins, for example Cry1Ab, Cry1Ac, Cry1F, Cry1Fa2, Cry2Ab, Cry3A, Cry3Bb1 or Cry9C, or vegetative insecticidal proteins (Vip), for example Vip1, Vip2, Vip3 or Vip3A, expressly also hybrid toxins, truncated toxins and modified toxins. Hybrid toxins are produced recombinantly by a new combination of different domains of those proteins (see, for example, WO 02/15701). Truncated toxins, for example a truncated Cry1Ab, are known. In the case of modified toxins, one or more amino acids of the naturally occurring toxin are replaced. In such amino acid replacements, preferably non-naturally present protease recognition sequences are inserted into the toxin, such as, for example, in the case of Cry3A055, a cathepsin-G-recognition sequence is inserted into a Cry3A toxin (see WO 03/018810).

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Examples of such toxins or transgenic plants capable of synthesising such toxins are disclosed, for example, in EP-A-0 374 753, WO 93/07278, WO 95/34656, EP-A-0 427 529, EP-A-451 878 and WO 03/052073.

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

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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 moths (Lepidoptera).

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

Transgenic crops of insect-resistant plants are also described in BATS (Zentrum für Biosicherheit und Nachhaltigkeit, Zentrum BATS, Clarastrasse 13, 4058 Basel, Switzerland) Report 2003, (<http://bats.ch>).

The term "crops" is to be understood as including also crop 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.

Crops may also be modified for enhanced resistance to fungal (for example Fusarium, Anthracnose, or Phytophthora), bacterial (for example Pseudomonas) or viral (for example potato leafroll virus, tomato spotted wilt virus, cucumber mosaic virus) pathogens.

Crops also include those that have enhanced resistance to nematodes, such as the soybean cyst nematode.

Crops that are tolerance to abiotic stress include those that have enhanced tolerance to drought, high salt, high temperature, chill, frost, or light radiation, for example through expression of NF-YB or other proteins known in the art.

Antipathogenic substances which can be expressed by such transgenic plants include, for example, ion channel blockers, such as blockers for sodium and calcium channels, for example the viral KP1, KP4 or KP6 toxins; stilbene synthases; bibenzyl synthases; chitinases; glucanases; the so-called "pathogenesis-related proteins" (PRPs; see e.g. EP-A-0 392 225); antipathogenic substances produced by microorganisms, for example peptide antibiotics or heterocyclic antibiotics (see e.g. WO 95/33818) or protein or polypeptide factors involved in plant pathogen defence (so-called "plant disease resistance genes", as described in WO 03/000906).

Further areas of use of the compositions according to the invention are the protection of stored goods and store rooms and the protection of raw materials, such as wood, textiles, floor coverings or

buildings, and also in the hygiene sector, especially the protection of humans, domestic animals and productive livestock against pests of the mentioned type.

The present invention also provides a method for controlling pests (such as mosquitoes and other disease vectors; see also http://www.who.int/malaria/vector_control/irs/en/). In one embodiment, the method for controlling pests comprises applying the compositions of the invention to the target pests, to their locus or to a surface or substrate by brushing, rolling, spraying, spreading or dipping. By way of example, an IRS (indoor residual spraying) application of a surface such as a wall, ceiling or floor surface is contemplated by the method of the invention. In another embodiment, it is contemplated to apply such compositions to a substrate such as non-woven or a fabric material in the form of (or which can be used in the manufacture of) netting, clothing, bedding, curtains and tents.

In one embodiment, the method for controlling such pests comprises applying a pesticidally effective amount of the compositions of the invention to the target pests, to their locus, or to a surface or substrate so as to provide effective residual pesticidal activity on the surface or substrate. Such application may be made by brushing, rolling, spraying, spreading or dipping the pesticidal composition of the invention. By way of example, an IRS application of a surface such as a wall, ceiling or floor surface is contemplated by the method of the invention so as to provide effective residual pesticidal activity on the surface. In another embodiment, it is contemplated to apply such compositions for residual control of pests on a substrate such as a fabric material in the form of (or which can be used in the manufacture of) netting, clothing, bedding, curtains and tents.

Substrates including non-woven, fabrics or netting to be treated may be made of natural fibres such as cotton, raffia, jute, flax, sisal, hessian, or wool, or synthetic fibres such as polyamide, polyester, polypropylene, polyacrylonitrile or the like. The polyesters are particularly suitable. The methods of textile treatment are known, e.g. WO 2008/151984, WO 2003/034823, US 5631072, WO 2005/64072, WO2006/128870, EP 1724392, WO 2005113886 or WO 2007/090739.

Further areas of use of the compositions according to the invention are the field of tree injection/trunk treatment for all ornamental trees as well all sort of fruit and nut trees.

In the field of tree injection/trunk treatment, the compounds according to the present invention are especially suitable against wood-boring insects from the order *Lepidoptera* as mentioned above and from the order *Coleoptera*, especially against woodborers listed in the following tables A and B:

Table A. Examples of exotic woodborers of economic importance.

Family	Species	Host or Crop Infested
Buprestidae	<i>Agrilus planipennis</i>	Ash

Cerambycidae	<i>Anoplura glabripennis</i>	Hardwoods
Scolytidae	<i>Xylosandrus crassiusculus</i>	Hardwoods
	<i>X. mutilatus</i>	Hardwoods
	<i>Tomicus piniperda</i>	Conifers

Table B. Examples of native woodborers of economic importance.

Family	Species	Host or Crop Infested
Buprestidae	<i>Agrilus anxius</i>	Birch
	<i>Agrilus politus</i>	Willow, Maple
	<i>Agrilus sayi</i>	Bayberry, Sweetfern
	<i>Agrilus vittaticollis</i>	Apple, Pear, Cranberry, Serviceberry, Hawthorn
	<i>Chrysobothris femorata</i>	Apple, Apricot, Beech, Boxelder, Cherry, Chestnut, Currant, Elm, Hawthorn, Hackberry, Hickory, Horsechestnut, Linden, Maple, Mountain-ash, Oak, Pecan, Pear, Peach, Persimmon, Plum, Poplar, Quince, Redbud, Serviceberry, Sycamore, Walnut, Willow
	<i>Texania campestris</i>	Basswood, Beech, Maple, Oak, Sycamore, Willow, Yellow-poplar
Cerambycidae	<i>Goes pulverulentus</i>	Beech, Elm, Nuttall, Willow, Black oak, Cherrybark oak, Water oak, Sycamore
	<i>Goes tigrinus</i>	Oak
	<i>Neoclytus acuminatus</i>	Ash, Hickory, Oak, Walnut, Birch, Beech, Maple, Eastern hophornbeam, Dogwood, Persimmon, Redbud, Holly,

Family	Species	Host or Crop Infested
		Hackberry, Black locust, Honeylocust, Yellow-poplar, Chestnut, Osage-orange, Sassafras, Lilac, Mountain-mahogany, Pear, Cherry, Plum, Peach, Apple, Elm, Basswood, Sweetgum
	<i>Neoptychodes trilineatus</i>	Fig, Alder, Mulberry, Willow, Netleaf hackberry
	<i>Oberea ocellata</i>	Sumac, Apple, Peach, Plum, Pear, Currant, Blackberry
	<i>Oberea tripunctata</i>	Dogwood, Viburnum, Elm, Sourwood, Blueberry, Rhododendron, Azalea, Laurel, Poplar, Willow, Mulberry
	<i>Oncideres cingulata</i>	Hickory, Pecan, Persimmon, Elm, Sourwood, Basswood, Honeylocust, Dogwood, Eucalyptus, Oak, Hackberry, Maple, Fruit trees
	<i>Saperda calcarata</i>	Poplar
	<i>Strophiona nitens</i>	Chestnut, Oak, Hickory, Walnut, Beech, Maple
Scolytidae	<i>Corthylus columbianus</i>	Maple, Oak, Yellow-poplar, Beech, Boxelder, Sycamore, Birch, Basswood, Chestnut, Elm
	<i>Dendroctonus frontalis</i>	Pine
	<i>Dryocoetes betulae</i>	Birch, Sweetgum, Wild cherry, Beech, Pear
	<i>Monarthrum fasciatum</i>	Oak, Maple, Birch, Chestnut, Sweetgum, Blackgum, Poplar, Hickory, Mimosa, Apple, Peach, Pine

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Family	Species	Host or Crop Infested
	<i>Phloeotribus liminaris</i>	Peach, Cherry, Plum, Black cherry, Elm, Mulberry, Mountain-ash
	<i>Pseudopityophthorus pruinosis</i>	Oak, American beech, Black cherry, Chickasaw plum, Chestnut, Maple, Hickory, Hornbeam, Hophornbeam
Sesiidae	<i>Paranthrene simulans</i>	Oak, American chestnut
	<i>Sannina uroceriformis</i>	Persimmon
	<i>Synanthedon exitiosa</i>	Peach, Plum, Nectarine, Cherry, Apricot, Almond, Black cherry
	<i>Synanthedon pictipes</i>	Peach, Plum, Cherry, Beach, Black Cherry
	<i>Synanthedon rubrofascia</i>	Tupelo
	<i>Synanthedon scitula</i>	Dogwood, Pecan, Hickory, Oak, Chestnut, Beech, Birch, Black cherry, Elm, Mountain-ash, Viburnum, Willow, Apple, Loquat, Ninebark, Bayberry
	<i>Vitacea polistiformis</i>	Grape

The present invention may be also used to control any insect pests that may be present in turfgrass, including for example beetles, caterpillars, fire ants, ground pearls, millipedes, sow bugs, mites, mole crickets, scales, mealybugs ticks, spittlebugs, southern chinch bugs and white grubs. The present invention may be used to control insect pests at various stages of their life cycle, including eggs, larvae, nymphs and adults.

In particular, the present invention may be used to control insect pests that feed on the roots of turfgrass including white grubs (such as *Cyclocephala* spp. (e.g. masked chafer, *C. lurida*), *Rhizotrogus* spp. (e.g. European chafer, *R. majalis*), *Cotinus* spp. (e.g. Green June beetle, *C. nitida*), *Popillia* spp. (e.g. Japanese beetle, *P. japonica*), *Phyllophaga* spp. (e.g. May/June beetle), *Ataenius* spp. (e.g. Black turfgrass ataenius, *A. spretulus*), *Maladera* spp. (e.g. Asiatic garden beetle, *M. castanea*) and *Tomarus* spp.), ground pearls (*Margarodes* spp.), mole crickets (tawny, southern, and

short-winged; *Scapteriscus* spp., *Gryllotalpa africana*) and leatherjackets (European crane fly, *Tipula* spp.).

The present invention may also be used to control insect pests of turfgrass that are thatch dwelling, including armyworms (such as fall armyworm *Spodoptera frugiperda*, and common armyworm *Pseudaletia unipuncta*), cutworms, billbugs (*Sphenophorus* spp., such as *S. venatus verstitus* and *S. parvulus*), and sod webworms (such as *Crambus* spp. and the tropical sod webworm, *Herpetogramma phaeopteralis*).

The present invention may also be used to control insect pests of turfgrass that live above the ground and feed on the turfgrass leaves, including chinch bugs (such as southern chinch bugs, *Blissus insularis*), Bermudagrass mite (*Eriophyes cynodoniensis*), rhodesgrass mealybug (*Antonina graminis*), two-lined spittlebug (*Prosapia bicincta*), leafhoppers, cutworms (*Noctuidae* family), and greenbugs. The present invention may also be used to control other pests of turfgrass such as red imported fire ants (*Solenopsis invicta*) that create ant mounds in turf.

In the hygiene sector, the compositions according to the invention are active against ectoparasites such as hard ticks, soft ticks, mange mites, harvest mites, flies (biting and licking), parasitic fly larvae, lice, hair lice, bird lice and fleas.

Examples of such parasites are:

Of the order Anoplurida: *Haematopinus* spp., *Linognathus* spp., *Pediculus* spp. and *Phtirus* spp., *Solenopotes* spp..

Of the order Mallophagida: *Trimenopon* spp., *Menopon* spp., *Trinoton* spp., *Bovicola* spp., *Werneckiella* spp., *Lepikentron* spp., *Damalina* spp., *Trichodectes* spp. and *Felicola* spp..

Of the order Diptera and the suborders Nematocera and Brachycera, for example *Aedes* spp., *Anopheles* spp., *Culex* spp., *Simulium* spp., *Eusimulium* spp., *Phlebotomus* spp., *Lutzomyia* spp., *Culicoides* spp., *Chrysops* spp., *Hybomitra* spp., *Atylotus* spp., *Tabanus* spp., *Haematopota* spp., *Philipomyia* spp., *Braula* spp., *Musca* spp., *Hydrotaea* spp., *Stomoxys* spp., *Haematobia* spp., *Morellia* spp., *Fannia* spp., *Glossina* spp., *Calliphora* spp., *Lucilia* spp., *Chrysomyia* spp., *Wohlfahrtia* spp., *Sarcophaga* spp., *Oestrus* spp., *Hypoderma* spp., *Gasterophilus* spp., *Hippobosca* spp., *Lipoptena* spp. and *Melophagus* spp..

Of the order Siphonaptera, for example *Pulex* spp., *Ctenocephalides* spp., *Xenopsylla* spp., *Ceratophyllus* spp..

Of the order Heteropterida, for example *Cimex* spp., *Triatoma* spp., *Rhodnius* spp., *Panstrongylus* spp..

5 Of the order Blattarida, for example *Blatta orientalis*, *Periplaneta americana*, *Blattella germanica* and *Supella* spp..

Of the subclass Acaria (Acarida) and the orders Meta- and Meso-stigmata, for example *Argas* spp., *Ornithodoros* spp., *Otobius* spp., *Ixodes* spp., *Amblyomma* spp., *Boophilus* spp., *Dermacentor* spp., *Haemophysalis* spp., *Hyalomma* spp., *Rhipicephalus* spp., *Dermanyssus* spp., *Raillietia* spp.,
10 *Pneumonyssus* spp., *Sternostoma* spp. and *Varroa* spp..

Of the orders Actinedida (Prostigmata) and Acaridida (Astigmata), for example *Acarapis* spp., *Cheyletiella* spp., *Ornithocheyletia* spp., *Myobia* spp., *Psorergates* spp., *Demodex* spp., *Trombicula* spp., *Listrophorus* spp., *Acarus* spp., *Tyrophagus* spp., *Caloglyphus* spp., *Hypodectes* spp.,
15 *Pterolichus* spp., *Psoroptes* spp., *Chorioptes* spp., *Otodectes* spp., *Sarcoptes* spp., *Notoedres* spp., *Knemidocoptes* spp., *Cytodites* spp. and *Laminosioptes* spp..

The compositions according to the invention are also suitable for protecting against insect infestation in the case of materials such as wood, textiles, plastics, adhesives, glues, paints, paper and card,
20 leather, floor coverings and buildings.

The compositions according to the invention can be used, for example, against the following pests: beetles such as *Hylotrupes bajulus*, *Chlorophorus pilosis*, *Anobium punctatum*, *Xestobium rufovillosum*, *Ptilinuspecticornis*, *Dendrobium pertinex*, *Ernobius mollis*, *Priobium carpini*, *Lyctus*
25 *brunneus*, *Lyctus africanus*, *Lyctus planicollis*, *Lyctus linearis*, *Lyctus pubescens*, *Trogoxylon aequale*, *Minthesrugicollis*, *Xyleborus* spec., *Tryptodendron* spec., *Apate monachus*, *Bostrychus capucins*, *Heterobostrychus brunneus*, *Sinoxylon* spec. and *Dinoderus minutus*, and also hymenopterans such as *Sirex juvencus*, *Urocera* *gigas*, *Urocera* *gigas taignus* and *Urocera* *augur*, and termites such as *Kaloterms flavicollis*, *Cryptoterms brevis*, *Heteroterms indicola*, *Reticulitermes flavipes*,
30 *Reticulitermes santonensis*, *Reticulitermes lucifugus*, *Mastoterms darwiniensis*, *Zootermopsis nevadensis* and *Coptoterms formosanus*, and bristletails such as *Lepisma saccharina*.

The compounds according to the invention can be used as pesticidal agents in unmodified form, but they are generally formulated into compositions in various ways using formulation adjuvants, such as
35 carriers, solvents and surface-active substances. The formulations can be in various physical forms, e.g. in the form of dusting powders, gels, wettable powders, water-dispersible granules, water-dispersible tablets, effervescent pellets, emulsifiable concentrates, microemulsifiable concentrates, oil-in-water emulsions, oil-flowables, aqueous dispersions, oily dispersions, suspo-emulsions, capsule suspensions, emulsifiable granules, soluble liquids, water-soluble concentrates (with water or a water-

miscible organic solvent as carrier), impregnated polymer films or in other forms known e.g. from the Manual on Development and Use of FAO and WHO Specifications for Pesticides, United Nations, First Edition, Second Revision (2010). Such formulations can either be used directly or diluted prior to use. The dilutions can be made, for example, with water, liquid fertilisers, micronutrients, biological organisms, oil or solvents.

The formulations can be prepared e.g. by mixing the active ingredient with the formulation adjuvants in order to obtain compositions in the form of finely divided solids, granules, solutions, dispersions or emulsions. The active ingredients can also be formulated with other adjuvants, such as finely divided solids, mineral oils, oils of vegetable or animal origin, modified oils of vegetable or animal origin, organic solvents, water, surface-active substances or combinations thereof.

The active ingredients can also be contained in very fine microcapsules. Microcapsules contain the active ingredients in a porous carrier. This enables the active ingredients to be released into the environment in controlled amounts (e.g. slow-release). Microcapsules usually have a diameter of from 0.1 to 500 microns. They contain active ingredients in an amount of about from 25 to 95 % by weight of the capsule weight. The active ingredients can be in the form of a monolithic solid, in the form of fine particles in solid or liquid dispersion or in the form of a suitable solution. The encapsulating membranes can comprise, for example, natural or synthetic rubbers, cellulose, styrene/butadiene copolymers, polyacrylonitrile, polyacrylate, polyesters, polyamides, polyureas, polyurethane or chemically modified polymers and starch xanthates or other polymers that are known to the person skilled in the art. Alternatively, very fine microcapsules can be formed in which the active ingredient is contained in the form of finely divided particles in a solid matrix of base substance, but the microcapsules are not themselves encapsulated.

The formulation adjuvants that are suitable for the preparation of the compositions according to the invention are known *per se*. As liquid carriers there may be used: water, toluene, xylene, petroleum ether, vegetable oils, acetone, methyl ethyl ketone, cyclohexanone, acid anhydrides, acetonitrile, acetophenone, amyl acetate, 2-butanone, butylene carbonate, chlorobenzene, cyclohexane, cyclohexanol, alkyl esters of acetic acid, diacetone alcohol, 1,2-dichloropropane, diethanolamine, p-diethylbenzene, diethylene glycol, diethylene glycol abietate, diethylene glycol butyl ether, diethylene glycol ethyl ether, diethylene glycol methyl ether, *N,N*-dimethylformamide, dimethyl sulfoxide, 1,4-dioxane, dipropylene glycol, dipropylene glycol methyl ether, dipropylene glycol dibenzoate, diproxitol, alkylpyrrolidone, ethyl acetate, 2-ethylhexanol, ethylene carbonate, 1,1,1-trichloroethane, 2-heptanone, alpha-pinene, d-limonene, ethyl lactate, ethylene glycol, ethylene glycol butyl ether, ethylene glycol methyl ether, gamma-butyrolactone, glycerol, glycerol acetate, glycerol diacetate, glycerol triacetate, hexadecane, hexylene glycol, isoamyl acetate, isobornyl acetate, isooctane, isophorone, isopropylbenzene, isopropyl myristate, lactic acid, laurylamine, mesityl oxide, methoxypropanol, methyl isoamyl ketone, methyl isobutyl ketone, methyl laurate, methyl octanoate, methyl oleate, methylene chloride, m-xylene, n-hexane, n-octylamine, octadecanoic acid, octylamine acetate,

oleic acid, oleylamine, o-xylene, phenol, polyethylene glycol, propionic acid, propyl lactate, propylene carbonate, propylene glycol, propylene glycol methyl ether, p-xylene, toluene, triethyl phosphate, triethylene glycol, xylenesulfonic acid, paraffin, mineral oil, trichloroethylene, perchloroethylene, ethyl acetate, amyl acetate, butyl acetate, propylene glycol methyl ether, diethylene glycol methyl ether, 5 methanol, ethanol, isopropanol, and alcohols of higher molecular weight, such as amyl alcohol, tetrahydrofurfuryl alcohol, hexanol, octanol, ethylene glycol, propylene glycol, glycerol, *N*-methyl-2-pyrrolidone and the like.

Suitable solid carriers are, for example, talc, titanium dioxide, pyrophyllite clay, silica, attapulgite clay, 10 kieselguhr, limestone, calcium carbonate, bentonite, calcium montmorillonite, cottonseed husks, wheat flour, soybean flour, pumice, wood flour, ground walnut shells, lignin and similar substances.

A large number of surface-active substances can advantageously be used in both solid and liquid formulations, especially in those formulations which can be diluted with a carrier prior to use. Surface-active substances may be anionic, cationic, non-ionic or polymeric and they can be used as 15 emulsifiers, wetting agents or suspending agents or for other purposes. Typical surface-active substances include, for example, salts of alkyl sulfates, such as diethanolammonium lauryl sulfate; salts of alkylarylsulfonates, such as calcium dodecylbenzenesulfonate; alkylphenol/alkylene oxide addition products, such as nonylphenol ethoxylate; alcohol/alkylene oxide addition products, such as tridecylalcohol ethoxylate; soaps, such as sodium stearate; salts of alkyl naphthalenesulfonates, such 20 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 lauryltrimethylammonium 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 di-alkylphosphate esters; and also further substances described e.g. in McCutcheon's Detergents and 25 Emulsifiers Annual, MC Publishing Corp., Ridgewood New Jersey (1981).

Further adjuvants that can be used in pesticidal formulations include crystallisation inhibitors, viscosity modifiers, suspending agents, dyes, anti-oxidants, foaming agents, light absorbers, mixing auxiliaries, antifoams, complexing agents, neutralising or pH-modifying substances and buffers, corrosion 30 inhibitors, fragrances, wetting agents, take-up enhancers, micronutrients, plasticisers, glidants, lubricants, dispersants, thickeners, antifreezes, microbicides, and liquid and solid fertilisers.

The compositions according to the invention can include an additive comprising an oil of vegetable or animal origin, a mineral oil, alkyl esters of such oils or mixtures of such oils and oil derivatives. The amount of oil additive in the composition according to the invention is generally from 0.01 to 10 %, 35 based on the mixture to be applied. For example, the oil additive can be added to a spray tank in the desired concentration after a spray mixture has been prepared. Preferred oil additives comprise mineral oils or an oil of vegetable origin, for example rapeseed oil, olive oil or sunflower oil, emulsified vegetable oil, alkyl esters of oils of vegetable origin, for example the methyl derivatives, or an oil of animal origin, such as fish oil or beef tallow. Preferred oil additives comprise alkyl esters of C₈-C₂₂ fatty

acids, especially the methyl derivatives of C₁₂-C₁₈ fatty acids, for example the methyl esters of lauric acid, palmitic acid and oleic acid (methyl laurate, methyl palmitate and methyl oleate, respectively). Many oil derivatives are known from the Compendium of Herbicide Adjuvants, 10th Edition, Southern Illinois University, 2010.

5

The inventive compositions generally comprise from 0.1 to 99 % by weight, especially from 0.1 to 95 % by weight, of compounds of the present invention and from 1 to 99.9 % by weight of a formulation adjuvant which preferably includes from 0 to 25 % by weight of a surface-active substance.

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

10

The rates of application vary within wide limits and depend on the nature of the soil, the method of application, the crop plant, the pest to be controlled, the prevailing climatic conditions, and other factors governed by the method of application, the time of application and the target crop. As a general guideline compounds may be applied at a rate of from 1 to 2000 l/ha, especially from 10 to

15

1000 l/ha.

Preferred formulations can have the following compositions (weight %):

Emulsifiable concentrates:

active ingredient:	1 to 95 %, preferably 60 to 90 %
20 surface-active agent:	1 to 30 %, preferably 5 to 20 %
liquid carrier:	1 to 80 %, preferably 1 to 35 %

Dusts:

active ingredient:	0.1 to 10 %, preferably 0.1 to 5 %
25 solid carrier:	99.9 to 90 %, preferably 99.9 to 99 %

Suspension concentrates:

active ingredient:	5 to 75 %, preferably 10 to 50 %
water:	94 to 24 %, preferably 88 to 30 %
30 surface-active agent:	1 to 40 %, preferably 2 to 30 %

Wettable powders:

active ingredient:	0.5 to 90 %, preferably 1 to 80 %
surface-active agent:	0.5 to 20 %, preferably 1 to 15 %
35 solid carrier:	5 to 95 %, preferably 15 to 90 %

Granules:

active ingredient:	0.1 to 30 %, preferably 0.1 to 15 %
solid carrier:	99.5 to 70 %, preferably 97 to 85 %

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

<u>Wettable powders</u>	a)	b)	c)
active ingredients	25 %	50 %	75 %
sodium lignosulfonate	5 %	5 %	-
sodium lauryl sulfate	3 %	-	5 %
sodium diisobutylphenylsulfonate	-	6 %	10 %
phenol polyethylene glycol ether (7-8 mol of ethylene oxide)	-	2 %	-
highly dispersed silicic acid	5 %	10 %	10 %
Kaolin	62 %	27 %	-

The combination 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.

5

<u>Powders for dry seed treatment</u>	a)	b)	c)
active ingredients	25 %	50 %	75 %
light mineral oil	5 %	5 %	5 %
highly dispersed silicic acid	5 %	5 %	-
Kaolin	65 %	40 %	-
Talcum	-	-	20 %

The combination 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.

10

<u>Emulsifiable concentrate</u>	
active ingredients	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.

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<u>Dusts</u>	a)	b)	c)
Active ingredients	5 %	6 %	4 %
Talcum	95 %	-	-
Kaolin	-	94 %	-
mineral filler	-	-	96 %

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

<u>Extruder granules</u>	
Active ingredients	15 %
sodium lignosulfonate	2 %
carboxymethylcellulose	1 %
Kaolin	82 %

The combination is mixed and ground with the adjuvants, and the mixture is moistened with water.

- 5 The mixture is extruded and then dried in a stream of air.

<u>Coated granules</u>	
Active ingredients	8 %
polyethylene glycol (mol. wt. 200)	3 %
Kaolin	89 %

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

15

Flowable concentrate for seed treatment

active ingredients	40 %
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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 %

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

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Slow Release Capsule Suspension

28 parts of the combination are mixed with 2 parts of an aromatic solvent and 7 parts of toluene diisocyanate/polymethylene-polyphenylisocyanate-mixture (8:1). This mixture is emulsified in a mixture of 1.2 parts of polyvinylalcohol, 0.05 parts of a defoamer and 51.6 parts of water until the desired particle size is achieved. To this emulsion a mixture of 2.8 parts 1,6-diaminohexane in 5.3 parts of water is added. The mixture is agitated until the polymerization reaction is completed. The obtained capsule suspension is stabilized by adding 0.25 parts of a thickener and 3 parts of a dispersing agent. The capsule suspension formulation contains 28% of the active ingredients. The medium capsule diameter is 8-15 microns. The resulting formulation is applied to seeds as an aqueous suspension in an apparatus suitable for that purpose.

15

Formulation types include 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), a soluble granule (SG) or any technically feasible formulation in combination with agriculturally acceptable adjuvants.

20

Preparatory Examples:

“Mp” means melting point in °C. Free radicals represent methyl groups. ¹H NMR measurements were recorded on a Bruker 400MHz spectrometer, chemical shifts are given in ppm relevant to a TMS standard. Spectra measured in deuterated solvents as indicated. Either one of the LCMS or GCMS methods below was used to characterize the compounds. The characteristic LCMS and GCMS values obtained for each compound were the retention time (“Rt”, recorded in minutes) and the measured molecular ion (M+H)⁺, (M-H)⁻ or (M)⁺.

30

LCMS Methods:

Method 1:

Spectra were recorded on a Mass Spectrometer from Waters (SQ Detector 2 Mass Spectrometer) equipped with an electrospray source (Polarity: positive or negative ions, Full Scan, Capillary: 3.00 kV, Cone range: 41 V, Source Temperature: 150°C, Desolvation Temperature: 500°C, Cone Gas Flow: 50 L/Hr, Desolvation Gas Flow: 1000 L/Hr, Mass range: 110 to 800 Da) and a H-Class UPLC from Waters: Binary pump, heated column compartment and diode-array detector. Column: Waters UPLC HSS T3 C18, 1.8 µm, 30 x 2.1 mm, Temp: 40 °C, DAD Wavelength range (nm): 200 to 400, Solvent Gradient: A = water + 5% Acetonitrile + 0.1 % HCOOH, B= Acetonitrile + 0.05 % HCOOH: gradient: 0 min 10% B; 0-0.2 min 10-50%B; 0.2-0.7 min 50-100% B; 0.7-1.3 min 100% B; 1.3-1.4 min 100-10% B; 1.4-1.6 min 10% B; Flow (mL/min) 0.6.

Method 2:

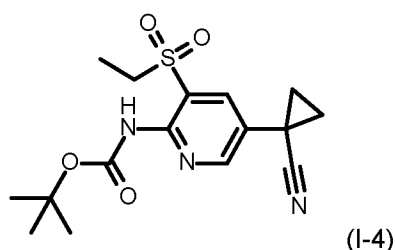
Spectra were recorded on a Mass Spectrometer from Agilent Technologies (6410 Triple Quadrupole mass spectrometer) equipped with an electrospray source (Polarity: positive or negative ions, MS2 Scan, Capillary: 4.00 kV, Fragmentor: 100 V, Desolvation Temperature: 350°C, Gas Flow: 11 L/min, Nebulizer Gas: 45 psi, Mass range: 100 to 800 Da) and a 1200 Series HPLC from Agilent: quaternary pump, heated column compartment and diode-array detector. Column: KINETEX EVO C18, 2.6 µm, 50 x 4.6 mm, Temp: 40 °C, DAD Wavelength range (nm): 210 to 400, Solvent Gradient: A = water + 5% Acetonitrile + 0.1 % HCOOH, B= Acetonitrile + 0.1 % HCOOH: gradient: 0 min 10% B, 90%A; 2.0-5.0 min 100% B; 5.0-6.0 min 100% B; 6.0-7.0 min 10% B, 90%A; 7.0-8.0 min 10% B, 90%A; Flow (mL/min) 1.2.

GCMS Method:Method 3:

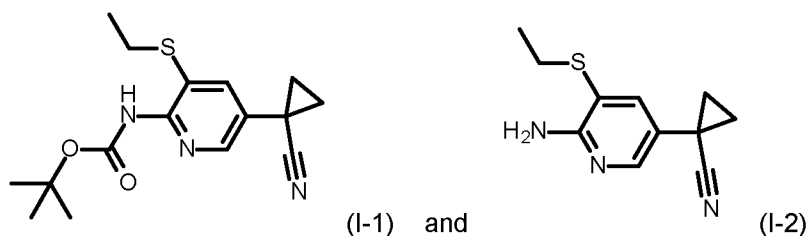
Spectra were recorded on a Gas Chromatography Mass Spectrometer (GC-MS) from Shimadzu Corporation equipped with AOC-20i autosampler, GC-2010 gas chromatography spectrometer with electron ionization (EI) source. Ion Source Temperature 200°C; Interface Temperature 220°C; Solvent Cut Time 2.00 min. Detector Gain Mode-Relative; Detector Gain: +0.00 kV. Threshold: 1000; Column: Rtx-17 sil MS (L: 3m, Thickness: 0.25mm, φ: 25 mm); MS Table: Start Time: 4.00 min; End Time: 18.00 min; ACQ Mode: Scan; Event Time: 0.30 sec; Scan Speed: 1666; Start m/z: 50.00; End m/z: 500.00; GC parameters: Column Oven Temp.: 40°C; Injection Temp.: 250°C; Injection Mode: Split; Pressure: 49.5 kPa; Total Flow: 33.0 mL/min; Column Flow: 1.00 mL/min; Linear Velocity: 36.1 cm/sec; Purge Flow: 2.0 mL/min; Split ratio: 30.0; Oven Temp. Program: Rate: 0; 40 °C, Hold 1.00 min; Rate: 20.00; 280°C, Hold 5.00 min.

Example I-4: Preparation of tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-4)

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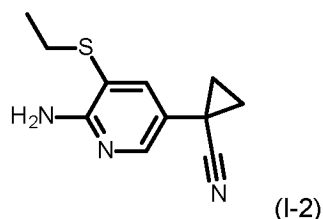


Step 1: Preparation of tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfanyl-2-pyridyl]carbamate (intermediate I-1) and 1-(6-amino-5-ethylsulfanyl-3-pyridyl)cyclopropanecarbonitrile (intermediate I-2)



- 5 To a solution of 5-(1-cyanocyclopropyl)-3-ethylsulfanyl-pyridine-2-carboxylic acid (CAS 2225113-77-7, prepared as described in WO 2018/108726) (50.0 g, 191.3 mmol) in toluene (500 mL) was added triethylamine (47.1 mL, 334.8 mmol), followed by tert-butanol (260 mL, 2755 mmol) at room temperature. The reaction mass was heated at 90°C and diphenylphosphoryl azide (71.94 mL, 327.1 mmol) was added in two hours. The reaction mixture was stirred at 90°C for one hour, then allowed to cool to room
- 10 temperature. After dilution with water (400 mL) and with a saturated aqueous solution of sodium bicarbonate (300 mL), the aqueous layer was extracted with ethyl acetate (400 mL). The organic layer was concentrated *in vacuo* to afford tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfanyl-2-pyridyl]carbamate (I-1) and 1-(6-amino-5-ethylsulfanyl-3-pyridyl)cyclopropanecarbonitrile (I-2) as a mixture. This crude material was used as such for the next step. LCMS (Method 1): Rt = 1.05 min, m/z=
- 15 318 (M-H)⁻ for intermediate (I-1).

Step 2: Preparation of 1-(6-amino-5-ethylsulfanyl-3-pyridyl)cyclopropanecarbonitrile (intermediate I-2)



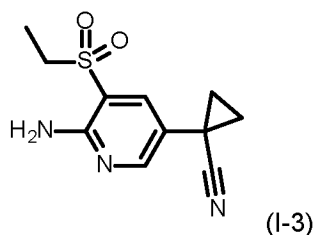
- To a mixture of tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfanyl-2-pyridyl]carbamate (I-1) and 1-(6-amino-5-ethylsulfanyl-3-pyridyl)cyclopropanecarbonitrile (I-2) (84 g, 163.1 mmol) in dichloromethane (250 mL) was added 2,2,2-trifluoroacetic acid (275 mL, 3587 mmol) at 5°C. The reaction mixture was stirred at room temperature overnight, then concentrated *in vacuo*, diluted with water (300 mL), and neutralised with an aqueous sodium bicarbonate solution (2500 mL). The aqueous layer was extracted with dichloromethane (3x 400 mL), the combined organic layers dried over sodium sulfate, filtered and
- 20

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concentrated *in vacuo*. The crude material was taken into tert-butyl methyl ether (265 mL), heated to 55°C and filtered at 30°C. The solid obtained was washed with methanol (60 mL) to afford pure 1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropanecarbonitrile (I-2). ¹H NMR (400 MHz, CDCl₃) δ ppm 1.21-1.33 (m, 5H) 1.61-1.69 (m, 2H) 2.80 (q, 2H) 5.26 (br s, 2H) 7.56 (d, 1H) 7.97 (d, 1H).

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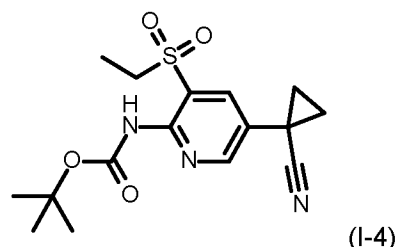
Step 3: Preparation of 1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropanecarbonitrile (intermediate I-3)



To a solution of 1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropanecarbonitrile (intermediate I-2 prepared as described above) (3.00 g, 13.68 mmol) in dichloromethane (60 mL) at 0°C was added 3-chlorobenzenecarboperoxoic acid (7.41 g, 30.10 mmol, 70 mass%). The mixture was stirred at room temperature for 30 minutes. The reaction mass was basified with a 10% sodium hydroxide solution (30 mL) and the organic layer separated. The aqueous layer was extracted with ethyl acetate (2x 50 mL). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate and concentrated *in vacuo*. The crude product was purified by combiflash (silica gel, 40% ethylacetate in cyclohexane) to afford 1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropanecarbonitrile (I-3) as an off-white solid. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.26-1.38 (m, 5H) 1.62-1.75 (m, 2H) 3.19 (q, 2H) 5.88 (br s, 2H) 7.84 (d, 1H) 8.35-8.39 (m, 1H).

20

Step 4: Preparation of tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-4)



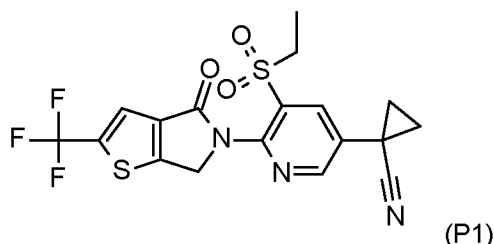
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To a solution of 1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropanecarbonitrile (intermediate I-3 prepared as described above) (1.9 g, 7.6 mmol) in N,N-dimethylformamide (20 mL) at 0°C was added sodium hydride (0.70 g, 17 mmol) and the reaction mixture was stirred at 0°C for one hour. A solution of tert-butoxycarbonyl tert-butyl carbonate (2.0 g, 9.1 mmol) in N,N-dimethylformamide (10 mL) was added at 0°C, and stirring continued at room temperature overnight. The reaction mass was quenched with ice water (20 mL) and extracted in ethyl acetate (3x 50 mL). The combined organic layers were washed with water (20 mL) and brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by combiflash (silica gel, 40% ethyl acetate in cyclohexane) to afford

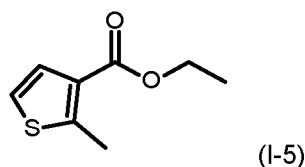
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pure tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]carbamate (I-4) as an off-white solid. LCMS (Method 1): Rt = 0.99 min, m/z = 296 [(M+H)-56]⁺.

Example P1: Preparation of 1-[5-ethylsulfonyl-6-[4-oxo-2-(trifluoromethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropanecarbonitrile (compound P1)

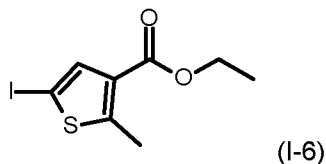


Step 1: Preparation of ethyl 2-methylthiophene-3-carboxylate (intermediate I-5)



To a solution of 2-methylthiophene-3-carboxylic acid (5.00 g, 35.16 mmol) in N,N-dimethylformamide (30 mL) was added cesium carbonate (13.75 g, 42.20 mmol). The reaction mixture was stirred at room temperature for 5 minutes, then iodoethane (4.44 mL, 52.75 mmol) was added and stirring continued at room temperature overnight. The mixture was diluted with ice water (100 mL) and extracted with ethyl acetate (2x 50 mL). The combined organic layers were washed with ice water (50 mL) and brine (50 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by combiflash (silica gel, 10-15% ethyl acetate in cyclohexane) to afford ethyl 2-methylthiophene-3-carboxylate (I-5). ¹H NMR (400 MHz, CDCl₃) δ ppm 1.37 (t, 3H) 2.75 (s, 3H) 4.32 (q, 2H) 6.98 (d, 1H) 7.40 (d, 1H).

Step 2: Preparation of ethyl 5-iodo-2-methyl-thiophene-3-carboxylate (Intermediate I-6)

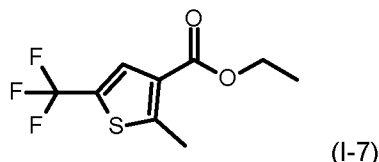


To a solution of ethyl 2-methylthiophene-3-carboxylate (intermediate I-5 prepared as described above) (5.00 g, 29.37 mmol) in acetonitrile (58 mL) containing 1-iodopyrrolidine-2,5-dione (6.60 g, 29.37 mmol) was added perchloric acid (0.295 mL, 2.93 mmol). The reaction mixture was stirred at 50°C for 5 hours. The reaction mixture was poured into a mixture of water (80 mL) and diethyl ether (50 mL), the layers separated and the organic layer washed with brine (50 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by combiflash (silica gel, 5-10% ethyl acetate in cyclohexane) to afford pure ethyl 5-iodo-2-methyl-thiophene-3-carboxylate (I-6). LCMS (method 1): 297 (M+H)⁺, Rt 1.23 min. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.36 (t, 3H) 2.71 (s,

-70-

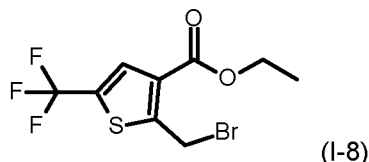
3H) 4.30 (q, 2H) 7.54 (s, 1H).

Step 3: Preparation of ethyl 2-methyl-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-7)



- 5 To a solution of ethyl 5-iodo-2-methyl-thiophene-3-carboxylate (intermediate I-6 prepared as described above) (0.100 g, 0.33 mmol) and 1,3-dimethylhexahydropyrimidin-2-one (0.245 mL, 2.02 mmol) in N,N-dimethylformamide (1.5 mL) were added methyl 2,2-difluoro-2-(fluorosulfonyl)acetate (0.265 mL, 2.02 mmol) and cuprous iodide (0.193 g, 1.01 mmol) at room temperature. The reaction mixture was stirred at 80°C under nitrogen atmosphere for 5 hours. The reaction mixture was cooled and poured
- 10 into a mixture of diethyl ether and water (10 mL, 1:1), filtered through a pad of celite and the celite bed washed with diethyl ether (10 mL). The layers of the filtrate were separated, the organic layer washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by combiflash (silica gel, 2-3% ethyl acetate in cyclohexane) to afford pure ethyl 2-methyl-5-(trifluoromethyl)thiophene-3-carboxylate (I-7). ¹H NMR (400 MHz, CDCl₃) δ ppm 1.38 (t, 3H) 2.78 (s,
- 15 3H) 4.33 (q, 2H) 7.73 (d, 1H).

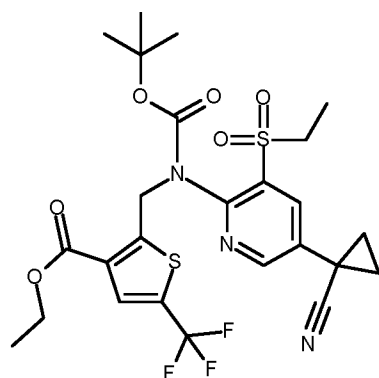
Step 4: Preparation of ethyl 2-(bromomethyl)-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-8)



- 20 To a solution of ethyl 2-methyl-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-7 prepared as described above) (0.950 g, 3.98 mmol) in tetrachloromethane (63.8 mL) was added N-bromo-succinimide (0.993 g, 5.58 mmol), followed by addition of benzoyl peroxide (0.321 g, 0.99 mmol, 75 mass%). The reaction mixture was heated to 90°C for 7 hours, then diluted with ice cold water (20 mL) and extracted with dichloromethane (20 mL). The organic layer was washed with brine (20 mL), dried
- 25 over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by combiflash (silica gel, 10-15% ethyl acetate in cyclohexane) to afford pure ethyl 2-(bromomethyl)-5-(trifluoromethyl)thiophene-3-carboxylate (I-8). ¹H NMR (400 MHz, CDCl₃) δ ppm 1.43 (t, 3H) 4.40 (q, 2H) 5.09 (s, 2H) 7.77-7.81 (m, 1H).

- 30 Step 5: Preparation of ethyl 2-[[tert-butoxycarbonyl]-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl]-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-9)

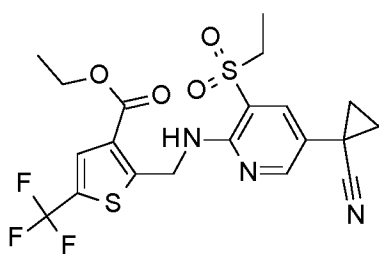
-71-



(I-9)

To a solution of tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-4 prepared as described above) (300 mg, 0.85 mmol) in N,N-dimethylformamide (6 mL) at 0°C was added sodium hydride (60 mass%, 44 mg, 1.11 mmol) and the mixture stirred at 0°C for 15 minutes. A solution of ethyl 2-(bromomethyl)-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-8 prepared as described above) (379 mg, 1.19 mmol) in N,N-dimethylformamide (0.5 mL) was added to the previous mixture at 0°C and stirring then continued at room temperature for one hour. The reaction mixture was quenched with ice water (10 mL) and extracted with ethyl acetate (2x 10 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by combiflash (silica gel, 10-15% ethyl acetate in cyclohexane) to afford ethyl 2-[[tert-butoxycarbonyl-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate (I-9). LCMS (Method 1): $R_t = 1.27$ min, $m/z = 488$ [(M+H)-100]⁺.

Step 6: Preparation of ethyl 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-10)



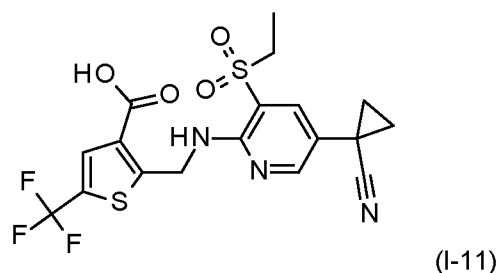
(I-10)

To a solution of ethyl 2-[[tert-butoxycarbonyl-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-9 prepared as described above) (470 mg, 0.79 mmol) in dichloromethane (10 mL) was added 2,2,2-trifluoroacetic acid (0.92 mL, 12.00 mmol) dropwise at room temperature. The reaction mixture was stirred at 40°C for 3 hours, then quenched with an aqueous saturated solution of potassium carbonate (10 mL), followed by water (15 mL) and the product extracted with dichloromethane (2x 10 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford ethyl 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate (I-10). This material was used as such for the next step. LCMS (Method 1): $R_t = 1.19$ min,

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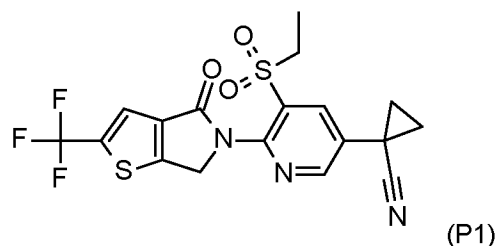
$m/z = 488$ ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.33 (t, 3H) 1.42 (t, 3H) 1.56 (m, 2H) 1.73 (m, 2H) 3.18 (q, 2H) 4.40 (q, 2H) 5.17 (d, 2H) 7.55 (br t, 1H) 7.76 (d, 1H) 7.84 (d, 1H) 8.42 (d, 1H).

Step 7: Preparation of 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylic acid (intermediate I-11)



To a solution of ethyl 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate (intermediate I-10 prepared as described above) (360 mg, 0.73 mmol) in methanol (14.4 mL) and water (7.2 mL) was added barium hydroxide octahydrate (465 mg, 1.47 mmol) at room temperature. The reaction mixture was stirred at 50°C for 4 hours, then evaporated. The residue was acidified with aqueous 2N hydrochloric acid and diluted with water. The aqueous layer was extracted with ethyl acetate (3x 15 mL), the combined organic layers were washed with brine (20 mL), dried over sodium sulfate, filtered and concentrated *in vacuo* to afford crude 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylic acid (I-11). This material was used as such for the next step. LCMS (Method 1): $R_t = 1.02$ min, $m/z = 460$ ($M+H$)⁺.

Step 8: Preparation of 1-[5-ethylsulfonyl-6-[4-oxo-2-(trifluoromethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropanecarbonitrile (compound P1)

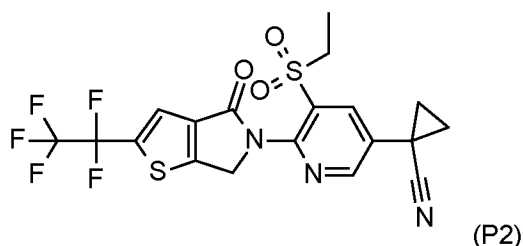


To a solution of 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylic acid (intermediate I-11 prepared as described above) (270 mg, 0.58 mmol) in pyridine (5 mL) at 0°C was added phosphorus oxychloride (0.166 mL, 1.76 mmol). The reaction mixture was stirred at room temperature for 3 hours, then evaporated. Water (20 mL) was added to the residue and the product extracted with ethyl acetate (2x 10 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by combiflash (silica gel, 30-40% ethyl acetate in cyclohexane) to afford 1-[5-ethylsulfonyl-6-[4-oxo-2-(trifluoromethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropanecarbonitrile

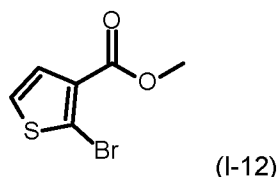
-73-

(compound P1). LCMS (Method 2): $R_t = 1.45$ min, $m/z = 442$ ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.39 (t, 3H) 1.61 (m, 2H) 1.98 (m, 2H) 3.55 (q, 2H) 5.12 (s, 2H) 7.67 (s, 1H) 8.18 (d, 1H) 8.83 (d, 1H).

5 Example P2: Preparation of 1-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropanecarbonitrile (compound P2)

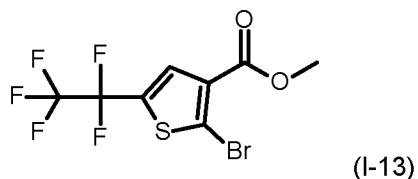


Step 1: Preparation of methyl 2-bromothiophene-3-carboxylate (intermediate I-12)



10 To a solution of 2-bromothiophene-3-carboxylic acid (4.00 g, 19.3 mmol) in N,N-dimethylformamide (30 mL) was added cesium carbonate (7.55 g, 23.2 mmol). The reaction mixture was stirred at room temperature for 5 minutes, then iodomethane (1.80 mL, 29.0 mmol) was added and stirring continued at room temperature for 5 hours. The reaction mixture was diluted with ice water (50 mL) and extracted with ethyl acetate (2x 50 mL). The combined organic layers were washed with ice water (50 mL) and brine (50 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by by combiflash (silica gel, 10-15% ethyl acetate in cyclohexane) to afford methyl 2-bromothiophene-3-carboxylate (I-12). ¹H NMR (400 MHz, CDCl₃) δ ppm 3.89 (s, 3H) 7.23 (d, 1H) 7.37 (d, 1H).

20 Step 2: Preparation of methyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-13)



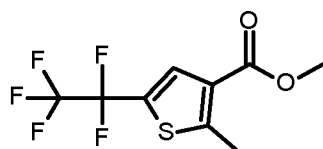
To a solution of methyl 2-bromothiophene-3-carboxylate (intermediate I-12 prepared as described above) (3.50 g, 16.0 mmol) in acetonitrile (30 mL) was added tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate (1.20 g, 1.60 mmol) and 1-oxido-4-phenyl-pyridin-1-ium (11.0 g, 63.0 mmol). The reaction mixture was degassed with nitrogen for 20 minutes, then 2,2,3,3,3-pentafluoropropanoyl 2,2,3,3,3-pentafluoropropanoate (13.0 mL, 63.0 mmol) was added and stirring continued under irradiation of blue LED light (465 nm; 50 W) for 22 hours. Completion of reaction was monitored by TLC and GCMS.

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After the irradiation time, the mixture was added to water (100 mL) and extracted with cyclohexane (2x 50 mL). The combined organic layers were washed with brine (50 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by combiflash (silica gel, ethyl acetate in cyclohexane) to afford methyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-13).

5 GCMS (method 3): 338/340 (M)⁺, Rt 6.67 min. ¹H NMR (400 MHz, CDCl₃) δ ppm 3.92 (s, 3H) 7.72 (s, 1H).

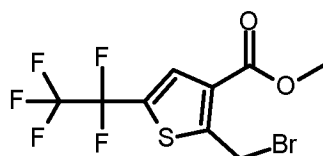
Step 3: Preparation of methyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-14)



(I-14)

Methyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-13 prepared as described above) (0.700 g, 2.06 mmol), methylboronic acid (0.637 g, 10.3 mmol), tricyclohexylphosphane (0.347 g, 1.24 mmol) and tripotassium phosphate (2.19 g, 10.3 mmol) were stirred in toluene (8 mL) and water (1.60 mL) while purged with nitrogen for 15 minutes. Palladium(II) acetate (0.139 g, 0.62 mmol) was added and the mixture heated in the microwave at 101°C for 1.5 hours. Additional methylboronic acid (0.319 g, 5.16 mmol), tricyclohexylphosphane (0.174 g, 0.62 mmol), tripotassium phosphate (1.10 g, 5.16 mmol) and palladium(II) acetate (0.069 g, 0.310 mmol) were added, the mixture degassed with nitrogen for 10 minutes and heating continued in the microwave at 101°C for an additional hour. Completion of reaction was monitored by GCMS. The reaction mixture was diluted with water (30 mL) and ethyl acetate (30 mL), then filtered through a pad of celite. The cake was washed with ethyl acetate (20 mL), then the two layers of the filtrate were separated. The organic layer was washed with brine (30 mL), dried over sodium sulfate, filtered and concentrated *in vacuo* to afford the crude methyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-14). This material was used as such for the next step. GCMS (Method 3): Rt = 5.86 min, m/z = 274 (M)⁺.

Step 4: Preparation of methyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-15)



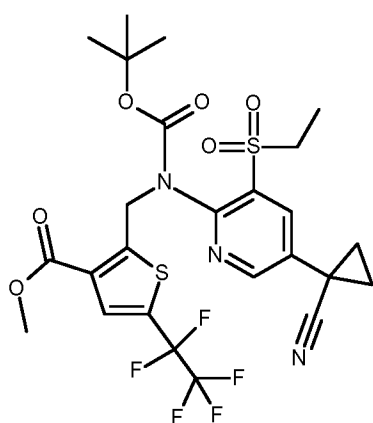
(I-15)

A mixture of methyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-14 prepared as described above) (1.20 g, 4.38 mmol), N-bromosuccinimide (0.795 g, 4.38 mmol) and 2,2'-azobis(isobutyronitrile) (0.071 g, 0.43 mmol) in trifluoromethyl benzene (12 mL) was stirred under nitrogen at 100°C for 5 hours. More N-bromosuccinimide (0.039 g, 2.19 mmol) and 2,2'-azobis(iso-

-75-

butyronitrile) (0.036 g, 0.21 mmol) were added and stirring continued at 100°C for an additional 5 hours. Completion of reaction was monitored by GCMS. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by combiflash by combiflash (silica gel, ethyl acetate in cyclohexane) to afford methyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-15). GCMS (Method 3): Rt = 7.74 min, m/z= 352/354 (M)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 3.94 (s, 3 H) 5.10 (s, 2 H) 7.79 (s, 1 H).

Step 5: Preparation of methyl 2-[[tert-butoxycarbonyl]-5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-16)

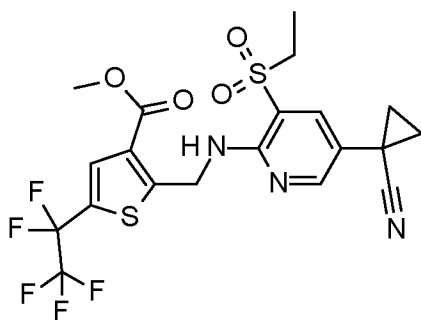


(I-16)

To a solution of tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl] carbamate (intermediate I-4 prepared as described above) (0.540 g, 1.54 mmol) in acetonitrile (10 mL) at room temperature were added cesium carbonate (0.752 g, 2.31 mmol) and methyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (Intermediate I-15 prepared as described above) (0.673 g, 1.91 mmol). The reaction mixture was stirred at 50°C for 5 hours, completion of reaction was monitored by TLC and LCMS. The reaction mass was quenched with ice cold water (20 mL) and extracted with ethyl acetate (2x 50 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 30% ethyl acetate in cyclohexane) to afford methyl 2-[[tert-butoxycarbonyl]-5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-16). LCMS (Method 1): Rt = 1.29 min, m/z= 524 [(M+H)-100]⁺.

Step 6: Preparation of methyl 2-[[[5-(1-cyanocyclopropyl)-3-methylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-17)

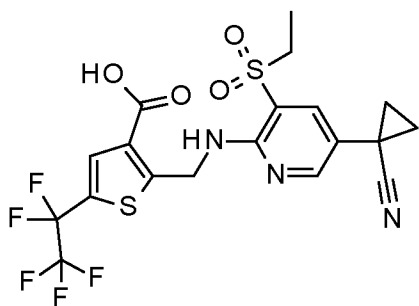
-76-



(I-17)

To a solution of methyl 2-[[tert-butoxycarbonyl-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-16 prepared as described above) (0.170 g, 0.27 mmol) in trifluoromethylbenzene (3.4 mL) was added 2,2,2-trifluoroacetic acid (0.417 mL, 5.45 mmol) dropwise at room temperature. The reaction mixture was stirred at room temperature for 5 hours, then additional 2,2,2-trifluoroacetic acid (0.417 mL, 5.45 mmol) was added and stirring continued at room temperature overnight. Completion of reaction was monitored by TLC and LCMS. The reaction mixture was slowly added to a saturated aqueous solution of potassium carbonate (10 mL) and extracted with ethyl acetate (2x 10 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, filtered and concentrated *in vacuo* to afford the crude methyl 2-[[[5-(1-cyanocyclopropyl)-3-methylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-17). This material was used directly for the next step. LCMS (Method 1): $R_t = 1.19$ min, $m/z = 524$ ($M+H$)⁺.

Step 7: Preparation of 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-18)



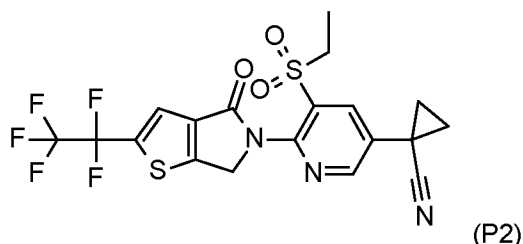
(I-18)

To a solution of methyl 2-[[[5-(1-cyanocyclopropyl)-3-methylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-17 prepared as described above) (0.105 g, 0.20 mmol) in methanol (4.2 mL) and water (2.1 mL) was added barium hydroxide octahydrate (0.126 g, 0.40 mmol) at room temperature. The reaction mixture was stirred at room temperature for 4 hours, then evaporated. Ice water was added to the residue and the mixture was acidified with aqueous 2N hydrochloric acid. The aqueous layer was extracted with ethyl acetate (2x 5 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, filtered and concentrated *in vacuo* to afford the crude 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-

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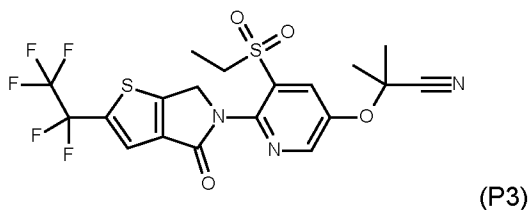
pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (I-18). This material was used as such for the next step. LCMS (Method 1): $R_t = 1.08$ min, $m/z = 510$ ($M+H$)⁺.

Step 8: Preparation of 1-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropanecarbonitrile (compound P2)



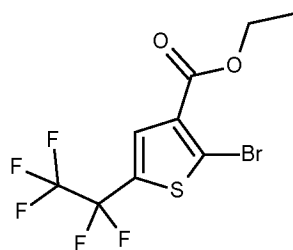
To a solution of 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-18 prepared as described above) (0.090 g, 0.17 mmol) in pyridine (3 mL) at 0°C was added phosphorus oxychloride (0.05 mL, 0.53 mmol). The reaction mixture was stirred at room temperature for 3 hours, then additional phosphorus oxychloride (0.10 mL, 1.06 mmol) was added and stirring continued at room temperature overnight. Completion of reaction was monitored by TLC and LCMS. The reaction mixture was added to water (10 mL) and extracted with ethyl acetate (2x 10 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 40-50% ethyl acetate in cyclohexane) to afford 1-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropanecarbonitrile (compound P2) as an off-white solid. LCMS (Method 1): $R_t = 1.08$ min, $m/z = 492$ ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.40 (t, 3H) 1.59 (m, 2H) 1.97 (m, 2H) 3.56 (q, 2H) 5.13 (br s, 2H) 7.67 (s, 1H) 8.18 (d, 1H) 8.83 (d, 1H).

Example P3: Preparation of 2-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]oxy]-2-methyl-propanenitrile (compound P3)



Step-1: Preparation of ethyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-19)

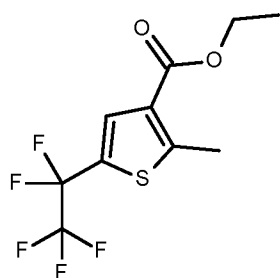
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(I-19)

To a solution of methyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-13 prepared as described above) (30.0 g, 61.93 mmol) in ethanol (300 mL) was added cesium carbonate (2.019 g, 6.193 mmol) at room temperature. The reaction mass was heated to 50°C for 12 hours, then quenched with water (400 mL) and the product extracted with cyclohexane (300 mL). The combined organic layers were washed with an aqueous 1N HCl solution (200 mL), water (100 mL) followed by brine (200 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 0-20% ethyl acetate in cyclohexane) to afford ethyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-19). ¹H NMR (400 MHz, CDCl₃) δ ppm 1.41 (t, 3H) 4.38 (q, 2H), 7.71 (s, 1H).

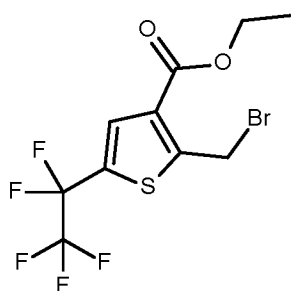
Step-2: Preparation of ethyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-20)



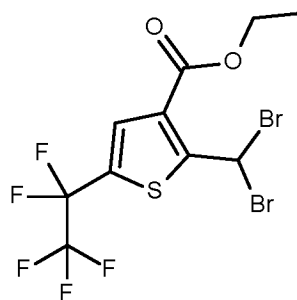
(I-20)

To a solution of ethyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-19 prepared as described above) (20.0 g, 39.649 mmol) in ethanol (160 mL) and water (40 mL) were added methylboronic acid (13.19 g, 198.24 mmol), followed by a solution of potassium carbonate (16.44 g, 118.95 mmol) in water (3 mL) while purged with nitrogen for 10 minutes. 1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (1.6690 g, 1.9824 mmol) was added and the reaction mixture heated at 90°C for 15 hours. The reaction mass was quenched with water and the product extracted with ethyl acetate. The combined organic layers were washed with water followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 0-30% ethyl acetate in cyclohexane) to afford ethyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate as brown oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.39 (t, 3H) 2.79 (s, 3H) 4.33 (q, 2H), 7.74 (s, 1H).

Step-3: Preparation of ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-21) and ethyl 2-(dibromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-22)



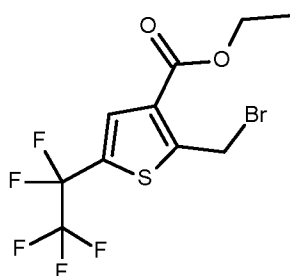
(I-21) and



(I-22)

- 5 To a solution of ethyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-20 prepared as described above) (5.5 g, 18 mmol) in benzotrifluoride (55 mL) were added N-bromosuccinimide (7.6 g, 42 mmol) and 2,2'-azobis(isobutyronitrile) (0.31 g, 1.8 mmol) and the reaction mass was heated at 90 °C for 5 hours. The mixture was cooled to room temperature and then filtered through a pad of celite. The filtrate was concentrated *in vacuo* and the residue purified by
- 10 combiflash (silica gel, 0-30% ethyl acetate in cyclohexane) to afford ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-21) and ethyl 2-(dibromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-22) as a colourless oil. ¹H NMR for intermediate I-21: ¹H NMR (400 MHz, CDCl₃) δ ppm 1.40-1.42 (m, 3H), 4.33 (q, 2H), 5.08 (s, 2H) 7.77 (s, 1H). ¹H NMR for intermediate I-22: ¹H NMR (400 MHz, CDCl₃) δ ppm 1.42 (t, 3H) 4.40 (q, 2H), 7.72 (s, 1H), 7.85 (s,
- 15 1H).

Step-4: Preparation of ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-21)



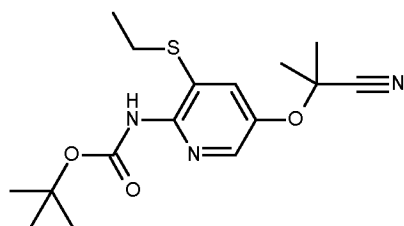
(I-21)

- 20 To a solution of ethyl 2-(dibromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-22 prepared as described above) (9 g, 19.169 mmol) in acetonitrile (76.6 mL) and water (1.5 mL) was added N,N-diisopropylethylamine (5.02 mL, 28.754 mmol) and the reaction mixture was stirred at 0°C for 5 minutes, then diethyl phosphite (3.704 mL, 28.754 mmol) was added dropwise at 0°C. The reaction mixture was stirred at 0-5°C for 2 hours. The reaction mass was
- 25 quenched with a cold aqueous 1N HCl solution (100 mL) and the product extracted with cyclohexane (2x 150 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 100% cyclohexane) to afford ethyl 2-

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(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-21) as a thick oil. ^1H NMR (400 MHz, CDCl_3) δ ppm 1.41 (t, 3H) 4.33 (q, 2H), 5.08 (s, 2H) 7.77 (s, 1H).

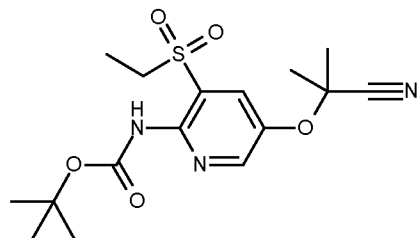
Step-5: Preparation of tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfanyl-2-pyridyl]carbamate (intermediate I-23)



(I-23)

To a solution of 5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfanyl-pyridine-2-carboxylic acid (CAS 2417036-66-7, prepared as described in WO2020141136) (4 g, 14.27 mmol) in tert-butanol (40 mL) was added triethylamine (3.21 mL, 22.83 mmol) and the reaction mass was heated at 90 °C. After 10 minutes diphenylphosphoryl azide (5.021 mL, 22.83 mmol) was added dropwise over a period of 15 minutes and the resulting reaction mass was stirred at 90 °C for 40 minutes. The reaction mixture was quenched with water (30 ml) and brine (20 ml), and the product extracted with ethyl acetate (2x 50 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 40-60% ethyl acetate in cyclohexane) to afford tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfanyl-2-pyridyl]carbamate (I-23). LCMS (Method 1): R_t = 1.17 min, m/z = 282 $[(M+H)-56]^+$.

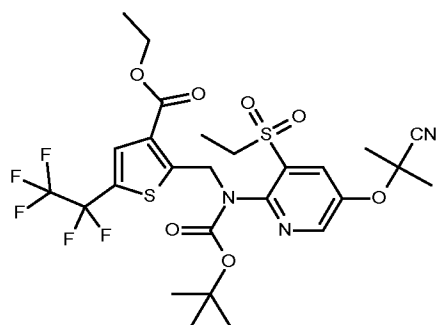
Step-6: Preparation of tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate-24)



(I-24)

To a solution of tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfanyl-2-pyridyl]carbamate (intermediate I-23 prepared as described above) (1.5 g, 4.2 mmol) in ethanol (15 mL) was added 3-chlorobenzoic acid (0.7 g, 4 mmol) at 15-20°C. The reaction mass was stirred at room temperature for 12 hours. The reaction was quenched with saturated sodium sulfite (5 mL), then the resulting reaction mass was added to an ice-cold solution of sodium carbonate (0.4 g, 4 mmol) in water (200 mL) and stirred for 30 minutes. The resulting white precipitate was filtered through a Buchner funnel and the solid residue washed with cold water followed by cyclohexane, dried *in vacuo* to afford tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (I-24) as white solid. LCMS (Method 2): R_t = 1.37 min, m/z = 314 $[(M+H)-56]^+$.

Step-7: Preparation of ethyl 2-[[tert-butoxycarbonyl-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-25)

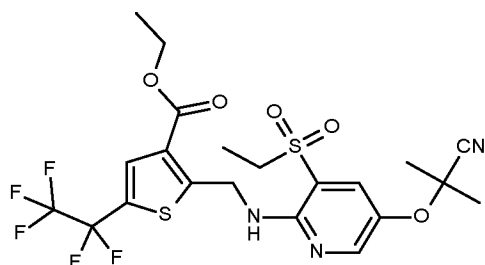


(I-25)

- 5 To solution of tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-24 prepared as described above) (0.8 g, 2.057 mmol) in acetonitrile (20 mL) were added ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-21 prepared as described above) (0.8309 g, 2.263 mmol) and cesium carbonate (1.341 g, 4.115 mmol). The reaction mixture was heated at 60 °C for 18 hours. The reaction mass was diluted with water and
- 10 extracted with ethyl acetate. The organic layer was washed with water (2x), then brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 10-50% ethyl acetate in cyclohexane) to afford ethyl 2-[[tert-butoxycarbonyl-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-25) as gummy mass. LCMS (Method 1): $R_t = 1.64$ min, $m/z = 556$ ($M+H$)⁺.

15

Step-8: Preparation of ethyl 2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate-26)



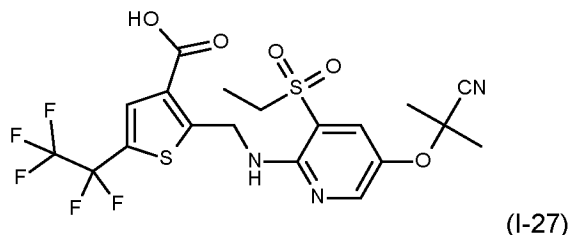
(I-26)

- To a solution of ethyl 2-[[tert-butoxycarbonyl-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-25 prepared as described above) (0.39 g, 0.5651 mmol) in benzotrifluoride (3.9 mL) was added trifluoroacetic acid (0.439 mL, 5.651 mmol) and the reaction mass was stirred for 3 hours at room temperature. After completion, the reaction mass was neutralised with an aqueous sodium bicarbonate solution. The aqueous layer was extracted with ethyl acetate (2x 50 mL), the combined
- 25 organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford ethyl 6-[[[3-ethylsulfonyl-6-(trifluoromethyl)imidazo[1,2-a]pyridin-2-yl]amino]methyl]-2,2-difluoro-1,3-benzodioxole-

-82-

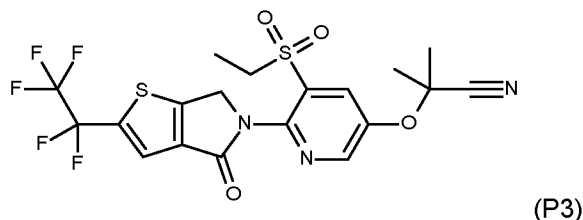
5-carboxylate (I-26). The crude was used as such for next step. LCMS (Method 1): $R_t = 1.64$ min, $m/z = 556$ ($M+H$)⁺.

Step-9: Preparation of 2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate-27)



To solution of ethyl 2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-26 prepared as described above) (0.42 g, 0.5293 mmol) in tetrahydrofuran (10.5 mL) was added a solution of lithium hydroxide monohydrate (0.1379 g, 3.176 mmol) in water (4.2 mL) at room temperature. The reaction mixture was stirred at room temperature overnight. More lithium hydroxide monohydrate (0.1379 g, 3.176 mmol) was added and stirring continued for an additional 12 hours. Upon completion, the reaction mass was concentrated *in vacuo*, acidified with an aqueous 1N hydrochloric acid solution, and the product extracted with ethyl acetate (2x 50 mL). The organic layer was washed with water (50 mL) followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 50-70% ethyl acetate in cyclohexane) to afford 2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (I-27) as off white solid. LCMS (Method 1): $R_t = 1.17$ min, $m/z = 528$ ($M+H$)⁺.

Step-10: Preparation of 2-[[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]oxy]-2-methyl-propanenitrile (compound P3)

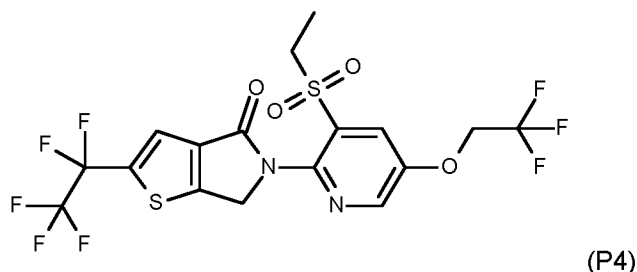


To a 0°C cooled solution of 2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-27 prepared as described above) (0.08 g, 0.1517 mmol) in pyridine (3 mL) was added phosphorus oxychloride (0.05683 mL, 0.6066 mmol). The reaction mixture stirred at room temperature for 2 hours, then more phosphorus oxychloride (0.028 mL, 0.303 mmol) was added and stirring continued at room temperature for an additional 2 hours. The reaction mass was acidified with an aqueous 2N hydrochloric acid (15 mL) solution and the product extracted with ethyl acetate (2x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by

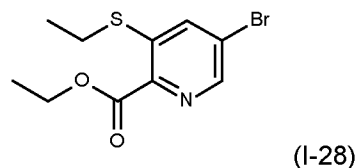
-83-

combiflash (silica gel, 50% ethyl acetate in cyclohexane) to afford 2-[[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]oxy]-2-methyl-propanenitrile (compound P3) as a white solid. LCMS (Method 2): Rt= 1.50 min, m/z= 510 (M+H)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.41 (t, 3 H) 1.88 (s, 6 H) 3.56 (q, 2 H) 5.13 (s, 2 H) 7.69 (s, 1 H) 8.23 (d, 1 H) 8.67 (d, 1 H).

Example P4: Preparation of 5-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P4)

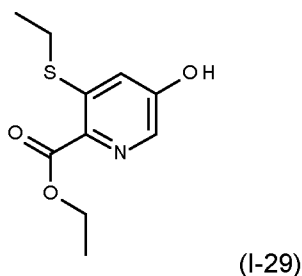


Step-1: Preparation of ethyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-28)



To a solution of 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylic acid (CAS 1857366-13-2) (10.0 g, 34.31 mmol, 89.94 mass%) in ethyl alcohol (85 mL) was added sulfuric acid (1.9 mL, 34.31 mmol) dropwise and heated at 80 °C for 3 hours. The reaction mass was cooled to 24 °C and basified with a saturated aqueous sodium bicarbonate solution (50 mL), then diluted with brine. The aqueous layer was extracted with ethyl acetate (3x 100 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude material was triturated with cold methyl tert-butyl ether (20 mL) and stirred for 15 minutes at 24 °C. The resulting precipitate was filtered through a Buchner funnel and dried *in vacuo* to afford ethyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (I-28) as a light brown solid. The crude was used as such for next step. LCMS (Method 1): Rt= 1.05 min, m/z= 290/292 (M+H)⁺.

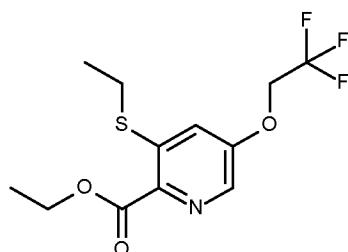
Step-2: Preparation of ethyl 3-ethylsulfanyl-5-hydroxy-pyridine-2-carboxylate (intermediate I-29)



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To a solution of ethyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-28 prepared as described above) (15.0 g, 47.99 mmol) in N,N-dimethylformamide (95.98 mL) were added cesium carbonate (34.4 g, 105.6 mmol), followed by (E)-benzaldehyde oxime (6.81 mL, 62.39 mmol) and the reaction mass was stirred reaction at 80 °C for 15 hours. The reaction mass was quenched with ice-cold water, acidified with an aqueous 2N hydrochloric acid and extracted in ethyl acetate (3x100 mL). The combined organic layers were washed with water (100 mL), dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The obtained residue was triturated with tert-butyl methyl ether, the solid isolated by filtration and dried *in vacuo* to afford ethyl 3-ethylsulfanyl-5-hydroxy-pyridine-2-carboxylate (I-29) as a brown solid. The crude was used as such for next step. LCMS (Method 1): Rt = 0.98 min, m/z= 228 (M+H)⁺.

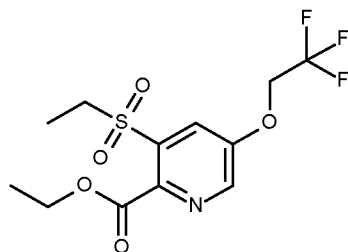
Step-3: Preparation of ethyl 3-ethylsulfanyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylate (intermediate I-30)



(I-30)

To a solution of ethyl 3-ethylsulfanyl-5-hydroxy-pyridine-2-carboxylate (intermediate I-29 prepared as described above) (4.108 g, 18.07 mmol) N,N-dimethylformamide (20 mL) were added potassium carbonate (4.99 g, 36.15 mmol) and 2,2,2-trifluoroethyl 4-methylbenzenesulfonate (5.97 g, 23.50 mmol) under nitrogen and the reaction mixture was stirred at 75 °C for 15 hours. The reaction mass was diluted with ice cold water (200 mL), and the product extracted with ethyl acetate (3x 60 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 0-40% ethyl acetate in cyclohexane) to afford ethyl 3-ethylsulfanyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylate (I-30) as an off white solid. LCMS (Method 1): Rt = 1.15 min, m/z= 310 (M+H)⁺.

Step-4: Preparation of ethyl 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylate (intermediate I-31)

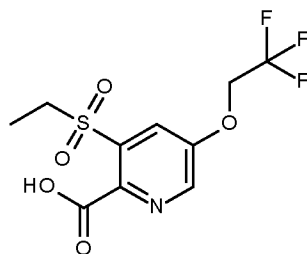


(I-31)

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To 0 °C cooled solution of ethyl 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylate (intermediate I-30 prepared as described above) (2.424 g, 7.837 mmol) in acetonitrile (20 mL) was added 3-chlorobenzenecarboperoxoic acid (4.25 g, 17.24 mmol, 70 mass%). The reaction mass was stirred at room temperature for 1.5 hours. The reaction mass was concentrated carefully *in vacuo* and the residue quenched with an aqueous 2N sodium hydroxide solution (20 mL). Water (60 mL) and ethyl acetate (40 mL) were added and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (2x 50 mL). The combined organic layers were washed with brine (60 mL), dried over sodium sulfate and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 0-40% ethyl acetate in cyclohexane) to afford ethyl 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylate (I-31) as an off white solid. LCMS (Method 2): Rt =1.09 min, m/z=342 (M+H)⁺.

Step-5: Preparation of 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylic acid (intermediate I-32)

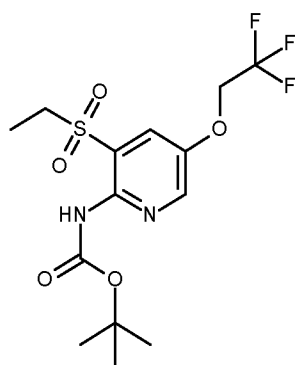


(I-32)

To a solution of ethyl 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylate (intermediate I-31 prepared as described above) (2.080 g, 6.094 mmol) in tetrahydrofuran (20 mL) was added a solution of lithium hydroxide monohydrate (1.077 g, 24.38 mmol) in water (7 mL) and the reaction mixture was stirred at room temperature overnight. The reaction mass was concentrated *in vacuo*, acidified with an aqueous 1N hydrochloric acid solution, and the product extracted with ethyl acetate (2x 50 mL). The combined organic layers were washed with water (50 mL) and brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylic acid (I-32) as an off white solid. The crude was used as such for next step. LCMS (Method 2): Rt =0.91 min, m/z=314 (M+H)⁺.

Step-6: Preparation of tert-butyl N-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]carbamate (intermediate I-33)

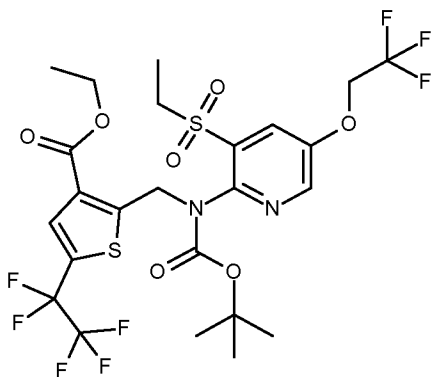
-86-



(I-33)

To a solution of 3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylic acid (intermediate I-32 prepared as described above) (2 g, 6.3847 mmol) in tert-butanol (40 mL) was added triethylamine (1.0441 g, 10.215 mmol) and the reaction mass was heated at 90 °C for 10 minutes. Diphenylphosphoryl azide (2.24 mL, 10.21 mmol) was added dropwise over a period of 15 minutes and the resulting reaction mass was stirred at 90 °C for 45 minutes. The reaction mass was quenched with ice-cold water (50 mL) and the product extracted with ethyl acetate (3x 70 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 0-50% ethyl acetate in cyclohexane) to afford tert-butyl N-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]carbamate (I-33). LCMS (Method 1): R_t = 1.14 min, m/z = 383 [(M-H)]⁻.

Step-7: Preparation of ethyl 2-[[tert-butoxycarbonyl-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-34)



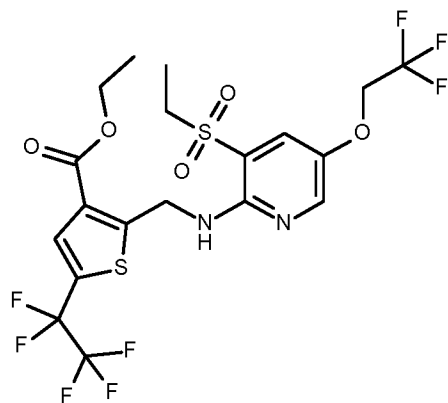
(I-34)

To a solution of tert-butyl N-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]carbamate (intermediate I-33 prepared as described above) (0.600 g, 1.561 mmol) in acetonitrile (10 mL) were added cesium carbonate (0.764 g, 2.341 mmol) and ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-21 prepared as described above) (0.85 g, 1.87 mmol) at room temperature. The reaction mixture was heated at 50 °C for 5 hours. The reaction mass was diluted with water and the product extracted with ethyl acetate (3x 50 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford ethyl 2-[[tert-butoxycarbonyl-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-

-87-

3-carboxylate (I-34) as gummy mass. The crude was used as such for next step. LCMS (Method 1): R_t = 1.39 min, m/z = 571 [(M+H)-100]⁺.

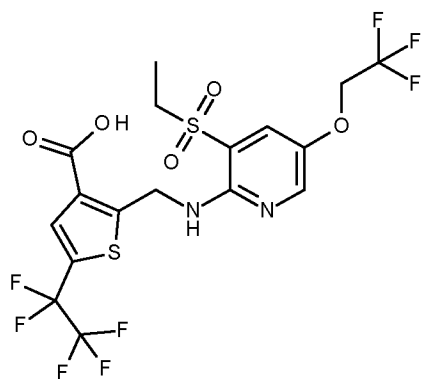
Step-8: Preparation of ethyl 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-35)



(I-35)

To a solution of ethyl 2-[[tert-butoxycarbonyl-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-34 prepared as described above) (1.135 g, 1.693 mmol) in trifluoromethylbenzene (20 mL) was added trifluoroacetic acid (2.05 mL, 25.39 mmol) at room temperature. The reaction mass was stirred at room temperature for 12 hours. After completion, the reaction mass was concentrated *in vacuo* and neutralised with an aqueous sodium carbonate solution. The aqueous layer was extracted with ethyl acetate (2x 50 mL), the combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 0-30% ethyl acetate in cyclohexane) to afford ethyl 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-35) as solid. LCMS (Method 1): R_t = 1.30 min, m/z = 571 (M+H)⁺.

Step-9: Preparation of 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-36)

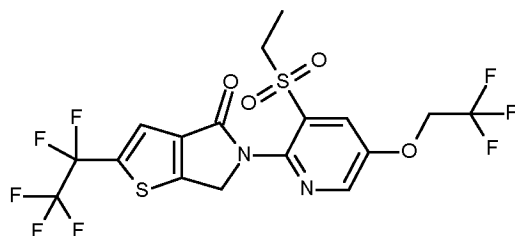


(I-36)

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To solution of ethyl 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-35 prepared as described above) (0.535 g, 0.9378 mmol) in tetrahydrofuran (10 mL) was added a solution of lithium hydroxide monohydrate (0.1657 g, 3.751 mmol) in water (3.5 mL) at room temperature. The reaction mixture was stirred at room temperature overnight, then concentrated *in vacuo*. The residue was acidified with an aqueous 1N hydrochloric acid solution and the product extracted with ethyl acetate (2x 50 mL). The organic layer was washed with water (50 mL) followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (I-36) as off white solid. The crude was used as such for next step. LCMS (Method 1): $R_t = 1.17$ min, $m/z = 543$ (M+H)⁺.

Step-10: Preparation of 5-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P4)

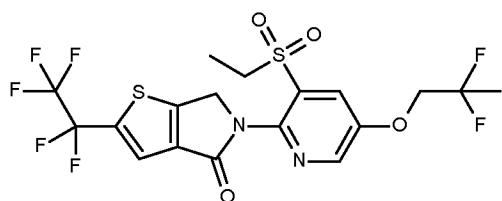


(P4)

To a 0°C cooled solution of 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-36 prepared as described above) (0.545 g, 1.0 mmol) in pyridine (6 mL) was added phosphorus oxychloride (0.369 mL, 4.02 mmol). The reaction mixture was allowed to come at room temperature and stirred for 30 minutes under nitrogen atmosphere. The reaction mass was quenched with water (30 mL), and the product extracted with ethyl acetate (3x 30 mL). The combined organic layers were washed with water (3x 40 mL), brine (30 mL), dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 0-25% ethyl acetate in cyclohexane) to afford 5-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P4) as brown solid. LCMS (Method 1): $R_t = 1.16$ min, $m/z = 525$ (M+H)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.37 (t, 3H) 3.49 (q, 2H) 4.55 (q, 2H) 5.07 (s, 2H) 7.67 (s, 1H) 7.95 (d, 1H) 8.56 (d, 1H).

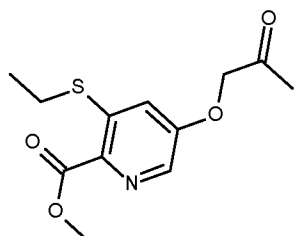
Example P6: Preparation of 5-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P6)

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(P6)

Step-1: Preparation of methyl 5-acetonyloxy-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-37)

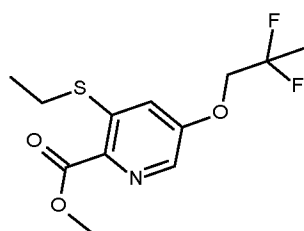


(I-37)

- 5 To a solution of methyl 3-ethylsulfanyl-5-hydroxy-pyridine-2-carboxylate (CAS 2417036-63-4) (8.0 g, 38.0 mmol) in N,N-dimethylformamide (80 mL) was added potassium carbonate (16.0 g, 110.0 mmol), followed by 1-chloropropan-2-one (10.0 g, 110.0 mmol). The reaction mixture was stirred at room temperature overnight. After completion, the reaction mass was diluted with water (150 mL) and extracted with ethyl acetate (3x 150 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 30% ethyl acetate in cyclohexane) to afford methyl 5-acetonyloxy-3-ethylsulfanyl-pyridine-2-carboxylate (I-37). LCMS (Method 1): $R_t = 0.84$ min, $m/z = 270$ ($M+H$)⁺.

Step-2: Preparation of methyl 5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylate

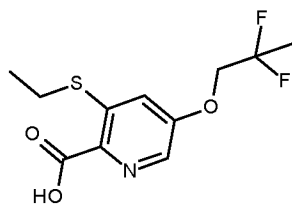
- 15 (intermediate I-38)



(I-38)

- To a 0 °C cooled solution of methyl 5-acetonyloxy-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-37 prepared as described above) (8.3 g, 31 mmol) in dichloromethane (170 mL) was added N-ethyl-N-(trifluoro- λ^4 -sulfanyl)ethanamine (16 mL, 120 mmol). The reaction mixture was allowed to come to room temperature and stirred for 16 hours. The reaction mass was quenched with solid sodium bicarbonate, diluted with water (100 mL), and the product extracted with dichloromethane (3x 80 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 30% ethyl acetate in cyclohexane) to afford methyl 5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylate (I-38). LCMS (Method 1): $R_t = 1.43$ min, $m/z = 292$ ($M+H$)⁺.

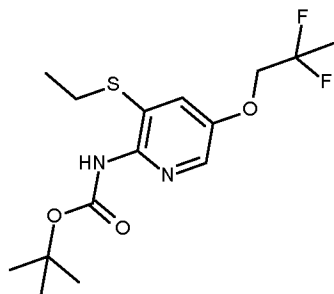
Step-3: Preparation of 5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylic acid
(intermediate I-39)



(I-39)

- 5 To a solution of methyl 5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-38 prepared as described above) (8.4 g, 29 mmol) in tetrahydrofuran (130 mL) was added a solution lithium hydroxide monohydrate (1.8 g, 43 mmol) in water (34 mL). The reaction mixture was stirred at room temperature for 2 hours. The reaction mass was acidified with an aqueous 2N HCl solution, diluted with water (100 mL) and the product extracted with ethyl acetate (3x 100 mL). The combined
 10 organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford 5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylic acid (I-39). The crude was used as such for next step. LCMS (Method 1): Rt = 0.91 min, m/z= 276 (M-H)⁻.

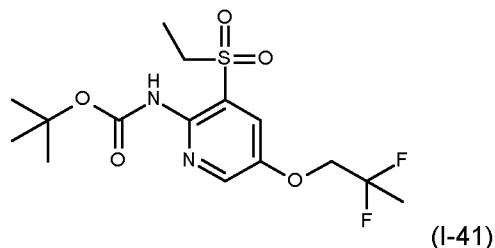
Step-4: Preparation of tert-butyl N-[5-(2,2-difluoropropoxy)-3-ethylsulfanyl-2-pyridyl]carbamate
(intermediate I-40)



(I-40)

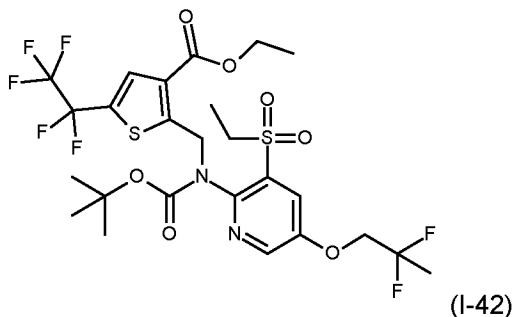
- To a solution of 5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylic acid (intermediate I-39 prepared as described above) (4.5 g, 15 mmol) in tert-butanol (68 mL) was added triethylamine (3.5 mL, 25 mmol) and the reaction mass was heated at 90 °C for 10 minutes. Diphenylphosphoryl azide
 20 (5.4 mL, 25 mmol) was then added dropwise over a period of 10 minutes and the resulting reaction mass was stirred at 90 °C for 60 minutes. The reaction mixture was quenched with ice-cold water (100 mL) and the product extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 20-70% ethyl acetate in cyclohexane) to afford tert-butyl N-[5-(2,2-
 25 difluoropropoxy)-3-ethylsulfanyl-2-pyridyl]carbamate (I-40). LCMS (Method 1): Rt = 1.16 min, m/z= 293 [(M+H)-56]⁺.

Step-5: Preparation of tert-butyl N-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-41)



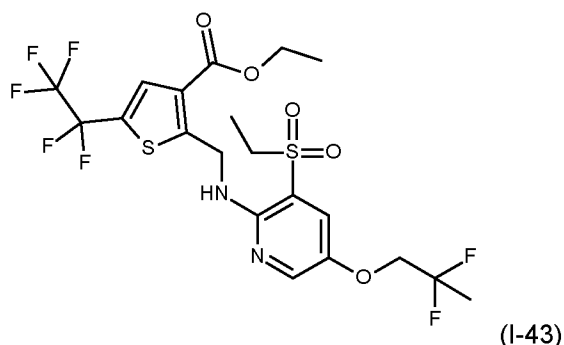
To a solution of tert-butyl N-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-40 prepared as described above) (4.5 g, 12 mmol) in ethanol (45 mL) was added 3-chlorobenzoic acid (2 g, 12.135 mmol) was added at 15-20°C. The reaction mass was stirred at room temperature for 12 hours. The reaction was quenched with saturated sodium sulfite (5 mL), then the resulting reaction mass was added to an ice-cold solution of sodium carbonate (1.5 g, 14 mmol) in water (200 mL) and stirred for 30 minutes. The resulting white precipitate was filtered through a Buchner funnel and the solid residue washed with cold water followed by cyclohexane, dried *in vacuo* to afford tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (I-41) as white solid. LCMS (Method 1): Rt = 1.13 min, m/z = 325 [(M+H)-56]⁺.

Step-6: Preparation of ethyl 2-[[tert-butoxycarbonyl-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-42)



To a solution of tert-butyl N-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-41 prepared as described above) (0.8 g, 1.998 mmol) in acetonitrile (20 mL) were added ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-21 prepared as described above) (0.9780 g, 2.397 mmol) and cesium carbonate (1.303 g, 3.996 mmol). The reaction mixture was heated at 75 °C for 3 hours. The reaction mass was diluted with water and extracted with ethyl acetate. The organic layer was washed with water (2x), then brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 10-50% ethyl acetate in cyclohexane) to afford ethyl 2-[[tert-butoxycarbonyl-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-42) as gummy mass. LCMS (Method 1): Rt = 1.30 min, m/z = 567 [(M+H)-100]⁺.

Step-7: Preparation of ethyl 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-43)

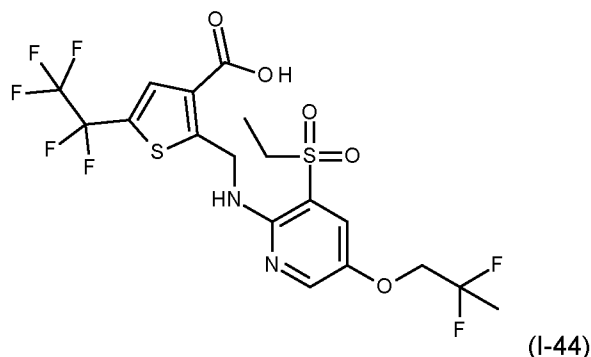


A solution of ethyl 2-[[tert-butoxycarbonyl-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-

- 5 pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-42 prepared as described above) (1 g, 1.425 mmol) in trifluoroacetic acid (5 mL, 64.3 mmol) was stirred for 12 hours. After completion, the reaction mass was neutralised with an aqueous sodium bicarbonate solution. The aqueous layer was extracted with ethyl acetate (2x), the combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford ethyl 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-43). The crude was used as such for next step. LCMS (Method 1): $R_t = 1.11$ min, $m/z = 567$ ($M+H$)⁺.

Step-8: Preparation of 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-44)

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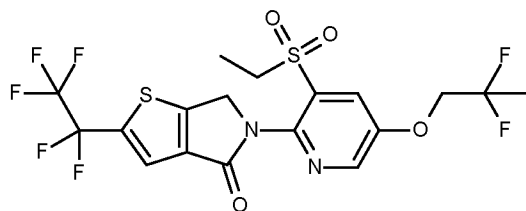
To solution of ethyl 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-43 prepared as described above) (0.72 g, 1.207 mmol) in tetrahydrofuran (6 mL) was added a solution barium hydroxide octahydrate (0.80 g, 2.41 mmol) in water (2 mL) at 10 °C. The reaction mixture was stirred at room temperature for 12 hours. After completion, the reaction mass was concentrated *in vacuo*. The reaction mass was acidified with an aqueous 1N hydrochloric acid solution, and the product extracted with ethyl acetate. The combined organic layers were washed with water (2x) followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo* to afford 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (I-44). The crude was

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used as such for next step. LCMS (Method 1): R_t = 1.20 min, m/z = 539 ($M+H$)⁺.

Step-9: Preparation of 5-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P6)



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(P6)

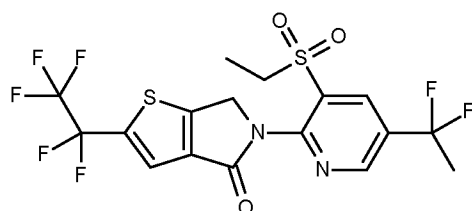
To a 0 °C cooled solution of 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-44 prepared as described above) (0.73 g, 1.288 mmol) in pyridine (2 mL) was added phosphorus oxychloride (0.2425 mL, 2.576 mmol). The reaction mixture was allowed to come at room temperature and stirred for 2 hours under nitrogen atmosphere. The reaction mass was acidified with an aqueous 2N hydrochloric acid (15 mL) solution, and the product extracted with ethyl acetate (2x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 50% ethyl acetate in cyclohexane) to afford 5-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P6) as a white solid. LCMS (Method 1): R_t = 1.17 min, m/z = 521 ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.38 (t, 3H) 1.84 (t, 3H) 3.47-3.50 (m, 2H) 4.31 (t, 2H) 5.08 (s, 2H) 7.68 (s, 1H) 7.95 (d, 1H) 8.54 (d, 1H).

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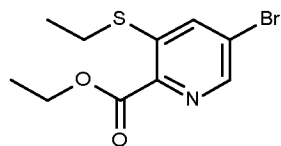
Example P8: Preparation of 5-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P8)

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(P8)

Step-1: Preparation of ethyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-45)



(I-45)

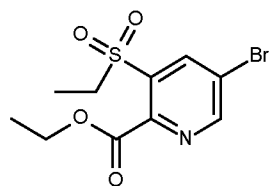
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To a solution of 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylic acid (CAS 1857366-13-2) (10.0 g, 34.31 mmol, 89.94 mass%) in ethyl alcohol (85 mL) was added sulfuric acid (1.9 mL, 34.31 mmol) dropwise and the mixture refluxed at 80 °C for 3 hours. The reaction mass was cooled to 24 °C and

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basified with a saturated aqueous sodium bicarbonate solution (50 mL), then diluted with brine. The aqueous layer was extracted with ethyl acetate (3x 100 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude material was triturated with cold methyl tert-butyl ether (20 mL) and stirred for 15 minutes at 24 °C. The resulting precipitate was
 5 filtered through a Buchner funnel and dried *in vacuo* to afford ethyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (I-45) as a light brown solid. The crude was used as such for next step. LCMS (Method 1): $R_t = 1.05$ min, $m/z = 290/292$ ($M+H$)⁺.

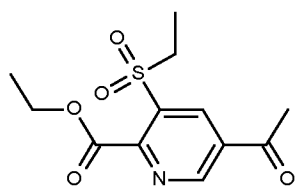
Step-2: Preparation of ethyl 5-bromo-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-46)



(I-46)

To a solution of ethyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (intermediate I-45 prepared as described above) (20.0 g, 65.47 mmol) in ethanol (200 mL) was added 3-chlorobenzenecarboxoperoxoic acid (61.63 g, 196.43 mmol) at 0°C. The reaction mass was stirred at room temperature for 12 hours. After completion, the reaction mass was quenched with a saturated aqueous solution of sodium sulfite (5 mL), then the resulting reaction mass was added to an ice-cold solution of sodium carbonate (7.1 g, 67 mmol) in water (200 mL) and stirred for 30 minutes. The resulting white precipitate was filtered
 15 through a Buchner funnel, the solid residue washed with cold water followed by cyclohexane, dried *in vacuo* to afford ethyl 5-bromo-3-ethylsulfonyl-pyridine-2-carboxylate (I-46) as a white solid. LCMS (Method 1): $R_t = 1.06$ min, $m/z = 322/324$ [$(M+H)$]⁺.

Step-3: Preparation of ethyl 5-acetyl-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-47)



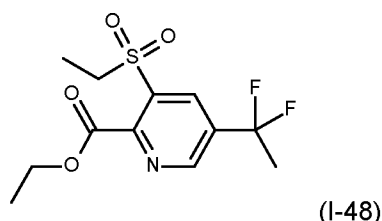
(I-47)

To a solution of ethyl 5-bromo-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-46 prepared as described above) (5 g, 14.743 mmol) in N,N-dimethylformamide (58.97 mL) was added tributyl(1-ethoxyvinyl)tin (6.727 g, 17.692 mmol) and the reaction mass was degassed with nitrogen for 15 minutes. Bis(triphenylphosphine)palladium(II) dichloride (0.522 g, 0.737 mmol) was added and to the reaction mass heated at 80 °C for 3 hours. The reaction mixture was cooled and an aqueous 2N HCl solution (20 mL) was added. After stirring at room temperature for 30 minutes, the reaction mass was quenched with an aqueous KF solution, diluted with water (100 mL) and ethyl acetate (100 mL). The
 25 solution was filtered through celite and the residue washed with ethyl acetate (20 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude
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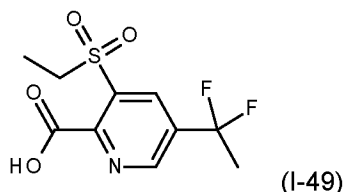
compound was purified by combiflash (silica gel, 30-40% ethyl acetate in cyclohexane) to afford ethyl 5-acetyl-3-ethylsulfonyl-pyridine-2-carboxylate (I-47). LCMS (Method 2): $R_t = 1.16$ min, $m/z = 286$ $[(M+H)]^+$.

5 Step-4: Preparation of ethyl 5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-48)



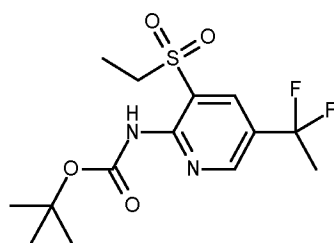
To a solution of ethyl 5-acetyl-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-47 prepared as described above) (3.5 g, 12 mmol) in toluene (35 mL) was added bis(2-methoxyethyl)aminosulfur trifluoride (13 mL, 35 mmol) dropwise under a nitrogen atmosphere. The reaction mixture was stirred at 80 °C for 12 hours, then quenched with a saturated sodium bicarbonate solution and diluted with ice-cold water (100 mL). The aqueous phase was extracted with ethyl acetate (3x 75 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 30-40% ethyl acetate in cyclohexane) to afford ethyl 5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylate (I-48). LCMS (Method 1): $R_t = 1.02$ min, $m/z = 308$ $(M+H)^+$.

Step-5: Preparation of 5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (intermediate I-49)



To a solution of ethyl 5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-48 prepared as described above) (3.0 g, 9.27 mmol) in tetrahydrofuran (24 mL) was added a solution of lithium hydroxide monohydrate (0.6799 g, 27.82 mmol) in water (6 mL) at 5°C. The reaction mixture was stirred at room temperature for 12 hours. Upon completion, the reaction mass was concentrated *in vacuo* and acidified with an aqueous 2N hydrochloric acid solution. The formed white precipitate was filtered through a Buchner funnel, and washed with cold water followed by cyclohexane, dried *in vacuo* to afford 5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (I-49) as a white solid. LCMS (Method 2): $R_t = 0.77$ min, $m/z = 280$ $(M+H)^+$.

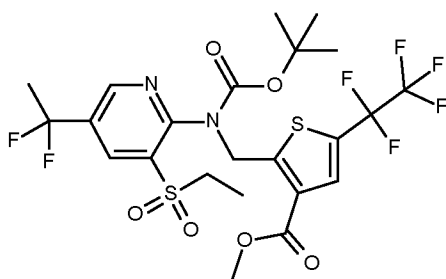
30 Step-6: Preparation of tert-butyl N-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-50)



(I-50)

To a solution of 5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid (intermediate I-49 prepared as described above) (2.4 g, 8.2 mmol) in tert-butanol (36 mL) was added triethylamine (1.8 mL, 13 mmol) and the reaction mass was heated at 90 °C for 10 minutes. Diphenylphosphoryl azide (2.9 mL, 13 mmol) was added dropwise over a period of 10 minutes and the resulting reaction mass was stirred at 90 °C for 40 minutes. The reaction mass was quenched with ice-cold water (30 mL) and the product extracted with ethyl acetate (2x). The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 60% ethyl acetate in cyclohexane) to afford tert-butyl N-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]carbamate. LCMS (Method 2): R_t = 1.37 min, m/z = 295 [(M+H)-56]⁺.

Step-7: Preparation of methyl 2-[[tert-butoxycarbonyl]-5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-51)

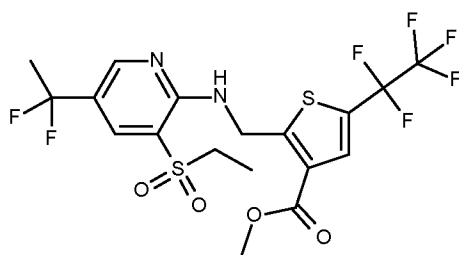


(I-51)

To a solution of tert-butyl N-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]carbamate (intermediate I-50 prepared as described above) (0.688 g, 1.865 mmol) in acetonitrile (20 mL) were added methyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-15 prepared as described above) (0.8320 g, 2.238 mmol), followed by cesium carbonate (1.216 g, 3.731 mmol). The reaction mixture was heated at 60 °C for 12 hours. The reaction mass was diluted with water and the product extracted with ethyl acetate. The organic layer was washed with water (2x) followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 10-50% ethyl acetate in cyclohexane) to afford methyl 2-[[tert-butoxycarbonyl]-5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-51) as gummy mass. LCMS (Method 1): R_t = 1.32 min, m/z = 523 [(M+H)-100]⁺.

Step-8: Preparation of methyl 2-[[[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-52)

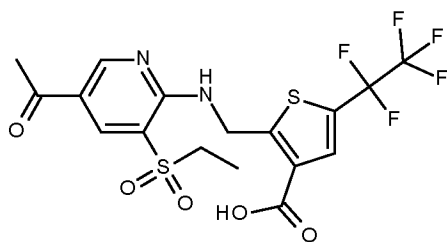
-97-



(I-52)

A solution of methyl 2-[[tert-butoxycarbonyl-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-51 prepared as described above) (0.4 g, 0.6103 mmol) in trifluoroacetic acid (3 mL, 38.6 mmol) was stirred for 3 hours. After completion, the reaction mass was neutralised with an aqueous sodium bicarbonate solution. The aqueous layer was extracted with ethyl acetate (2x), the combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford methyl 2-[[[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-52). The crude was used as such for next step. LCMS (Method 1): $R_t = 1.21$ min, $m/z = 523$ (M+H)⁺.

Step-9: Preparation of 2-[[[5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-53)

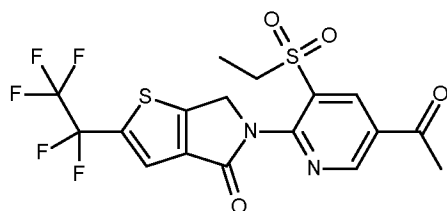


(I-53)

To solution of methyl 2-[[[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-52 prepared as described above) (0.23 g, 0.4182 mmol) in methanol (6 mL) was added a solution of barium hydroxide octahydrate (0.2777 g, 0.8364 mmol) in water (2 mL) at 10 °C. The reaction mixture was stirred at room temperature for 12 hours. After completion, the reaction mass was concentrated *in vacuo*, acidified with an aqueous 1N hydrochloric acid solution, and the product extracted with ethyl acetate. The organic layer was washed with water (2x) followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was triturated with acetonitrile to afford pure 2-[[[5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (I-53) as a light yellow solid. The crude was used as such for next step. LCMS (Method 1): $R_t = 1.06$ min, $m/z = 487$ (M+H)⁺.

Step-10: Preparation of 5-(5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P9)

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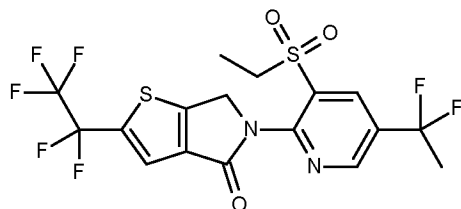


(P9)

To a 0°C cooled solution of 2-[[5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-53 prepared as described above) (0.215 g, 0.4199 mmol) in pyridine (2 mL) was added phosphorus oxychloride (0.08240 mL, 0.8398 mmol).

- 5 The reaction mixture was allowed to come at room temperature and stirred for 2 hours under nitrogen atmosphere. The reaction mass was acidified with an aqueous 2N hydrochloric acid (15 mL) solution, and the product extracted with ethyl acetate (2x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 10-50% ethyl acetate in cyclohexane) to afford 5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P9) as a light yellow solid. LCMS (Method 1): $R_t = 1.14$ min, $m/z = 469$ ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.45 (t, 3 H), 2.74 (s, 3H), 3.70 (q, 2 H), 5.26 (br s, 2 H), 7.69 (s, 1 H), 8.87 (d, 1 H), 9.26 (d, 1 H).

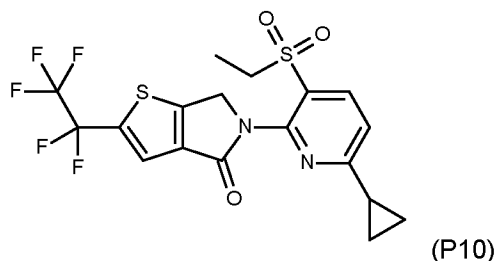
Step-11: Preparation of 5-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P8)



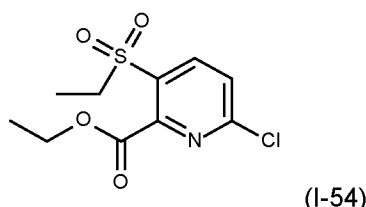
(P8)

To a solution of 5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P9 prepared as described above) (0.13 g, 0.2637 mmol) in toluene (1.3 mL) was added bis(2-methoxyethyl)aminosulfur trifluoride (0.39 mL, 1.055 mmol) dropwise under nitrogen atmosphere and the reaction mass was stirred at 80 °C for 24 hours. After completion, the reaction mixture was quenched with a saturated solution of sodium bicarbonate, followed by ice-cold water (500mL). The aqueous phase was extracted with ethyl acetate (3x 75 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 20-50% ethyl acetate in cyclohexane) to afford 5-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P8) as a white solid. LCMS (Method 1): $R_t = 1.11$ min, $m/z = 491$ ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.42 (t, 3H) 2.06 (t, 3H) 3.62 (q, 2H) 5.20 (br s, 2H) 7.70 (s, 1H) 8.53 (d, 1H) 8.93 (d, 1H).

Example P10: Preparation of 5-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P10)

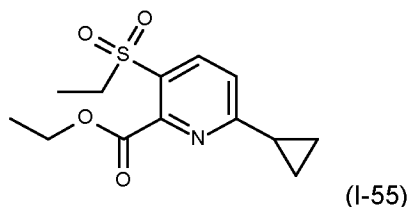


5 Step-1: Preparation of ethyl 6-chloro-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-54)



To 0°C cooled solution of 6-chloro-3-ethylsulfonyl-pyridine-2-carboxylic acid (CAS 1848219-28-2) (10 g, 40.05 mmol) in methanesulfinylmethane (100 mL) were added potassium carbonate (11.07 g, 80.106 mmol), followed by iodoethane (6.44 mL, 80.106 mmol) dropwise. The reaction mixture was stirred at room temperature overnight. The reaction mass was poured into ice-cold water and the product extracted with ethyl acetate (3x 100 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 20% ethyl acetate in cyclohexane) to afford ethyl 6-chloro-3-ethylsulfonyl-pyridine-2-carboxylate (I-54). LCMS (Method 1): $R_t = 1.05$ min, $m/z = 278$ (M+H)⁺.

15 Step-2: Preparation of ethyl 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-55)

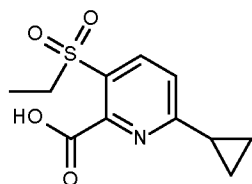


To a solution of ethyl 6-chloro-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-54 prepared as described above) (9.3 g, 33 mmol) in toluene (93 mL) and water (28 mL) were added potassium carbonate (14.0 g, 100 mmol), cyclopropyl boronic acid (7.6 g, 84 mmol) and the reaction mass was degassed with nitrogen for 10 minutes. 1,1'-Bis(diphenylphosphino)ferrocene-palladium(II)dichloride dichloromethane complex (1.4 g, 1.70 mmol) was added and the reaction mass was degassed with nitrogen for another 5 minutes and stirred for 5 hours at 110 °C under nitrogen atmosphere. The reaction mixture was allowed to cool to room temperature, diluted with water, extracted with ethyl acetate (3x) and washed with brine. The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 20%

-100-

ethyl acetate in cyclohexane) to afford ethyl 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylate (I-55) as a solid. LCMS (Method 1): $R_t = 1.08$ min, $m/z = 284$ ($M+H$)⁺.

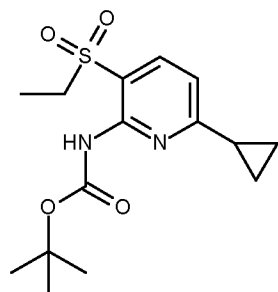
Step-3: Preparation of 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylic acid (intermediate I-56)



(I-56)

To a solution of ethyl 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylate (intermediate I-55 prepared as described above) (2.0 g, 7.1 mmol) in tetrahydrofuran (16 mL) and water (4 mL) was added lithium hydroxide monohydrate (0.89 g, 21 mmol) at 0-5°C. The reaction mixture was stirred at room temperature for 24 hours. Upon completion, the reaction mass was concentrated *in vacuo* and the residue acidified with an aqueous 2N hydrochloric acid solution. The formed white precipitate was filtered through a Buchner funnel and the solid residue washed with cold water followed by cyclohexane, then dried *in vacuo* to afford 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylic acid (I-56) as a solid. The crude was used as such for next step. LCMS (Method 1): $R_t = 0.66$ min, $m/z = 256$ ($M+H$)⁺.

Step-4: Preparation of tert-butyl N-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)carbamate (intermediate I-57)

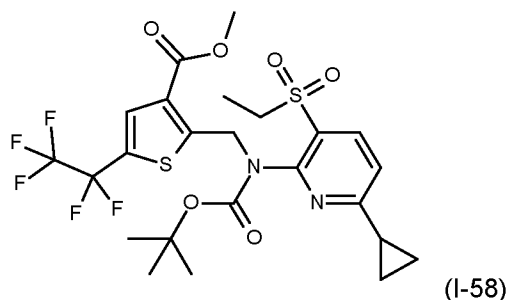


(I-57)

To a solution of 6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylic acid (intermediate I-56 prepared as described above) (1.7 g, 6.3 mmol) in tert-butanol (26 mL) was added triethylamine (1.4 mL, 10 mmol) and the reaction mass was heated at 90 °C for 10 minutes. Diphenylphosphoryl azide (2.2 mL, 10 mmol) was added dropwise over a period of 10 minutes and the resulting reaction mass was stirred at 90 °C for 60 minutes. The reaction mass was quenched with ice-cold water (100 mL) and the product extracted with ethyl acetate (2x). The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 20-70% ethyl acetate in cyclohexane) to afford tert-butyl N-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)carbamate (I-57). LCMS (Method 1): $R_t = 1.14$ min, $m/z = 327$ ($M+H$)⁺.

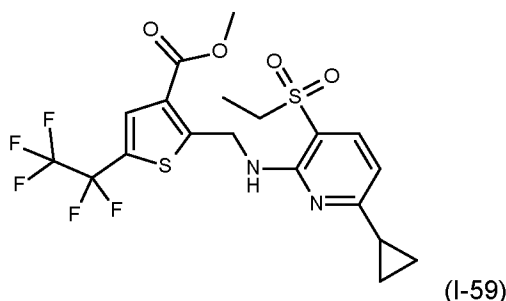
-101-

Step-5: Preparation of methyl 2-[[tert-butoxycarbonyl-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-58)



To solution of tert-butyl N-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)carbamate (intermediate I-57 prepared as described above) (0.55 g, 1.180 mmol) in acetonitrile (10 mL) were added methyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-15 prepared as described above) (0.5261 g, 1.415 mmol) and cesium carbonate (0.7690 g, 2.359 mmol). The reaction mixture was heated at 60 °C for 12 hours. The reaction mass was diluted with water and the product extracted with ethyl acetate. The organic layer was washed with water (2x) then brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was purified by combiflash (silica gel, 10-50% ethyl acetate in cyclohexane) to afford methyl 2-[[tert-butoxycarbonyl-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-58) as gummy mass. LCMS (Method 1): Rt = 1.35 min, m/z= 499 [(M+H)-100]⁺.

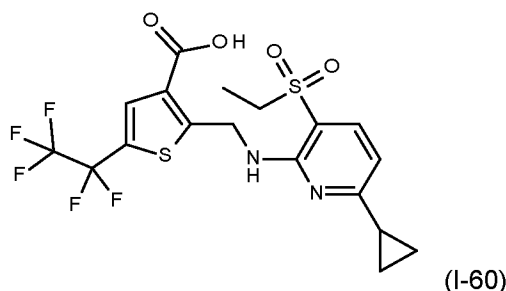
Step-6: Preparation of methyl 2-[[[(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-59)



A solution of methyl 2-[[tert-butoxycarbonyl-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-58 prepared as described above) (0.48 g, 0.7618 mmol) in trifluoroacetic acid (5 mL, 64.3 mmol) was stirred for 12 hours. After completion, the reaction mass was neutralised with an aqueous sodium bicarbonate solution. The aqueous layer was extracted with ethyl acetate (2x), the combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo* to afford methyl 2-[[[(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (I-59). The crude was used as such for next step. LCMS (Method 1): Rt = 1.23 min, m/z= 497 (M-H)⁻.

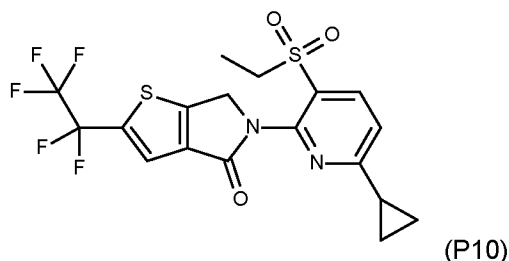
-102-

Step-7: Preparation of 2-[[[6-cyclopropyl-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-60)



To solution of methyl 2-[[[6-cyclopropyl-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate (intermediate I-59 prepared as described above) (0.23 g, 0.4383 mmol) in methanol (6 mL) was added a solution of barium hydroxide octahydrate (0.2911 g, 0.8766 mmol, 2.000) in water (2 mL) at 10 °C. The reaction mixture was stirred at room temperature for 12 hours. After completion, the reaction mass was concentrated *in vacuo*, acidified with an aqueous 1N hydrochloric acid solution, and the product extracted with ethyl acetate. The organic layer was washed with water (2x) followed by brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude was triturated with acetonitrile to afford 2-[[[6-cyclopropyl-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (I-60) as light yellow solid. LCMS (Method 1): $R_t = 1.22$ min, $m/z = 485$ ($M+H$)⁺.

Step-8: Preparation of 5-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P10)



To a 0°C cooled solution of 2-[[[6-cyclopropyl-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid (intermediate I-60 prepared as described above) (0.14 g, 0.2745 mmol) in pyridine (2 mL) was added phosphorus oxychloride (0.05169 mL, 0.5490 mmol). The reaction mixture was allowed to come at room temperature and stirred for 2 hours under nitrogen atmosphere. The reaction mass was acidified with an aqueous 2N hydrochloric acid (15 mL) solution and the product extracted with ethyl acetate (2x 30 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude compound was purified by combiflash (silica gel, 10-50% ethyl acetate in cyclohexane) to afford 5-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P10) as a light yellow solid.

LCMS (Method 1): $R_t = 1.21$ min, $m/z = 467$ ($M+H$)⁺. ¹H NMR (400 MHz, CDCl₃) δ ppm 1.11 - 1.19 (m, 4H) 1.38 (t, 3H) 2.11 - 2.18 (m, 1H) 3.52 (q, 2H) 5.09 (br s, 2H) 7.39 (d, 1H) 7.68 (s, 1H) 8.23 (d, 1H).

Table P: Examples of compounds of formula (I)

No.	IUPAC name	Structures	LCMS			Mp (°C)
			R _t (min)	[M+H] ⁺ (measured)	Method	
P1	1-[5-ethylsulfonyl-6-[4-oxo-2-(trifluoromethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropane-carbonitrile		1.45	442	2	175 - 177
P2	1-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropane-carbonitrile		1.08	492	1	-
P3	2-[[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]oxy]-2-methyl-propanenitrile		1.50	510	2	155 - 157
P4	5-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.16	525	1	123 - 125
P5	2-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]-2-methyl-propanenitrile		1.14	494	1	190 - 195
P6	5-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.17	521	1	114 - 118
P7	N-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]-N-methyl-acetamide		1.02	498	1	190 - 193

No.	IUPAC name	Structures	LCMS			Mp (°C)
			R _t (min)	[M+H] ⁺ (measured)	Method	
P8	5-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.11	491	1	154 - 156
P9	5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.14	469	1	126 - 130
P10	5-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.21	467	1	170 - 172
P11	5-(3-ethylsulfonyl-6-pyrimidin-2-yl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.02	505	1	120 - 125
P12	5-(3-ethylsulfonyl-6-methoxy-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.17	457	1	-
P13	5-[3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.04	494	1	147 - 150
P14	5-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.12	495	1	142 - 144

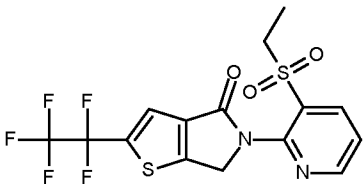
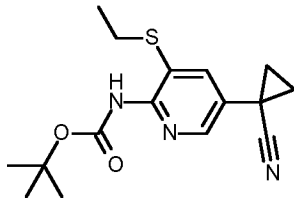
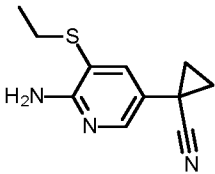
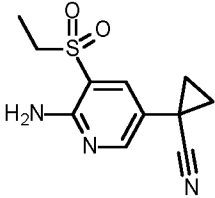
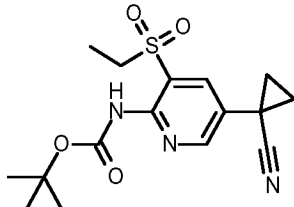
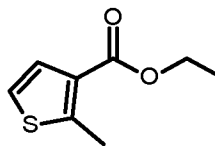
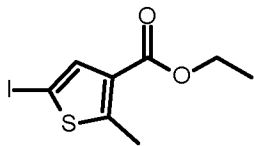
No.	IUPAC name	Structures	LCMS			Mp (°C)
			R _t (min)	[M+H] ⁺ (measured)	Method	
P15	5-(3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one		1.09	427	1	173 - 175

Table I: Examples of intermediates

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-1	tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]carbamate		1.05	318 (M-H) ⁻	1	-
I-2	1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropane-carbonitrile		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.21-1.33 (m, 5H), 1.61-1.69 (m, 2H), 2.80 (q, 2H), 5.26 (br s, 2H), 7.56 (d, 1H), 7.97 (d, 1H).			-
I-3	1-(6-amino-5-ethylsulfonyl-3-pyridyl)cyclopropane-carbonitrile		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.26-1.38 (m, 5H), 1.62-1.75 (m, 2H), 3.19 (q, 2H), 5.88 (br s, 2H), 7.84 (d, 1H), 8.35-8.39 (m, 1H).			-
I-4	tert-butyl N-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]carbamate		0.99	296 [(M+H) ⁺ - 56]	1	-
I-5	ethyl 2-methylthiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.37 (t, 3H), 2.75 (s, 3H), 4.32 (q, 2H), 6.98 (d, 1H), 7.40 (d, 1H).			-
I-6	ethyl 5-iodo-2-methylthiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.36 (t, 3H), 2.71 (s, 3H), 4.30 (q, 2H), 7.54 (s, 1H).			-

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-7	ethyl 2-methyl-5-(trifluoromethyl)thiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.38 (t, 3H), 2.78 (s, 3H), 4.33 (q, 2H), 7.73 (d, 1H).			-
I-8	ethyl 2-(bromomethyl)-5-(trifluoromethyl)thiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.43 (t, 3H), 4.40 (q, 2H), 5.09 (s, 2H), 7.77-7.81 (m, 1H).			-
I-9	ethyl 2-[[tert-butoxycarbonyl-[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate		1.27	488 [(M+H) ⁺ -100]	1	-
I-10	ethyl 2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylate		1.19	488	1	-
I-11	2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(trifluoromethyl)thiophene-3-carboxylic acid		1.02	460	1	-
I-12	methyl 2-bromothiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 3.89 (s, 3H), 7.23 (d, 1H), 7.37 (d, 1H).			-
I-13	methyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		6.67	338/340	3	-

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-14	methyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		5.86	274	3	-
I-15	methyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		8.43	352/354	3	-
I-16	methyl 2-[[[tert-butoxycarbonyl-5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.29	524 [(M+H) ⁺ -100]	1	-
I-17	methyl 2-[[[5-(1-cyanocyclopropyl)-3-methylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.19	524	1	-
I-18	2-[[[5-(1-cyanocyclopropyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.08	510	1	-
I-19	ethyl 2-bromo-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.41 (t, 3H) 4.38 (q, 2H), 7.71 (s, 1H).			
I-20	ethyl 2-methyl-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.39 (t, 3H) 2.79 (s, 3H) 4.33 (q, 2H), 7.74 (s, 1H).			

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-21	ethyl 2-(bromomethyl)-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		¹ H NMR (400 MHz, CDCl ₃) δ ppm 1.40-1.42 (m, 3H) 2.79 (s, 3H) 4.33 (q, 2H), 5.08 (s, 2H) 7.77 (s, 1H)			
I-23	tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]carbamate		1.17	282 [(M+H) ⁺ -56]	1	
I-24	tert-butyl N-[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]carbamate		1.37	314 [(M+H) ⁺ -56]	2	
I-25	ethyl 2-[[[tert-butoxycarbonyl-5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.39	556 [(M+H) ⁺ -100]	1	
I-26	ethyl 2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.64	556	1	
I-27	2-[[[5-(1-cyano-1-methyl-ethoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.17	528	1	
I-32	3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)pyridine-2-carboxylic acid		0.91	314	2	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-33	tert-butyl N-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]carbamate		1.14	383 (M-H) ⁻	1	
I-34	ethyl 2-[[[tert-butoxycarbonyl-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.39	571 [(M+H) ⁺ -100]	1	
I-35	ethyl 2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.30	571	1	
I-36	2-[[[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.17	543	1	

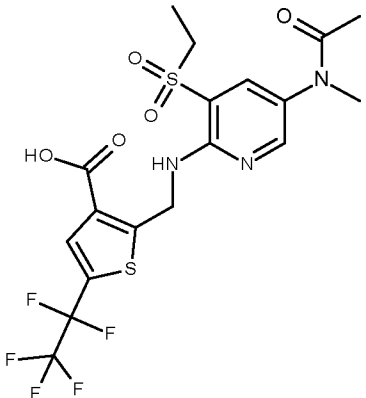
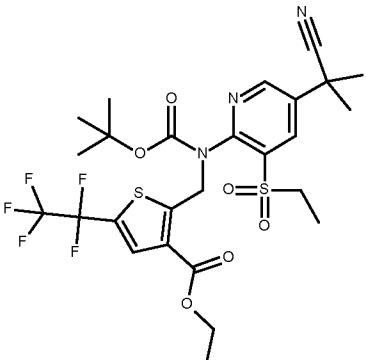
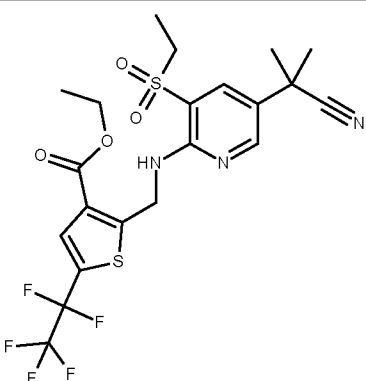
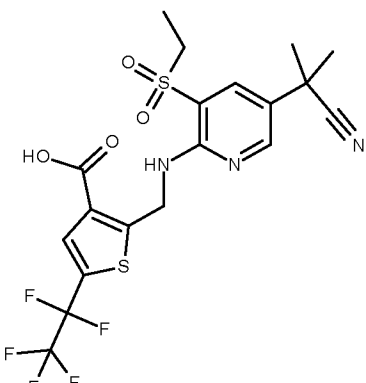
No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-39	5-(2,2-difluoropropoxy)-3-ethylsulfanyl-pyridine-2-carboxylic acid		0.91	276 (M-H) ⁻	1	
I-40	tert-butyl N-[5-(2,2-difluoropropoxy)-3-ethylsulfanyl-2-pyridyl]carbamate		1.16	293 [(M+H) ⁺ -56]	1	
I-41	tert-butyl N-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]carbamate		1.13	325 [(M+H) ⁺ -100]	1	
I-42	ethyl 2-[[[tert-butoxycarbonyl-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.30	567 [(M+H) ⁺ -100]	1	
I-43	ethyl 2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.11	567	1	
I-44	2-[[[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.20	539	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-49	5-(1,1-difluoroethyl)-3-ethylsulfonyl-pyridine-2-carboxylic acid		0.77	280	2	
I-50	tert-butyl N-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]carbamate		1.37	295 [(M+H) ⁺ - 56]	2	
I-51	methyl 2-[[tert-butoxycarbonyl-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.32	523 [(M+H) ⁺ - 100]	1	
I-52	methyl 2-[[[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.21	523	1	
I-53	2-[[[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.06	487	1	

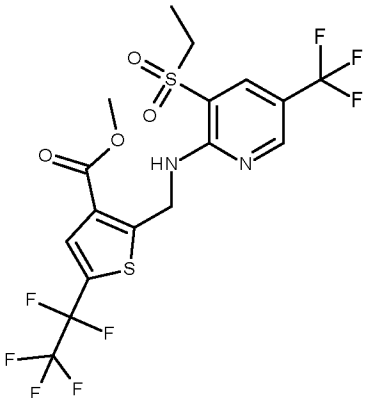
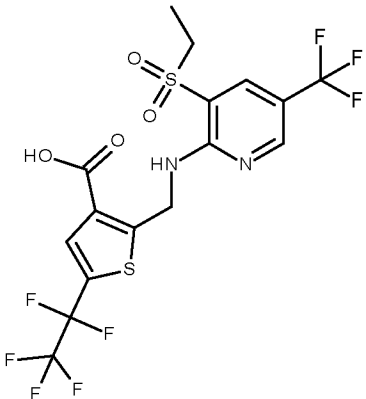
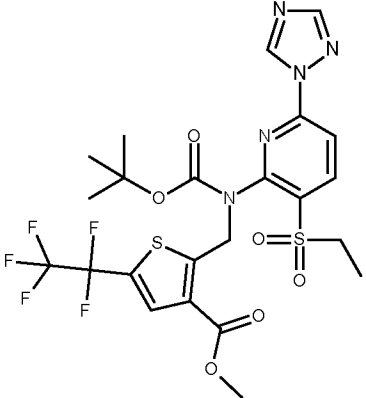
No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-54	6-cyclopropyl-3-ethylsulfonyl-pyridine-2-carboxylic acid		0.66	256	1	
I-57	tert-butyl N-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)carbamate		1.14	327	1	
I-58	methyl 2-[[tert-butoxycarbonyl-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.35	499 [(M+H) ⁺ -100]	1	
I-59	methyl 2-[(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.23	497 (M-H) ⁻	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-60	2-[[[(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.22	485	1	
I-61	tert-butyl N-[5-(1-cyano-1-methyl-ethyl)-3-ethylsulfonyl-2-pyridyl]carbamate		1.08	298 [(M+H) ⁺ -56]	1	
I-62	3-ethylsulfonyl-5-(trifluoromethyl)pyridin-2-amine		0.91	253 (M-H) ⁻	1	
I-63	tert-butyl N-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]carbamate		1.17	299 [(M+H) ⁺ -56]	1	
I-64	N-(6-amino-5-ethylsulfonyl-3-pyridyl)-N-methylacetamide		0.39	258	1	
I-65	tert-butyl N-[5-[acetyl(methyl)amino]-3-ethylsulfonyl-2-pyridyl]carbamate		0.93	356 (M-H) ⁻	1	

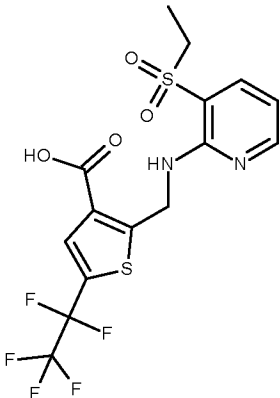
No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-66	3-ethylsulfonyl-6-pyrimidin-2-yl-pyridin-2-amine		0.84	265	1	
I-67	tert-butyl N-(3-ethylsulfonyl-6-pyrimidin-2-yl-2-pyridyl)carbamate		1.00	363 (M-H) ⁻	1	
I-68	methyl 2-[[[5-[acetyl(methyl)amino]-3-ethylsulfonyl-2-pyridyl]-tert-butoxycarbonyl-amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.16	530 [(M+H) ⁺ - 100]	1	
I-69	methyl 2-[[[5-[acetyl(methyl)amino]-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.10	530	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-70	2-[[[5-[acetyl(methyl)amino]-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.06	516	1	
I-71	ethyl 2-[[[tert-butoxycarbonyl-[5-(1-cyano-1-methyl-ethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.28	540 [(M+H) ⁺ - 100]	1	
I-72	ethyl 2-[[[5-(1-cyano-1-methyl-ethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.29	540	1	
I-73	2-[[[5-(1-cyano-1-methyl-ethyl)-3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.20	512	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-74	methyl 2-[[tert-butoxycarbonyl-(3-ethylsulfonyl-6-pyrimidin-2-yl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.25	637	1	
I-75	methyl 2-[[[(3-ethylsulfonyl-6-pyrimidin-2-yl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.11	537	1	
I-76	2-[[[(3-ethylsulfonyl-6-pyrimidin-2-yl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.04	523	1	
I-77	methyl 2-[[tert-butoxycarbonyl-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.41	527 [(M+H) ⁺ -100]	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-78	methyl 2-[[[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.21	527	1	
I-79	2-[[[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.37	513	1	
I-80	methyl 2-[[[tert-butoxycarbonyl-[3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.25	626	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-81	methyl 2-[[[3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.11	526	1	
I-82	2-[[[3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.16	512	1	
I-83	methyl 2-[[[tert-butoxycarbonyl-(3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.26	459 [(M+H) ⁺ - 100]	1	
I-84	methyl 2-[[[3-ethylsulfonyl-2-pyridyl]amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylate		1.21	459	1	

No.	IUPAC name	Structures	¹ H NMR, LCMS, GCMS			Mp (°C)
			R _t (min)	[M] ⁺ or [M+H] ⁺ (measured)	Method	
I-85	2-[[[(3-ethylsulfonyl-2-pyridyl)amino]methyl]-5-(1,1,2,2,2-pentafluoroethyl)thiophene-3-carboxylic acid		1.11	445	1	

The activity of the compositions according to the invention can be broadened considerably, and adapted to prevailing circumstances, by adding other insecticidally, acaricidally and/or fungicidally active ingredients. The mixtures of the compounds of formula I with other insecticidally, acaricidally and/or fungicidally active ingredients may also have further surprising advantages which can also be described, in a wider sense, as synergistic activity. For example, better tolerance by plants, reduced phytotoxicity, insects can be controlled in their different development stages or better behaviour during their production, for example during grinding or mixing, during their storage or during their use. Suitable additions to active ingredients here are, for example, representatives of the following classes of active ingredients: organophosphorus compounds, nitrophenol derivatives, thioureas, juvenile hormones, formamidines, benzophenone derivatives, ureas, pyrrole derivatives, carbamates, pyrethroids, chlorinated hydrocarbons, acylureas, pyridylmethyleamino derivatives, macrolides, neonicotinoids and *Bacillus thuringiensis* preparations.

The following mixtures of the compounds of formula I with active ingredients are preferred (the abbreviation "TX" means "one compound selected from the group consisting of the compounds described in Tables A-1 to A-12, Tables C-1 to C-12 and Table P of the present invention"):

an adjuvant selected from the group of substances consisting of petroleum oils (alternative name) (628) + TX;

an insect control active substance selected from abamectin + TX, acequinocyl + TX, acetamiprid + TX, acetoprole + TX, acrinathrin + TX, acynonapyr + TX, afidopyropen + TX, afoxolaner + TX, alanycarb + TX, allethrin + TX, alpha-cypermethrin + TX, alphamethrin + TX, amidoflumet + TX, aminocarb + TX, azocyclotin + TX, bensultap + TX, benzoximate + TX, benzpyrimoxan + TX, betacyfluthrin + TX, beta-cypermethrin + TX, bifenazate + TX, bifenthrin + TX, binapacryl + TX, bioallethrin + TX, S-bioallethrin + TX, bioresmethrin + TX, bistrifluron + TX, broflanilide + TX, brofluthrin + TX, brofluthrin + TX, bromophos-ethyl + TX, buprofezine + TX, butocarboxim + TX, cadusafos + TX, carbaryl + TX, carbosulfan + TX, cartap +

TX, CAS number: 1632218-00-8 + TX, CAS number: 1808115-49-2 + TX, CAS number: 2032403-97-5 + TX, CAS number: 2044701-44-0 + TX, CAS number: 2128706-05-6 + TX, CAS number: 2095470-94-1 + TX, CAS number: 2377084-09-6 + TX, CAS number: 1445683-71-5 + TX, CAS number: 2408220-94-8 + TX, CAS number: 2408220-91-5 + TX, CAS number: 1365070-72-9 + TX, CAS number: 2171099-09-3 + TX, CAS number: 2396747-83-2 + TX, CAS number: 2032403-97-5 + TX, CAS number: 1680187-98-7 + TX, CAS number: 1680188-04-8 + TX, CAS number: 1680188-06-0 + TX, CAS number: 1680188-09-3 + TX, CAS number: 1680188-56-0 + TX, CAS number: 1680188-55-9 + TX, CAS number: 1680188-65-1 + TX, CAS number: 1680188-68-4 + TX, CAS number: 1680188-69-5 + TX, CAS number: 1680188-91-3 + TX, CAS number: 1689545-27-4 + TX, CAS number: 2408908-90-5 + TX, CAS number: 2408908-91-6 + TX, CAS number: 2408908-92-7 + TX, CAS number: 2408908-93-8 + TX, CAS number: 2133042-31-4 + TX, CAS number: 2133042-44-9 + TX, CAS number: 1445684-82-1 + TX, CAS number: 1445684-82-1 + TX, CAS number: 1922957-45-6 + TX, CAS number: 1922957-46-7 + TX, CAS number: 1922957-47-8 + TX, CAS number: 1922957-48-9 + TX, CAS number: 2415706-16-8 + TX, CAS number: 1594624-87-9 + TX, CAS number: 1594637-65-6 + TX, CAS number: 1594626-19-3 + TX, chlorantraniliprole + TX, chlordane + TX, chlorfenapyr + TX, chlorprallethrin + TX, chromafenozide + TX, clenpirin + TX, cloethocarb + TX, clothianidin + TX, 2-chlorophenyl N-methylcarbamate (CPMC) + TX, cyanofenphos + TX, cyantraniliprole + TX, cyclaniliprole + TX, cyclobutrifluram + TX, cycloprothrin + TX, cycloxaprid + TX, cyenopyrafen + TX, cyetpyrafen + TX, cyflumetofen + TX, cyfluthrin + TX, cyhalodiamide + TX, cyhalothrin + TX, cypermethrin + TX, cyphenothrin + TX, cyproflanilide + TX, cyromazine + TX, deltamethrin + TX, diafenthiuron + TX, dialifos + TX, dibrom + TX, dicloromezotiaz + TX, diflovidazine + TX, diflubenzuron + TX, dimpropyridaz + TX, dinactin + TX, dinocap + TX, dinotefuran + TX, dioxabenzofos + TX, emamectin (or emamectin benzoate) + TX, empenthrin + TX, epsilon-momfluorothrin + TX, epsilon-metofluthrin + TX, esfenvalerate + TX, ethion + TX, ethiprole + TX, etofenprox + TX, etoxazole + TX, famphur + TX, fenazaquin + TX, fenfluthrin + TX, fenmezoditiaz + TX, fenitrothion + TX, fenobucarb + TX, fenothiocarb + TX, fenoxycarb + TX, fenpropathrin + TX, fenpyroximate + TX, fensulfothion + TX, fenthion + TX, fentinacetate + TX, fenvalerate + TX, fipronil + TX, flometoquin + TX, flonicamid + TX, fluacrypyrim + TX, fluazaindolizine + TX, fluazuron + TX, flubendiamide + TX, flubenzimine + TX, fluchlordiniliprole + TX, flucitrate + TX, flucycloxuron + TX, flucythrinate + TX, fluensulfone + TX, flufenerim + TX, flufenprox + TX, flufiprole + TX, fluhexafon + TX, flumethrin + TX, fluopyram + TX, flupentiofenox + TX, flupyradifurone + TX, flupyrimin + TX, fluralaner + TX, fluvalinate + TX, fluxametamide + TX, fosthiazate + TX, gamma-cyhalothrin + TX, Gossypure™ + TX, guadipyr + TX, halofenozide + TX, halfenprox + TX, heptafluthrin + TX, hexythiazox + TX, hydramethylnon + TX, imicyafos + TX, imidacloprid + TX, imiprothrin + TX, indoxacarb + TX, iodomethane + TX, iprodione + TX, isocycloseram + TX, isothioate + TX, ivermectin + TX, kappa-bifenthrin + TX, kappa-tefluthrin + TX, lambda-cyhalothrin + TX, lepimectin + TX, lotilaner + TX, lufenuron + TX, metaflumizone + TX, metaldehyde + TX, metam + TX, methomyl + TX, methoxyfenozide + TX, metofluthrin + TX, metolcarb + TX, mexacarbate + TX, milbemectin + TX, momfluorothrin + TX, niclosamide + TX, nicofluprole + TX; nitenpyram + TX, nithiazine + TX,

omethoate + TX, oxamyl + TX, oxazosulphyl + TX, parathion-ethyl + TX, permethrin + TX, phenothrin + TX, phosphocarb + TX, piperonylbutoxide + TX, pirimicarb + TX, pirimiphos-ethyl + TX, pirimiphos-methyl + TX, Polyhedrosis virus + TX, prallethrin + TX, profenofos + TX, profluthrin + TX, propargite + TX, propetamphos + TX, propoxur + TX, prothiophos + TX, protrifenbute + TX, pyflubumide + TX,

5 pymetrozine + TX, pyraclofos + TX, pyrafluprole + TX, pyridaben + TX, pyridalyl + TX, pyrifluquinazon + TX, pyrimidifen + TX, pyriminostrobin + TX, pyriprole + TX, pyriproxyfen + TX, resmethrin + TX, sarolaner + TX, selamectin + TX, silafluofen + TX, spinetoram + TX, spinosad + TX, spiroadiclofen + TX, spiromesifen + TX, spiropidion + TX, spirotetramat + TX, spidoxamat + TX, sulfoxaflor + TX, tebufenozide + TX, tebufenpyrad + TX, tebupirimiphos + TX, tefluthrin + TX, temephos + TX,

10 tetrachlorantraniliprole + TX, tetradiphon + TX, tetramethrin + TX, tetramethylfluthrin + TX, tetranactin + TX, tetraniliprole + TX, theta-cypermethrin + TX, thiacloprid + TX, thiamethoxam + TX, thiocyclam + TX, thiodicarb + TX, thiofanox + TX, thiometon + TX, thiosultap + TX, tigolaner + TX, tioazafen + TX, tolfenpyrad + TX, toxaphene + TX, tralomethrin + TX, transfluthrin + TX, triazamate + TX, triazophos + TX, trichlorfon + TX, trichloronate + TX, trichlorphon + TX, triflumezopyrim + TX, tyclopyrazoflor + TX,

15 zeta-cypermethrin + TX, Extract of seaweed and fermentation product derived from melasse + TX, Extract of seaweed and fermentation product derived from melasse comprising urea + TX, amino acids + TX, potassium and molybdenum and EDTA-chelated manganese + TX, Extract of seaweed and fermented plant products + TX, Extract of seaweed and fermented plant products comprising phytohormones + TX, vitamins + TX, EDTA-chelated copper + TX, zinc + TX, and iron + TX,

20 azadirachtin + TX, *Bacillus aizawai* + TX, *Bacillus chitosporus* AQ746 (NRRL Accession No B-21 618) + TX, *Bacillus firmus* + TX, *Bacillus kurstaki* + TX, *Bacillus mycoides* AQ726 (NRRL Accession No. B-21664) + TX, *Bacillus pumilus* (NRRL Accession No B-30087) + TX, *Bacillus pumilus* AQ717 (NRRL Accession No. B-21662) + TX, *Bacillus* sp. AQ178 (ATCC Accession No. 53522) + TX, *Bacillus* sp. AQ175 (ATCC Accession No. 55608) + TX, *Bacillus* sp. AQ177 (ATCC Accession No. 55609) + TX, *Bacillus subtilis* unspecified + TX, *Bacillus subtilis* AQ153 (ATCC Accession No. 55614) + TX, *Bacillus subtilis* AQ30002 (NRRL Accession No. B-50421) + TX, *Bacillus subtilis* AQ30004 (NRRL Accession No. B- 50455) + TX, *Bacillus subtilis* AQ713 (NRRL Accession No. B-21661) + TX, *Bacillus subtilis* AQ743 (NRRL Accession No. B-21665) + TX, *Bacillus thuringiensis* AQ52 (NRRL Accession No. B-21619) + TX, *Bacillus thuringiensis* BD#32 (NRRL Accession No B-21530) + TX,

30 *Bacillus thuringiensis* subspec. *kurstaki* BMP 123 + TX, *Beauveria bassiana* + TX, D-limonene + TX, Granulovirus + TX, Harpin + TX, *Helicoverpa armigera* Nucleopolyhedrovirus + TX, *Helicoverpa zea* Nucleopolyhedrovirus + TX, *Heliothis virescens* Nucleopolyhedrovirus + TX, *Heliothis punctigera* Nucleopolyhedrovirus + TX, *Metarhizium* spp. + TX, *Muscodor albus* 620 (NRRL Accession No. 30547) + TX, *Muscodor roseus* A3-5 (NRRL Accession No. 30548) + TX, Neem tree based products + TX, *Paecilomyces fumosoroseus* + TX, *Paecilomyces lilacinus* + TX, *Pasteuria nishizawae* + TX, *Pasteuria penetrans* + TX, *Pasteuria ramosa* + TX, *Pasteuria thornei* + TX, *Pasteuria usgae* + TX, P-cymene + TX, *Plutella xylostella* Granulosis virus + TX, *Plutella xylostella* Nucleopolyhedrovirus + TX, Polyhedrosis virus + TX, pyrethrum + TX, QRD 420 (a terpenoid blend) + TX, QRD 452 (a terpenoid blend) + TX, QRD 460 (a terpenoid blend) + TX, *Quillaja saponaria* + TX, *Rhodococcus globerulus*

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AQ719 (NRRL Accession No B-21663) + TX, *Spodoptera frugiperda* Nucleopolyhedrovirus + TX, *Streptomyces galbus* (NRRL Accession No. 30232) + TX, *Streptomyces* sp. (NRRL Accession No. B-30145) + TX, Terpenoid blend + TX, and *Verticillium* spp.;

5 an algicide selected from the group of substances consisting of bethoxazin [CCN] + TX, copper dioctanoate (IUPAC name) (170) + TX, copper sulfate (172) + TX, cybutryne [CCN] + TX, dichlone (1052) + TX, dichlorophen (232) + TX, endothal (295) + TX, fentin (347) + TX, hydrated lime [CCN] + TX, nabam (566) + TX, quinoxamine (714) + TX, quinonamid (1379) + TX, simazine (730) + TX, triphenyltin acetate (IUPAC name) (347) and triphenyltin hydroxide (IUPAC name) (347) + TX;

10 an anthelmintic selected from the group of substances consisting of abamectin (1) + TX, crufomate (1011) + TX, cyclobutifluram + TX, doramectin (alternative name) [CCN] + TX, emamectin (291) + TX, emamectin benzoate (291) + TX, eprinomectin (alternative name) [CCN] + TX, ivermectin (alternative name) [CCN] + TX, milbemycin oxime (alternative name) [CCN] + TX, moxidectin (alternative name) [CCN] + TX, piperazine [CCN] + TX, selamectin (alternative name) [CCN] + TX, spinosad (737) and thiophanate (1435) + TX;

an avicide selected from the group of substances consisting of chloralose (127) + TX, endrin (1122) + TX, fenthion (346) + TX, pyridin-4-amine (IUPAC name) (23) and strychnine (745) + TX;

a bactericide selected from the group of substances consisting of 1-hydroxy-1*H*-pyridine-2-thione (IUPAC name) (1222) + TX, 4-(quinoxalin-2-ylamino)benzenesulfonamide (IUPAC name) (748) + TX, 20 8-hydroxyquinoline sulfate (446) + TX, bronopol (97) + TX, copper dioctanoate (IUPAC name) (170) + TX, copper hydroxide (IUPAC name) (169) + TX, cresol [CCN] + TX, dichlorophen (232) + TX, dipyrithione (1105) + TX, dodicin (1112) + TX, fenaminosulf (1144) + TX, formaldehyde (404) + TX, hydrargaphen (alternative name) [CCN] + TX, kasugamycin (483) + TX, kasugamycin hydrochloride hydrate (483) + TX, nickel bis(dimethyldithiocarbamate) (IUPAC name) (1308) + TX, 25 nitrapyrin (580) + TX, octhilonone (590) + TX, oxolinic acid (606) + TX, oxytetracycline (611) + TX, potassium hydroxyquinoline sulfate (446) + TX, probenazole (658) + TX, streptomycin (744) + TX, streptomycin sesquisulfate (744) + TX, tecloftalam (766) + TX, and thiomersal (alternative name) [CCN] + TX;

a biological agent selected from the group of substances consisting of *Adoxophyes orana* GV (alternative name) (12) + TX, *Agrobacterium radiobacter* (alternative name) (13) + TX, *Amblyseius* spp. (alternative name) (19) + TX, *Anagrapha falcifera* NPV (alternative name) (28) + TX, *Anagrus atomus* (alternative name) (29) + TX, *Aphelinus abdominalis* (alternative name) (33) + TX, *Aphidius colemani* (alternative name) (34) + TX, *Aphidoletes aphidimyza* (alternative name) (35) + TX, *Autographa californica* NPV (alternative name) (38) + TX, *Bacillus firmus* (alternative name) (48) + 35 TX, *Bacillus sphaericus* Neide (scientific name) (49) + TX, *Bacillus thuringiensis* Berliner (scientific name) (51) + TX, *Bacillus thuringiensis* subsp. *aizawai* (scientific name) (51) + TX, *Bacillus thuringiensis* subsp. *israelensis* (scientific name) (51) + TX, *Bacillus thuringiensis* subsp. *japonensis* (scientific name) (51) + TX, *Bacillus thuringiensis* subsp. *kurstaki* (scientific name) (51) + TX, *Bacillus thuringiensis* subsp. *tenebrionis* (scientific name) (51) + TX, *Beauveria bassiana* (alternative

- name) (53) + TX, *Beauveria brongniartii* (alternative name) (54) + TX, *Chrysoperla carnea* (alternative name) (151) + TX, *Cryptolaemus montrouzieri* (alternative name) (178) + TX, *Cydia pomonella* GV (alternative name) (191) + TX, *Dacnusa sibirica* (alternative name) (212) + TX, *Diglyphus isaea* (alternative name) (254) + TX, *Encarsia formosa* (scientific name) (293) + TX,
- 5 *Eretmocerus eremicus* (alternative name) (300) + TX, *Helicoverpa zea* NPV (alternative name) (431) + TX, *Heterorhabditis bacteriophora* and *H. megidis* (alternative name) (433) + TX, *Hippodamia convergens* (alternative name) (442) + TX, *Leptomastix dactylopii* (alternative name) (488) + TX, *Macrolophus caliginosus* (alternative name) (491) + TX, *Mamestra brassicae* NPV (alternative name) (494) + TX, *Metaphycus helvolus* (alternative name) (522) + TX, *Metarhizium anisopliae* var.
- 10 *acridum* (scientific name) (523) + TX, *Metarhizium anisopliae* var. *anisopliae* (scientific name) (523) + TX, *Neodiprion sertifer* NPV and *N. lecontei* NPV (alternative name) (575) + TX, *Orius* spp. (alternative name) (596) + TX, *Paecilomyces fumosoroseus* (alternative name) (613) + TX, *Phytoseiulus persimilis* (alternative name) (644) + TX, *Spodoptera exigua* multicapsid nuclear polyhedrosis virus (scientific name) (741) + TX, *Steinernema bibionis* (alternative name) (742) + TX,
- 15 *Steinernema carpocapsae* (alternative name) (742) + TX, *Steinernema feltiae* (alternative name) (742) + TX, *Steinernema glaseri* (alternative name) (742) + TX, *Steinernema riobrave* (alternative name) (742) + TX, *Steinernema riobrave* (alternative name) (742) + TX, *Steinernema scapterisci* (alternative name) (742) + TX, *Steinernema* spp. (alternative name) (742) + TX, *Trichogramma* spp. (alternative name) (826) + TX, *Typhlodromus occidentalis* (alternative name) (844) and *Verticillium*
- 20 *lecanii* (alternative name) (848) + TX;
- a soil sterilant selected from the group of substances consisting of iodomethane (IUPAC name) (542) and methyl bromide (537) + TX;
- a chemosterilant selected from the group of substances consisting of apholate [CCN] + TX, bisazir (alternative name) [CCN] + TX, busulfan (alternative name) [CCN] + TX, diflubenzuron (250) + TX,
- 25 dimatif (alternative name) [CCN] + TX, hemel [CCN] + TX, hempa [CCN] + TX, metepa [CCN] + TX, methiotepa [CCN] + TX, methyl apholate [CCN] + TX, morzid [CCN] + TX, penfluron (alternative name) [CCN] + TX, tepa [CCN] + TX, thiohempa (alternative name) [CCN] + TX, thiotepa (alternative name) [CCN] + TX, tretamine (alternative name) [CCN] and uredepa (alternative name) [CCN] + TX;
- 30 an insect pheromone selected from the group of substances consisting of (*E*)-dec-5-en-1-yl acetate with (*E*)-dec-5-en-1-ol (IUPAC name) (222) + TX, (*E*)-tridec-4-en-1-yl acetate (IUPAC name) (829) + TX, (*E*)-6-methylhept-2-en-4-ol (IUPAC name) (541) + TX, (*E,Z*)-tetradeca-4,10-dien-1-yl acetate (IUPAC name) (779) + TX, (*Z*)-dodec-7-en-1-yl acetate (IUPAC name) (285) + TX, (*Z*)-hexadec-11-enal (IUPAC name) (436) + TX, (*Z*)-hexadec-11-en-1-yl acetate (IUPAC name) (437) + TX, (*Z*)-
- 35 hexadec-13-en-11-yn-1-yl acetate (IUPAC name) (438) + TX, (*Z*)-icos-13-en-10-one (IUPAC name) (448) + TX, (*Z*)-tetradec-7-en-1-yl acetate (IUPAC name) (782) + TX, (*Z*)-tetradec-9-en-1-yl acetate (IUPAC name) (783) + TX, (*Z*)-tetradec-9-en-1-yl acetate (IUPAC name) (784) + TX, (7*E*,9*Z*)-dodeca-7,9-dien-1-yl acetate (IUPAC name) (283) + TX, (9*Z*,11*E*)-tetradeca-9,11-dien-1-yl acetate (IUPAC name) (780) + TX, (9*Z*,12*E*)-tetradeca-9,12-dien-1-yl acetate (IUPAC name) (781) + TX, 14-methyloctadec-1-ene

(IUPAC name) (545) + TX, 4-methylnonan-5-ol with 4-methylnonan-5-one (IUPAC name) (544) + TX, alpha-multistriatin (alternative name) [CCN] + TX, brevicomin (alternative name) [CCN] + TX, codlure (alternative name) [CCN] + TX, codlemone (alternative name) (167) + TX, cuelure (alternative name) (179) + TX, disparlure (277) + TX, dodec-8-en-1-yl acetate (IUPAC name) (286) + TX, dodec-9-en-1-yl acetate (IUPAC name) (287) + TX, dodeca-8 + TX, 10-dien-1-yl acetate (IUPAC name) (284) + TX, dominicalure (alternative name) [CCN] + TX, ethyl 4-methyloctanoate (IUPAC name) (317) + TX, eugenol (alternative name) [CCN] + TX, frontalinal (alternative name) [CCN] + TX, gossyplure (alternative name) (420) + TX, grandlure (421) + TX, grandlure I (alternative name) (421) + TX, grandlure II (alternative name) (421) + TX, grandlure III (alternative name) (421) + TX, grandlure IV (alternative name) (421) + TX, hexalure [CCN] + TX, ipsdienol (alternative name) [CCN] + TX, ipsenol (alternative name) [CCN] + TX, japonilure (alternative name) (481) + TX, lineatin (alternative name) [CCN] + TX, litlure (alternative name) [CCN] + TX, looplure (alternative name) [CCN] + TX, medlure [CCN] + TX, megatomoic acid (alternative name) [CCN] + TX, methyl eugenol (alternative name) (540) + TX, muscalure (563) + TX, octadeca-2,13-dien-1-yl acetate (IUPAC name) (588) + TX, octadeca-3,13-dien-1-yl acetate (IUPAC name) (589) + TX, orfralure (alternative name) [CCN] + TX, oryctalure (alternative name) (317) + TX, ostramone (alternative name) [CCN] + TX, siglure [CCN] + TX, sordidin (alternative name) (736) + TX, sulcatol (alternative name) [CCN] + TX, tetradec-11-en-1-yl acetate (IUPAC name) (785) + TX, trimedlure (839) + TX, trimedlure A (alternative name) (839) + TX, trimedlure B₁ (alternative name) (839) + TX, trimedlure B₂ (alternative name) (839) + TX, trimedlure C (alternative name) (839) and trunc-call (alternative name) [CCN] + TX;

an insect repellent selected from the group of substances consisting of 2-(octylthio)ethanol (IUPAC name) (591) + TX, butopyronoxyl (933) + TX, butoxy(polypropylene glycol) (936) + TX, dibutyl adipate (IUPAC name) (1046) + TX, dibutyl phthalate (1047) + TX, dibutyl succinate (IUPAC name) (1048) + TX, diethyltoluamide [CCN] + TX, dimethyl carbate [CCN] + TX, dimethyl phthalate [CCN] + TX, ethyl hexanediol (1137) + TX, hexamide [CCN] + TX, methoquin-butyl (1276) + TX, methylneodecanamide [CCN] + TX, oxamate [CCN] and picaridin [CCN] + TX;

a molluscicide selected from the group of substances consisting of bis(tributyltin) oxide (IUPAC name) (913) + TX, bromoacetamide [CCN] + TX, calcium arsenate [CCN] + TX, cloethocarb (999) + TX, copper acetoarsenite [CCN] + TX, copper sulfate (172) + TX, fentin (347) + TX, ferric phosphate (IUPAC name) (352) + TX, metaldehyde (518) + TX, methiocarb (530) + TX, niclosamide (576) + TX, niclosamide-olamine (576) + TX, pentachlorophenol (623) + TX, sodium pentachlorophenoxide (623) + TX, tazimcarb (1412) + TX, thiodicarb (799) + TX, tributyltin oxide (913) + TX, trifenmorph (1454) + TX, trimethacarb (840) + TX, triphenyltin acetate (IUPAC name) (347) and triphenyltin hydroxide (IUPAC name) (347) + TX, pyriprole [394730-71-3] + TX;

a nematicide selected from the group of substances consisting of AKD-3088 (compound code) + TX, 1,2-dibromo-3-chloropropane (IUPAC/Chemical Abstracts name) (1045) + TX, 1,2-dichloropropane (IUPAC/ Chemical Abstracts name) (1062) + TX, 1,2-dichloropropane with 1,3-dichloropropene (IUPAC name) (1063) + TX, 1,3-dichloropropene (233) + TX, 3,4-dichlorotetrahydrothiophene 1,1-

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dioxide (IUPAC/Chemical Abstracts name) (1065) + TX, 3-(4-chlorophenyl)-5-methylrhodanine (IUPAC name) (980) + TX, 5-methyl-6-thioxo-1,3,5-thiadiazinan-3-ylacetic acid (IUPAC name) (1286) + TX, 6-isopentenylaminopurine (alternative name) (210) + TX, abamectin (1) + TX, acetoprole [CCN] + TX, alanycarb (15) + TX, aldicarb (16) + TX, aldoxycarb (863) + TX, AZ 60541 (compound code) + TX, benclonthiaz [CCN] + TX, benomyl (62) + TX, butylpyridaben (alternative name) + TX, cadusafos (109) + TX, carbofuran (118) + TX, carbon disulfide (945) + TX, carbosulfan (119) + TX, chloropicrin (141) + TX, chlorpyrifos (145) + TX, cloethocarb (999) + TX, cyclobutrifluram + TX, cytokinins (alternative name) (210) + TX, dazomet (216) + TX, DBCP (1045) + TX, DCIP (218) + TX, diamidafos (1044) + TX, dichlofenthion (1051) + TX, dicliphos (alternative name) + TX, dimethoate (262) + TX, doramectin (alternative name) [CCN] + TX, emamectin (291) + TX, emamectin benzoate (291) + TX, eprinomectin (alternative name) [CCN] + TX, ethoprophos (312) + TX, ethylene dibromide (316) + TX, fenamiphos (326) + TX, fenpyrad (alternative name) + TX, fensulfthion (1158) + TX, fosthiazate (408) + TX, fosthietan (1196) + TX, furfural (alternative name) [CCN] + TX, GY-81 (development code) (423) + TX, heterophos [CCN] + TX, iodomethane (IUPAC name) (542) + TX, isamidofos (1230) + TX, isazofos (1231) + TX, ivermectin (alternative name) [CCN] + TX, kinetin (alternative name) (210) + TX, mecarphon (1258) + TX, metam (519) + TX, metam-potassium (alternative name) (519) + TX, metam-sodium (519) + TX, methyl bromide (537) + TX, methyl isothiocyanate (543) + TX, milbemycin oxime (alternative name) [CCN] + TX, moxidectin (alternative name) [CCN] + TX, *Myrothecium verrucaria* composition (alternative name) (565) + TX, NC-184 (compound code) + TX, oxamyl (602) + TX, phorate (636) + TX, phosphamidon (639) + TX, phosphocarb [CCN] + TX, sebufos (alternative name) + TX, selamectin (alternative name) [CCN] + TX, spinosad (737) + TX, terbam (alternative name) + TX, terbufos (773) + TX, tetrachlorothiophene (IUPAC/ Chemical Abstracts name) (1422) + TX, thiafenox (alternative name) + TX, thionazin (1434) + TX, triazophos (820) + TX, triazuron (alternative name) + TX, xlenols [CCN] + TX, YI-5302 (compound code) and zeatin (alternative name) (210) + TX, fluensulfone [318290-98-1] + TX, fluopyram + TX;

a nitrification inhibitor selected from the group of substances consisting of potassium ethylxanthate [CCN] and nitrapyrin (580) + TX;

a plant activator selected from the group of substances consisting of acibenzolar (6) + TX, acibenzolar-S-methyl (6) + TX, probenazole (658) and *Reynoutria sachalinensis* extract (alternative name) (720) + TX;

a rodenticide selected from the group of substances consisting of 2-isovalerylindan-1,3-dione (IUPAC name) (1246) + TX, 4-(quinoxalin-2-ylamino)benzenesulfonamide (IUPAC name) (748) + TX, alpha-chlorohydrin [CCN] + TX, aluminium phosphide (640) + TX, antu (880) + TX, arsenous oxide (882) + TX, barium carbonate (891) + TX, bisthiosemi (912) + TX, brodifacoum (89) + TX, bromadiolone (including alpha-bromadiolone) + TX, bromethalin (92) + TX, calcium cyanide (444) + TX, chloralose (127) + TX, chlorophacinone (140) + TX, cholecalciferol (alternative name) (850) + TX, coumachlor (1004) + TX, coumafuryl (1005) + TX, coumatetralyl (175) + TX, crimidine (1009) + TX, difenacoum (246) + TX, difethialone (249) + TX, diphacinone (273) + TX, ergocalciferol

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- (301) + TX, flocoumafen (357) + TX, fluoroacetamide (379) + TX, flupropadine (1183) + TX, flupropadine hydrochloride (1183) + TX, gamma-HCH (430) + TX, HCH (430) + TX, hydrogen cyanide (444) + TX, iodomethane (IUPAC name) (542) + TX, lindane (430) + TX, magnesium phosphide (IUPAC name) (640) + TX, methyl bromide (537) + TX, norbormide (1318) + TX,
- 5 phosacetim (1336) + TX, phosphine (IUPAC name) (640) + TX, phosphorus [CCN] + TX, pindone (1341) + TX, potassium arsenite [CCN] + TX, pyrinuron (1371) + TX, scilliroside (1390) + TX, sodium arsenite [CCN] + TX, sodium cyanide (444) + TX, sodium fluoroacetate (735) + TX, strychnine (745) + TX, thallium sulfate [CCN] + TX, warfarin (851) and zinc phosphide (640) + TX; a synergist selected from the group of substances consisting of 2-(2-butoxyethoxy)ethyl piperonylate
- 10 (IUPAC name) (934) + TX, 5-(1,3-benzodioxol-5-yl)-3-hexylcyclohex-2-enone (IUPAC name) (903) + TX, farnesol with nerolidol (alternative name) (324) + TX, MB-599 (development code) (498) + TX, MGK 264 (development code) (296) + TX, piperonyl butoxide (649) + TX, piprotal (1343) + TX, propyl isomer (1358) + TX, S421 (development code) (724) + TX, sesamex (1393) + TX, sesasmolin (1394) and sulfoxide (1406) + TX;
- 15 an animal repellent selected from the group of substances consisting of anthraquinone (32) + TX, chloralose (127) + TX, copper naphthenate [CCN] + TX, copper oxychloride (171) + TX, diazinon (227) + TX, dicyclopentadiene (chemical name) (1069) + TX, guazatine (422) + TX, guazatine acetates (422) + TX, methiocarb (530) + TX, pyridin-4-amine (IUPAC name) (23) + TX, thiram (804) + TX, trimethacarb (840) + TX, zinc naphthenate [CCN] and ziram (856) + TX;
- 20 a virucide selected from the group of substances consisting of imanin (alternative name) [CCN] and ribavirin (alternative name) [CCN] + TX;
- a wound protectant selected from the group of substances consisting of mercuric oxide (512) + TX, octhilinone (590) and thiophanate-methyl (802) + TX;
- a biologically active substance selected from 1,1-bis(4-chloro-phenyl)-2-ethoxyethanol + TX, 2,4-
- 25 dichlorophenyl benzenesulfonate + TX, 2-fluoro-N-methyl-N-1-naphthylacetamide + TX, 4-chlorophenyl phenyl sulfone + TX, acetoprole + TX, aldoxycarb + TX, amidithion + TX, amidothioate + TX, amiton + TX, amiton hydrogen oxalate + TX, amitraz + TX, aramite + TX, arsenous oxide + TX, azobenzene + TX, azothoate + TX, benomyl + TX, benoxa-fos + TX, benzyl benzoate + TX, bixafen + TX, brofenvalerate + TX, bromo-cyclen + TX, bromophos + TX, bromopropylate + TX, buprofezin + TX,
- 30 butocarboxim + TX, butoxycarboxim + TX, butylpyridaben + TX, calcium polysulfide + TX, camphechlor + TX, carbanolate + TX, carbophenothion + TX, cymiazole + TX, chino-methionat + TX, chlorbenside + TX, chlordimeform + TX, chlordimeform hydrochloride + TX, chlorfenethol + TX, chlorfenson + TX, chlorfensulfide + TX, chlorobenzilate + TX, chloromebuform + TX, chloromethiuron + TX, chloropropylate + TX, chlorthiophos + TX, cinerin I + TX, cinerin II + TX, cinerins + TX, closantel + TX,
- 35 coumaphos + TX, crotamiton + TX, crotoxyphos + TX, cufraneb + TX, cyanthoate + TX, DCPM + TX, DDT + TX, demephion + TX, demephion-O + TX, demephion-S + TX, demeton-methyl + TX, demeton-O + TX, demeton-O-methyl + TX, demeton-S + TX, demeton-S-methyl + TX, demeton-S-methylsulfon + TX, dichlofluanid + TX, dichlorvos + TX, dicliphos + TX, dienochlor + TX, dimefox + TX, dinex + TX, dinex-diclexine + TX, dinocap-4 + TX, dinocap-6 + TX, dinocron + TX, dino-penton + TX, dinosulfon +

TX, dinoterbon + TX, dioxathion + TX, diphenyl sulfone + TX, disulfiram + TX, DNOC + TX, dofenapyn + TX, doramectin + TX, endothion + TX, eprinomectin + TX, ethoate-methyl + TX, etrimfos + TX, fenazaflor + TX, fenbutatin oxide + TX, fenothiocarb + TX, fenpyrad + TX, fen-pyroximate + TX, fenpyrazamine + TX, fenson + TX, fentrifanil + TX, flubenzimine + TX, flucycloxuron + TX, fluenetil + TX, fluorbenside + TX, FMC 1137 + TX, formetanate + TX, formetanate hydrochloride + TX, formparanate + TX, gamma-HCH + TX, glyodin + TX, halfenprox + TX, hexadecyl cyclopropanecarboxylate + TX, isocarbophos + TX, jasmolin I + TX, jasmolin II + TX, jodfenphos + TX, lindane + TX, malonoben + TX, mecarbam + TX, mephosfolan + TX, mesulfen + TX, methacrifos + TX, methyl bromide + TX, metolcarb + TX, mexacarbate + TX, milbemycin oxime + TX, mipafox + TX, monocrotophos + TX, morphothion + TX, moxidectin + TX, naled + TX, 4-chloro-2-(2-chloro-2-methylpropyl)-5-[(6-iodo-3-pyridyl)methoxy]pyridazin-3-one + TX, nifluridide + TX, nikkomycins + TX, nitrilacarb + TX, nitrilacarb 1:1 zinc chloride complex + TX, omethoate + TX, oxydeprofos + TX, oxydisulfoton + TX, pp'-DDT + TX, parathion + TX, permethrin + TX, phenkapton + TX, phosalone + TX, phosfolan + TX, phosphamidon + TX, polychloroterpenes + TX, polynactins + TX, proclonol + TX, promacyl + TX, propoxur + TX, prothidathion + TX, prothoate + TX, pyrethrin I + TX, pyrethrin II + TX, pyrethrins + TX, pyridaphenthion + TX, pyrimitate + TX, quinalphos + TX, quintiofos + TX, R-1492 + TX, phosglycin + TX, rotenone + TX, schradan + TX, sebufos + TX, selamectin + TX, sophamide + TX, SSI-121 + TX, sulfiram + TX, sulfluramid + TX, sulfotep + TX, sulfur + TX, diflovidazin + TX, tau-fluvalinate + TX, TEPP + TX, terbam + TX, tetradifon + TX, tetrasul + TX, thiafenox + TX, thiocarboxime + TX, thiofanox + TX, thiometon + TX, thioquinox + TX, thuringiensin + TX, triamiphos + TX, triarathene + TX, triazophos + TX, triazuron + TX, trifenofos + TX, trinactin + TX, vamidothion + TX, vaniliprole + TX, bethoxazin + TX, copper dioctanoate + TX, copper sulfate + TX, cybutryne + TX, dichlone + TX, dichlorophen + TX, endothal + TX, fentin + TX, hydrated lime + TX, nabam + TX, quinoclamine + TX, quinonamid + TX, simazine + TX, triphenyltin acetate + TX, triphenyltin hydroxide + TX, crufomate + TX, piperazine + TX, thiophanate + TX, chloralose + TX, fenthion + TX, pyridin-4-amine + TX, strychnine + TX, 1-hydroxy-1H-pyridine-2-thione + TX, 4-(quinoxalin-2-ylamino)benzenesulfonamide + TX, 8-hydroxyquinoline sulfate + TX, bronopol + TX, copper hydroxide + TX, cresol + TX, dipyrithione + TX, dodicin + TX, fenaminosulf + TX, formaldehyde + TX, hydrargaphen + TX, kasugamycin + TX, kasugamycin hydrochloride hydrate + TX, nickel bis(dimethyldithiocarbamate) + TX, nitrapyrin + TX, octhilinone + TX, oxolinic acid + TX, oxytetracycline + TX, potassium hydroxyquinoline sulfate + TX, probenazole + TX, streptomycin + TX, streptomycin sesquisulfate + TX, tecloftalam + TX, thiomersal + TX, Adoxophyes orana GV + TX, Agrobacterium radiobacter + TX, Amblyseius spp. + TX, Anagrapta falcifera NPV + TX, Anagrus atomus + TX, Aphelinus abdominalis + TX, Aphidius colemani + TX, Aphidoletes aphidimyza + TX, Autographa californica NPV + TX, Bacillus sphaericus Neide + TX, Beauveria brongniartii + TX, Chrysoperla carnea + TX, Cryptolaemus montrouzieri + TX, Cydia pomonella GV + TX, Dacnusa sibirica + TX, Diglyphus isaea + TX, Encarsia formosa + TX, Eretmocerus eremicus + TX, Heterorhabditis bacteriophora and H. megidis + TX, Hippodamia convergens + TX, Leptomastix dactylopii + TX, Macrolophus caliginosus + TX, Mamestra brassicae NPV + TX, Metaphycus helvolus + TX, Metarhizium anisopliae var. acridum + TX, Metarhizium anisopliae var.

anisopliae + TX, Neodiprion sertifer NPV and *N. lecontei* NPV + TX, *Orius* spp. + TX, *Paecilomyces fumosoroseus* + TX, *Phytoseiulus persimilis* + TX, *Steinernema bibionis* + TX, *Steinernema carpocapsae* + TX, *Steinernema feltiae* + TX, *Steinernema glaseri* + TX, *Steinernema riobrave* + TX, *Steinernema riobrave* + TX, *Steinernema scapterisci* + TX, *Steinernema* spp. + TX, *Trichogramma* spp. + TX, *Typhlodromus occidentalis* + TX, *Verticillium lecanii* + TX, apholate + TX, bisazir + TX, busulfan + TX, dimatif + TX, hemel + TX, hempa + TX, metepa + TX, methiotepa + TX, methyl apholate + TX, morzid + TX, penfluron + TX, tepa + TX, thiohempa + TX, thiotepa + TX, tretamine + TX, uredepa + TX, (E)-dec-5-en-1-yl acetate with (E)-dec-5-en-1-ol + TX, (E)-tridec-4-en-1-yl acetate + TX, (E)-6-methylhept-2-en-4-ol + TX, (E,Z)-tetradeca-4,10-dien-1-yl acetate + TX, (Z)-dodec-7-en-1-yl acetate + TX, (Z)-hexadec-11-enal + TX, (Z)-hexadec-11-en-1-yl acetate + TX, (Z)-hexadec-13-en-11-yn-1-yl acetate + TX, (Z)-icos-13-en-10-one + TX, (Z)-tetradec-7-en-1-al + TX, (Z)-tetradec-9-en-1-ol + TX, (Z)-tetradec-9-en-1-yl acetate + TX, (7E,9Z)-dodeca-7,9-dien-1-yl acetate + TX, (9Z,11E)-tetradeca-9,11-dien-1-yl acetate + TX, (9Z,12E)-tetradeca-9,12-dien-1-yl acetate + TX, 14-methyloctadec-1-ene + TX, 4-methylnonan-5-ol with 4-methylnonan-5-one + TX, alpha-multistriatin + TX, brevicomin + TX, codlure + TX, codlemone + TX, cuelure + TX, disparlure + TX, dodec-8-en-1-yl acetate + TX, dodec-9-en-1-yl acetate + TX, dodeca-8 + TX, 10-dien-1-yl acetate + TX, dominicalure + TX, ethyl 4-methyloctanoate + TX, eugenol + TX, frontaline + TX, grandlure + TX, grandlure I + TX, grandlure II + TX, grandlure III + TX, grandlure IV + TX, hexalure + TX, ipsdienol + TX, ipsenol + TX, japonilure + TX, lineatin + TX, litlure + TX, looplure + TX, medlure + TX, megatomoic acid + TX, methyl eugenol + TX, muscalure + TX, octadeca-2,13-dien-1-yl acetate + TX, octadeca-3,13-dien-1-yl acetate + TX, orfralure + TX, oryctalure + TX, ostramone + TX, siglure + TX, sordidin + TX, sulcatol + TX, tetradec-11-en-1-yl acetate + TX, trimedlure + TX, trimedlure A + TX, trimedlure B₁ + TX, trimedlure B₂ + TX, trimedlure C + TX, trunc-call + TX, 2-(octylthio)-ethanol + TX, butopyronoxyl + TX, butoxy(polypropylene glycol) + TX, dibutyl adipate + TX, dibutyl phthalate + TX, dibutyl succinate + TX, diethyltoluamide + TX, dimethyl carbamate + TX, dimethyl phthalate + TX, ethyl hexanediol + TX, hexamide + TX, methoquin-butyl + TX, methylneodecanamide + TX, oxamate + TX, picaridin + TX, 1-dichloro-1-nitroethane + TX, 1,1-dichloro-2,2-bis(4-ethylphenyl)-ethane + TX, 1,2-dichloropropane with 1,3-dichloropropene + TX, 1-bromo-2-chloroethane + TX, 2,2,2-trichloro-1-(3,4-dichloro-phenyl)ethyl acetate + TX, 2,2-dichlorovinyl 2-ethylsulfinyloxyethyl methyl phosphate + TX, 2-(1,3-dithiolan-2-yl)phenyl dimethylcarbamate + TX, 2-(2-butoxyethoxy)ethyl thiocyanate + TX, 2-(4,5-dimethyl-1,3-dioxolan-2-yl)phenyl methylcarbamate + TX, 2-(4-chloro-3,5-xylyloxy)ethanol + TX, 2-chlorovinyl diethyl phosphate + TX, 2-imidazolidone + TX, 2-isovalerylindan-1,3-dione + TX, 2-methyl(prop-2-ynyl)aminophenyl methylcarbamate + TX, 2-thiocyanatoethyl laurate + TX, 3-bromo-1-chloroprop-1-ene + TX, 3-methyl-1-phenylpyrazol-5-yl dimethyl-carbamate + TX, 4-methyl(prop-2-ynyl)amino-3,5-xylyl methylcarbamate + TX, 5,5-dimethyl-3-oxocyclohex-1-enyl dimethylcarbamate + TX, acethion + TX, acrylonitrile + TX, aldrin + TX, allosamidin + TX, allyxycarb + TX, alpha-ecdysone + TX, aluminium phosphide + TX, aminocarb + TX, anabasine + TX, athidathion + TX, azamethiphos + TX, *Bacillus thuringiensis* delta endotoxins + TX, barium hexafluorosilicate + TX, barium polysulfide + TX, barthrin + TX, Bayer 22/190 + TX, Bayer 22408 + TX, beta-cyfluthrin + TX, beta-cypermethrin + TX, bioethanomethrin + TX, biopermethrin + TX, bis(2-

chloroethyl) ether + TX, borax + TX, bromfeninfos + TX, bromo-DDT + TX, bufencarb + TX, butacarb + TX, butathiofos + TX, butonate + TX, calcium arsenate + TX, calcium cyanide + TX, carbon disulfide + TX, carbon tetrachloride + TX, cartap hydrochloride + TX, cevadine + TX, chlorbicyclen + TX, chlordane + TX, chlordecone + TX, chloroform + TX, chloropicrin + TX, chlorphoxim + TX, 5 chlorprazophos + TX, cis-resmethrin + TX, cismethrin + TX, clocythrins + TX, copper acetoarsenite + TX, copper arsenate + TX, copper oleate + TX, coumthioate + TX, cryolite + TX, CS 708 + TX, cyanofenphos + TX, cyanophos + TX, cyclothrin + TX, cythioate + TX, d-tetramethrin + TX, DAEP + TX, dazomet + TX, decarbofuran + TX, diamidafos + TX, dicapthon + TX, dichlofenthion + TX, dicresyl + TX, dicyclanil + TX, dieldrin + TX, diethyl 5-methylpyrazol-3-yl phosphate + TX, dilor + TX, dimefluthrin + TX, dimetan + TX, dimethrin + TX, dimethylvinphos + TX, dimetilan + TX, dinoprop + TX, dinosam + TX, dinoseb + TX, diofenolan + TX, dioxabenzofos + TX, dithicrofos + TX, DSP + TX, ecdysterone + TX, EI 1642 + TX, EMPC + TX, EPBP + TX, etaphos + TX, ethiofencarb + TX, ethyl formate + TX, ethylene dibromide + TX, ethylene dichloride + TX, ethylene oxide + TX, EXD + TX, fenchlorphos + TX, fenethacarb + TX, fenitrothion + TX, fenoxacrim + TX, fenpirithrin + TX, fensulfothion + TX, fenthion-ethyl + TX, flucufuron + TX, fosmethilan + TX, fospirate + TX, fosthietan + TX, furathiocarb + TX, furethrin + TX, guazatine + TX, guazatine acetates + TX, sodium tetrathiocarbonate + TX, halfenprox + TX, HCH + TX, HEOD + TX, heptachlor + TX, heterophos + TX, HHDN + TX, hydrogen cyanide + TX, hyquincarb + TX, IPSP + TX, isazofos + TX, isobenzan + TX, isodrin + TX, isofenphos + TX, isolane + TX, isoprothiolane + TX, isoxathion + TX, juvenile hormone I + TX, juvenile hormone II + TX, juvenile hormone III + TX, kelevan + TX, kinoprene + TX, lead arsenate + TX, leptophos + TX, lirimfos + TX, lythidathion + TX, m-cumenyl methylcarbamate + TX, magnesium phosphide + TX, mazidox + TX, mecarphon + TX, menazon + TX, mercurous chloride + TX, mesulfenfos + TX, metam + TX, metam-potassium + TX, metam-sodium + TX, methanesulfonyl fluoride + TX, methocrotophos + TX, methoprene + TX, methothrin + TX, methoxychlor + TX, methyl isothiocyanate + TX, methylchloroform + TX, methylene chloride + TX, 25 metoxadiazone + TX, mirex + TX, naftalofos + TX, naphthalene + TX, NC-170 + TX, nicotine + TX, nicotine sulfate + TX, nithiazine + TX, norm nicotine + TX, O-5-dichloro-4-iodophenyl O-ethyl ethylphosphonothioate + TX, O,O-diethyl O-4-methyl-2-oxo-2H-chromen-7-yl phosphorothioate + TX, O,O-diethyl O-6-methyl-2-propylpyrimidin-4-yl phosphorothioate + TX, O,O,O',O'-tetrapropyl dithiopyrophosphate + TX, oleic acid + TX, para-dichlorobenzene + TX, parathion-methyl + TX, 30 pentachlorophenol + TX, pentachlorophenyl laurate + TX, PH 60-38 + TX, phenkapton + TX, phosnichlor + TX, phosphine + TX, phoxim-methyl + TX, pirimetaphos + TX, polychlorodicyclopentadiene isomers + TX, potassium arsenite + TX, potassium thiocyanate + TX, precocene I + TX, precocene II + TX, precocene III + TX, primidophos + TX, profluthrin + TX, promecarb + TX, prothiofos + TX, pyrazophos + TX, pyresmethrin + TX, quassia + TX, quinalphos-methyl + TX, quinothion + TX, rafoxanide + TX, 35 resmethrin + TX, rotenone + TX, kadethrin + TX, ryania + TX, ryanodine + TX, sabadilla) + TX, schradan + TX, sebufos + TX, SI-0009 + TX, thiapronil + TX, sodium arsenite + TX, sodium cyanide + TX, sodium fluoride + TX, sodium hexafluorosilicate + TX, sodium pentachlorophenoxide + TX, sodium selenate + TX, sodium thiocyanate + TX, sulcofuron + TX, sulcofuron-sodium + TX, sulfuryl fluoride + TX, sulprofos + TX, tar oils + TX, tazimcarb + TX, TDE + TX, tebupirimfos + TX, temephos + TX, terallethrin + TX,

tetrachloroethane + TX, thicrofos + TX, thiocyclam + TX, thiocyclam hydrogen oxalate + TX, thionazin + TX, thiosultap + TX, thiosultap-sodium + TX, tralomethrin + TX, transpermethrin + TX, triazamate + TX, trichlormetaphos-3 + TX, trichloronat + TX, trimethacarb + TX, tolprocarb + TX, triclopyricarb + TX, triprene + TX, veratridine + TX, veratrine + TX, XMC + TX, zetamethrin + TX, zinc phosphide + TX,

5 zolaprofos + TX, and meperfluthrin + TX, tetramethylfluthrin + TX, bis(tributyltin) oxide + TX, bromoacetamide + TX, ferric phosphate + TX, niclosamide-olamine + TX, tributyltin oxide + TX, pyrimorph + TX, trifenmorph + TX, 1,2-dibromo-3-chloropropane + TX, 1,3-dichloropropene + TX, 3,4-dichlorotetrahydrothio-phenene 1,1-dioxide + TX, 3-(4-chlorophenyl)-5-methylrhodanine + TX, 5-methyl-6-thioxo-1,3,5-thiadiazinan-3-ylacetic acid + TX, 6-isopentenylaminopurine + TX, anisiflupurin + TX,

10 benclothiaz + TX, cytokinins + TX, DCIP + TX, furfural + TX, isamidofos + TX, kinetin + TX, Myrothecium verrucaria composition + TX, tetrachlorothiophene + TX, xylenols + TX, zeatin + TX, potassium ethylxanthate + TX, acibenzolar + TX, acibenzolar-S-methyl + TX, Reynoutria sachalinensis extract + TX, alpha-chlorohydrin + TX, antu + TX, barium carbonate + TX, bisthiosemi + TX, brodifacoum + TX, bromadiolone + TX, bromethalin + TX, chlorophacinone + TX, cholecalciferol + TX, coumachlor + TX,

15 coumafuryl + TX, coumatetralyl + TX, crimidine + TX, difenacoum + TX, difethialone + TX, diphacinone + TX, ergocalciferol + TX, flocoumafen + TX, fluoroacetamide + TX, flupropadine + TX, flupropadine hydrochloride + TX, norbormide + TX, phosacetim + TX, phosphorus + TX, pindone + TX, pyrinuron + TX, scilliroside + TX, -sodium fluoroacetate + TX, thallium sulfate + TX, warfarin + TX, -2-(2-butoxyethoxy)ethyl piperonylate + TX, 5-(1,3-benzodioxol-5-yl)-3-hexylcyclohex-2-enone + TX, farnesol

20 with nerolidol + TX, verbutin + TX, MGK 264 + TX, piperonyl butoxide + TX, piprotal + TX, propyl isomer + TX, S421 + TX, sesamex + TX, sesasmolin + TX, sulfoxide + TX, anthraquinone + TX, copper naphthenate + TX, copper oxychloride + TX, dicyclopentadiene + TX, thiram + TX, zinc naphthenate + TX, ziram + TX, imanin + TX, ribavirin + TX, chloroinconazide + TX, mercuric oxide + TX, thiophanate-methyl + TX, azaconazole + TX, bitertanol + TX, bromuconazole + TX, cyproconazole + TX,

25 difenoconazole + TX, diniconazole + TX, epoxiconazole + TX, fenbuconazole + TX, fluquinconazole + TX, flusilazole + TX, flutriafol + TX, furametpyr + TX, hexaconazole + TX, imazalil- + TX, imiben-conazole + TX, ipconazole + TX, metconazole + TX, myclobutanil + TX, paclobutrazole + TX, pefurazoate + TX, penconazole + TX, prothioconazole + TX, pyrifenox + TX, prochloraz + TX, propiconazole + TX, pyrisoxazole + TX, -simeconazole + TX, tebuconazole + TX, tetraconazole + TX,

30 triadimefon + TX, triadimenol + TX, triflumizole + TX, triticonazole + TX, ancymidol + TX, fenarimol + TX, nuarimol + TX, bupirimate + TX, dimethirimol + TX, ethirimol + TX, dodemorph + TX, fenpropidin + TX, fenpropimorph + TX, spiroxamine + TX, tridemorph + TX, cyprodinil + TX, mepanipyrim + TX, pyrimethanil + TX, fenpiclonil + TX, fludioxonil + TX, benalaxyl + TX, furalaxyl + TX, -metalaxyl + TX, Rmetalaxyl + TX, ofurace + TX, oxadixyl + TX, carbendazim + TX, debacarb + TX, fuberidazole + TX,

35 thiabendazole + TX, chlozolinate + TX, dichlozoline + TX, myclozoline- + TX, procymidone + TX, vinclozoline + TX, boscalid + TX, carboxin + TX, fenfuram + TX, flutolanil + TX, mepronil + TX, oxycarboxin + TX, penthiopyrad + TX, thifluzamide + TX, dodine + TX, iminoctadine + TX, azoxystrobin + TX, dimoxystrobin + TX, enestroburin + TX, fenaminstrobin + TX, flufenoxystrobin + TX, fluoxastrobin + TX, kresoxim--methyl + TX, metominostrobin + TX, trifloxystrobin + TX, orysastrobin + TX,

picoxystrobin + TX, pyraclostrobin + TX, pyrametostrobin + TX, pyraoxystrobin + TX, ferbam + TX, mancozeb + TX, maneb + TX, metiram + TX, propineb + TX, zineb + TX, captafol + TX, captan + TX, fluoroimide + TX, folpet + TX, tolylfluanid + TX, bordeaux mixture + TX, copper oxide + TX, mancopper + TX, oxine-copper + TX, nitrothal-isopropyl + TX, edifenphos + TX, iprobenphos + TX, phosdiphen + TX, tolclofos-methyl + TX, anilazine + TX, benthiavalicarb + TX, blasticidin-S + TX, chloroneb + TX, chloro-tha-lonil + TX, cyflufenamid + TX, cymoxanil + TX, cyclobutrifluram + TX, diclocymet + TX, diclomezine + TX, dicloran + TX, diethofencarb + TX, dimethomorph + TX, flumorph + TX, dithianon + TX, ethaboxam + TX, etridiazole + TX, famoxadone + TX, fenamidone + TX, fenoxanil + TX, ferimzone + TX, fluazinam + TX, flumetylsulforim + TX, fluopicolide + TX, fluoxytioconazole + TX, flusulfamide + TX, fluxapyroxad + TX, -fenhexamid + TX, fosetyl-aluminium + TX, hymexazol + TX, iprovalicarb + TX, cyazofamid + TX, methasulfocarb + TX, metrafenone + TX, pencycuron + TX, phthalide + TX, polyoxins + TX, propamocarb + TX, pyribencarb + TX, proquinazid + TX, pyroquilon + TX, pyriofenone + TX, quinoxifen + TX, quintozone + TX, tiadinil + TX, triazoxide + TX, tricyclazole + TX, triforine + TX, validamycin + TX, valifenalate + TX, zoxamide + TX, mandipropamid + TX, flubeneteram + TX, isopyrazam + TX, sedaxane + TX, benzovindiflupyr + TX, pydiflumetofen + TX, 3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid (3',4',5'-trifluoro-biphenyl-2-yl)-amide + TX, isoflucypram + TX, isotianil + TX, dipymetitron + TX, 6-ethyl-5,7-dioxo-pyrrolo[4,5][1,4]dithiino[1,2-c]isothiazole-3-carbonitrile + TX, 2-(difluoromethyl)-N-[3-ethyl-1,1-dimethyl-indan-4-yl]pyridine-3-carboxamide + TX, 4-(2,6-difluorophenyl)-6-methyl-5-phenyl-pyridazine-3-carbonitrile + TX, (R)-3-(difluoromethyl)-1-methyl-N-[1,1,3-trimethylindan-4-yl]pyrazole-4-carboxamide + TX, 4-(2-bromo-4-fluoro-phenyl)-N-(2-chloro-6-fluoro-phenyl)-2,5-dimethyl-pyrazol-3-amine + TX, 4-(2-bromo-4-fluorophenyl)-N-(2-chloro-6-fluorophenyl)-1,3-dimethyl-1H-pyrazol-5-amine + TX, fluindapyr + TX, coumethoxystrobin (jiaxiangjunzhi) + TX, lvbenmixianan + TX, dichlobentiazox + TX, mandestrobin + TX, 3-(4,4-difluoro-3,4-dihydro-3,3-dimethylisoquinolin-1-yl)quinolone + TX, 2-[2-fluoro-6-[(8-fluoro-2-methyl-3-quinolyl)oxy]phenyl]propan-2-ol + TX, oxathiapiroline + TX, tert-butyl N-[6-[[[(1-methyltetrazol-5-yl)-phenyl-methylene]amino]oxymethyl]-2-pyridyl]carbamate + TX, pyraziflumid + TX, inpyrfluxam + TX, troprocarb + TX, mefentrifluconazole + TX, ipfentrifluconazole + TX, 2-(difluoromethyl)-N-[(3R)-3-ethyl-1,1-dimethyl-indan-4-yl]pyridine-3-carboxamide + TX, N'-(2,5-dimethyl-4-phenoxy-phenyl)-N-ethyl-N-methyl-formamidine + TX, N'-[4-(4,5-dichlorothiazol-2-yl)oxy-2,5-dimethyl-phenyl]-N-ethyl-N-methyl-formamidine + TX, [2-[3-[2-[1-[2-[3,5-bis(difluoromethyl)pyrazol-1-yl]acetyl]-4-piperidyl]thiazol-4-yl]-4,5-dihydroisoxazol-5-yl]-3-chloro-phenyl]methanesulfonate + TX, but-3-ynyl N-[6-[(Z)-[(1-methyltetrazol-5-yl)-phenyl-methylene]amino]oxymethyl]-2-pyridyl]carbamate + TX, methyl N-[[5-[4-(2,4-dimethylphenyl)triazol-2-yl]-2-methyl-phenyl]methyl]carbamate + TX, 3-chloro-6-methyl-5-phenyl-4-(2,4,6-trifluorophenyl)pyridazine + TX, pyridachlometyl + TX, 3-(difluoromethyl)-1-methyl-N-[1,1,3-trimethylindan-4-yl]pyrazole-4-carboxamide + TX, 1-[2-[[1-(4-chlorophenyl)pyrazol-3-yl]oxymethyl]-3-methyl-phenyl]-4-methyl-tetrazol-5-one + TX, 1-methyl-4-[3-methyl-2-[[2-methyl-4-(3,4,5-trimethylpyrazol-1-yl)phenoxy]methyl]phenyl]tetrazol-5-one + TX, aminopyrifen + TX, ametoctradin + TX, amisulbrom + TX, penflufen + TX, (Z,2E)-5-[1-(4-chlorophenyl)pyrazol-3-yl]oxy-2-methoxyimino-N,3-dimethyl-pent-3-enamide + TX, florylpicoxamid + TX, fenpicoxamid + TX, metarylpicoxamid + TX,

tebufloquin + TX, ipflufenquin + TX, quinofumelin + TX, isofetamid + TX, N-[2-[2,4-dichlorophenoxy]phenyl]-3-(difluoromethyl)-1-methyl-pyrazole-4-carboxamide + TX, N-[2-[2-chloro-4-(trifluoromethyl)phenoxy]phenyl]-3-(difluoromethyl)-1-methyl-pyrazole-4-carboxamide + TX, benzoithiostrobin + TX, phenamacril + TX, 5-amino-1,3,4-thiadiazole-2-thiol zinc salt (2:1) + TX, fluopyram + TX, flufenoxadiazam + TX, flutianil + TX, fluopimomide + TX, pyrapropoyne + TX, picarbutrazox + TX, 2-(difluoromethyl)-N-(3-ethyl-1,1-dimethyl-indan-4-yl)pyridine-3-carboxamide + TX, 2-(difluoromethyl)-N-((3R)-1,1,3-trimethylindan-4-yl)pyridine-3-carboxamide + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(1,2,4-triazol-1-yl)propyl]-3-pyridyl]oxy]benzonitrile + TX, metyltetraprole + TX, 2-(difluoromethyl)-N-((3R)-1,1,3-trimethylindan-4-yl)pyridine-3-carboxamide + TX, α -(1,1-dimethylethyl)- α -[4'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]-5-pyrimidinemethanol + TX, fluoxapiprolin + TX, enoxastrobin + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(1,2,4-triazol-1-yl)propyl]-3-pyridyl]oxy]benzonitrile + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(5-sulfanyl-1,2,4-triazol-1-yl)propyl]-3-pyridyl]oxy]benzonitrile + TX, 4-[[6-[2-(2,4-difluorophenyl)-1,1-difluoro-2-hydroxy-3-(5-thioxo-4H-1,2,4-triazol-1-yl)propyl]-3-pyridyl]oxy]benzonitrile + TX, trinexapac + TX, coumoxystrobin + TX, zhongshengmycin + TX, thiodiazole copper + TX, zinc thiazole + TX, amectotractin + TX, iprodione + TX, seboctylamine + TX; N'-[5-bromo-2-methyl-6-[(1S)-1-methyl-2-propoxy-ethoxy]-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-bromo-2-methyl-6-[(1R)-1-methyl-2-propoxy-ethoxy]-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-bromo-2-methyl-6-(1-methyl-2-propoxy-ethoxy)-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-chloro-2-methyl-6-(1-methyl-2-propoxy-ethoxy)-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX, N'-[5-bromo-2-methyl-6-(1-methyl-2-propoxy-ethoxy)-3-pyridyl]-N-isopropyl-N-methyl-formamidine + TX (these compounds may be prepared from the methods described in WO2015/155075); N'-[5-bromo-2-methyl-6-(2-propoxypropoxy)-3-pyridyl]-N-ethyl-N-methyl-formamidine + TX (this compound may be prepared from the methods described in IPCOM000249876D); N-isopropyl-N'-[5-methoxy-2-methyl-4-(2,2,2-trifluoro-1-hydroxy-1-phenyl-ethyl)phenyl]-N-methyl-formamidine + TX, N'-[4-(1-cyclopropyl-2,2,2-trifluoro-1-hydroxy-ethyl)-5-methoxy-2-methyl-phenyl]-N-isopropyl-N-methyl-formamidine + TX (these compounds may be prepared from the methods described in WO2018/228896); N-ethyl-N'-[5-methoxy-2-methyl-4-[(2-trifluoromethyl)oxetan-2-yl]phenyl]-N-methyl-formamidine + TX, N-ethyl-N'-[5-methoxy-2-methyl-4-[(2-trifluoromethyl)tetrahydrofuran-2-yl]phenyl]-N-methyl-formamidine + TX (these compounds may be prepared from the methods described in WO2019/110427); N-[(1R)-1-benzyl-3-chloro-1-methyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-3-chloro-1-methyl-but-3-enyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1R)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-3,3,3-trifluoro-1-methyl-propyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-7,8-difluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-1,3-dimethyl-butyl]-7,8-difluoro-quinoline-3-carboxamide + TX, 8-fluoro-N-[(1R)-1-[(3-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide + TX, 8-fluoro-N-[(1S)-1-[(3-fluorophenyl)methyl]-1,3-dimethyl-butyl]quinoline-3-carboxamide + TX, N-[(1R)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide + TX, N-[(1S)-1-benzyl-1,3-dimethyl-butyl]-8-fluoro-quinoline-3-carboxamide + TX, N-((1R)-1-benzyl-3-chloro-1-

methyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide + TX, N-((1S)-1-benzyl-3-chloro-1-methyl-but-3-enyl)-8-fluoro-quinoline-3-carboxamide + TX (these compounds may be prepared from the methods described in WO2017/153380);

1-(6,7-dimethylpyrazolo[1,5-a]pyridin-3-yl)-4,4,5-trifluoro-3,3-dimethyl-isoquinoline + TX, 1-(6,7-dimethylpyrazolo[1,5-a]pyridin-3-yl)-4,4,6-trifluoro-3,3-dimethyl-isoquinoline + TX, 4,4-difluoro-3,3-dimethyl-1-(6-methylpyrazolo[1,5-a]pyridin-3-yl)isoquinoline + TX, 4,4-difluoro-3,3-dimethyl-1-(7-methylpyrazolo[1,5-a]pyridin-3-yl)isoquinoline + TX, 1-(6-chloro-7-methyl-pyrazolo[1,5-a]pyridin-3-yl)-4,4-difluoro-3,3-dimethyl-isoquinoline + TX (these compounds may be prepared from the methods described in WO2017/025510);

1-(4,5-dimethylbenzimidazol-1-yl)-4,4,5-trifluoro-3,3-dimethyl-isoquinoline + TX, 1-(4,5-dimethylbenzimidazol-1-yl)-4,4-difluoro-3,3-dimethyl-isoquinoline + TX, 6-chloro-4,4-difluoro-3,3-dimethyl-1-(4-methylbenzimidazol-1-yl)isoquinoline + TX, 4,4-difluoro-1-(5-fluoro-4-methyl-benzimidazol-1-yl)-3,3-dimethyl-isoquinoline + TX, 3-(4,4-difluoro-3,3-dimethyl-1-isoquinolyl)-7,8-dihydro-6H-cyclopenta[e]benzimidazole + TX (these compounds may be prepared from the methods described in WO2016/156085);

N-methoxy-N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]cyclopropanecarboxamide + TX, N,2-dimethoxy-N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]propanamide + TX, N-ethyl-2-methyl-N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]propanamide + TX, 1-methoxy-3-methyl-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]urea + TX, 1,3-dimethoxy-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]urea + TX, 3-ethyl-1-methoxy-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]urea + TX, N-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]propanamide + TX, 4,4-dimethyl-2-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]isoxazolidin-3-one + TX, 5,5-dimethyl-2-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]isoxazolidin-3-one + TX, ethyl 1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]pyrazole-4-carboxylate + TX, N,N-dimethyl-1-[[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methyl]-1,2,4-triazol-3-amine + TX. The

compounds in this paragraph may be prepared from the methods described in WO 2017/055473, WO 2017/055469, WO 2017/093348 and WO 2017/118689; 2-[6-(4-chlorophenoxy)-2-(trifluoromethyl)-3-pyridyl]-1-(1,2,4-triazol-1-yl)propan-2-ol + TX (this compound may be prepared from the methods described in WO 2017/029179); 2-[6-(4-bromophenoxy)-2-(trifluoromethyl)-3-pyridyl]-1-(1,2,4-triazol-1-yl)propan-2-ol + TX (this compound may be prepared from the methods described in WO 2017/029179);

3-[2-(1-chlorocyclopropyl)-3-(2-fluorophenyl)-2-hydroxy-propyl]imidazole-4-carbonitrile + TX (this compound may be prepared from the methods described in WO 2016/156290); 3-[2-(1-chlorocyclopropyl)-3-(3-chloro-2-fluoro-phenyl)-2-hydroxy-propyl]imidazole-4-carbonitrile + TX (this compound may be prepared from the methods described in WO 2016/156290);

(4-phenoxyphenyl)methyl 2-amino-6-methyl-pyridine-3-carboxylate + TX (this compound may be prepared from the methods described in WO 2014/006945); 2,6-Dimethyl-1H,5H-[1,4]dithiino[2,3-c:5,6-c']dipyrrole-1,3,5,7(2H,6H)-tetrone + TX (this compound may be prepared from the methods described in WO 2011/138281); N-methyl-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzenecarbothioamide + TX; N-methyl-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX; (Z,E)-5-[1-(2,4-dichlorophenyl)pyrazol-3-yl]oxy-2-methoxyimino-N,3-dimethyl-pent-3-enamide + TX (this compound

may be prepared from the methods described in WO 2018/153707); N'-(2-chloro-5-methyl-4-phenoxy-phenyl)-N-ethyl-N-methyl-formamidine + TX; N'-[2-chloro-4-(2-fluorophenoxy)-5-methyl-phenyl]-N-ethyl-N-methyl-formamidine + TX (this compound may be prepared from the methods described in WO 2016/202742); 2-(difluoromethyl)-N-[(3S)-3-ethyl-1,1-dimethyl-indan-4-yl]pyridine-3-carboxamide + TX
 5 (this compound may be prepared from the methods described in WO 2014/095675); (5-methyl-2-pyridyl)-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methanone + TX, (3-methylisoxazol-5-yl)-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]methanone + TX (these compounds may be prepared from the methods described in WO 2017/220485); 2-oxo-N-propyl-2-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]acetamide + TX (this compound may be prepared from the methods described in
 10 WO 2018/065414); ethyl 1-[[5-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-2-thienyl]methyl]pyrazole-4-carboxylate + TX (this compound may be prepared from the methods described in WO 2018/158365); 2,2-difluoro-N-methyl-2-[4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]phenyl]acetamide + TX, N-[(E)-methoxyiminomethyl]-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX, N-[(Z)-methoxyiminomethyl]-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX, N-[N-methoxy-C-
 15 methyl-carbonimidoyl]-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]benzamide + TX (these compounds may be prepared from the methods described in WO 2018/202428);
 microbials including: *Acinetobacter lwoffii* + TX, *Acremonium alternatum* + TX + TX, *Acremonium cephalosporium* + TX + TX, *Acremonium diospyri* + TX, *Acremonium obclavatum* + TX, *Adoxophyes orana granulovirus* (AdoxGV) (Capex®) + TX, *Agrobacterium radiobacter* strain K84 (Galltrol-A®) + TX,
 20 *Alternaria alternate* + TX, *Alternaria cassia* + TX, *Alternaria destruens* (Smolder®) + TX, *Ampelomyces quisqualis* (AQ10®) + TX, *Aspergillus flavus* AF36 (AF36®) + TX, *Aspergillus flavus* NRRL 21882 (Aflaguard®) + TX, *Aspergillus* spp. + TX, *Aureobasidium pullulans* + TX, *Azospirillum* + TX, (MicroAZ® + TX, TAZO B®) + TX, *Azotobacter* + TX, *Azotobacter chroococcum* (Azotomeal®) + TX, *Azotobacter* cysts (Bionatural Blooming Blossoms®) + TX, *Bacillus amyloliquefaciens* + TX, *Bacillus cereus* + TX,
 25 *Bacillus chitinosporus* strain CM-1 + TX, *Bacillus chitinosporus* strain AQ746 + TX, *Bacillus licheniformis* strain HB-2 (Biostart™ Rhizoboost®) + TX, *Bacillus licheniformis* strain 3086 (EcoGuard® + TX, Green Releaf®) + TX, *Bacillus circulans* + TX, *Bacillus firmus* (BioSafe® + TX, BioNem-WP® + TX, VOTIVO®) + TX, *Bacillus firmus* strain I-1582 + TX, *Bacillus macerans* + TX, *Bacillus marismortui* + TX, *Bacillus megaterium* + TX, *Bacillus mycoides* strain AQ726 + TX, *Bacillus papillae* (Milky Spore Powder®) + TX,
 30 *Bacillus pumilus* spp. + TX, *Bacillus pumilus* strain GB34 (Yield Shield®) + TX, *Bacillus pumilus* strain AQ717 + TX, *Bacillus pumilus* strain QST 2808 (Sonata® + TX, Ballad Plus®) + TX, *Bacillus spahericus* (VectoLex®) + TX, *Bacillus* spp. + TX, *Bacillus* spp. strain AQ175 + TX, *Bacillus* spp. strain AQ177 + TX, *Bacillus* spp. strain AQ178 + TX, *Bacillus subtilis* strain QST 713 (CEASE® + TX, Serenade® + TX, Rhapsody®) + TX, *Bacillus subtilis* strain QST 714 (JAZZ®) + TX, *Bacillus subtilis* strain AQ153 + TX,
 35 *Bacillus subtilis* strain AQ743 + TX, *Bacillus subtilis* strain QST3002 + TX, *Bacillus subtilis* strain QST3004 + TX, *Bacillus subtilis* var. *amyloliquefaciens* strain FZB24 (Taegro® + TX, Rhizopro®) + TX, *Bacillus thuringiensis* Cry 2Ae + TX, *Bacillus thuringiensis* Cry1Ab + TX, *Bacillus thuringiensis aizawai* GC 91 (Agree®) + TX, *Bacillus thuringiensis israelensis* (BMP123® + TX, Aquabac® + TX, VectoBac®) + TX, *Bacillus thuringiensis kurstaki* (Javelin® + TX, Deliver® + TX, CryMax® + TX, Bonide® + TX,

Scutella WP® + TX, Turilav WP® + TX, Astuto® + TX, Dipel WP® + TX, Biobit® + TX, Foray® + TX, *Bacillus thuringiensis kurstaki* BMP 123 (Baritone®) + TX, *Bacillus thuringiensis kurstaki* HD-1 (Bioprotec-CAF / 3P®) + TX, *Bacillus thuringiensis* strain BD#32 + TX, *Bacillus thuringiensis* strain AQ52 + TX, *Bacillus thuringiensis* var. *aizawai* (XenTari® + TX, DiPel®) + TX, bacteria spp. (GROWMEND® + TX, GROWSWEET® + TX, Shootup®) + TX, bacteriophage of *Clavipacter michiganensis* (AgriPhage®) + TX, Bakflor® + TX, *Beauveria bassiana* (Beaugenic® + TX, Brocaril WP®) + TX, *Beauveria bassiana* GHA (Mycotrol ES® + TX, Mycotrol O® + TX, BotaniGuard®) + TX, *Beauveria brongniartii* (Engerlingspilz® + TX, Schweizer Beauveria® + TX, Melocont®) + TX, *Beauveria* spp. + TX, *Botrytis cinerea* + TX, *Bradyrhizobium japonicum* (TerraMax®) + TX, *Brevibacillus brevis* + TX, *Bacillus thuringiensis tenebrionis* (Novodor®) + TX, BtBooster + TX, *Burkholderia cepacia* (Deny® + TX, Intercept® + TX, Blue Circle®) + TX, *Burkholderia gladii* + TX, *Burkholderia gladioli* + TX, *Burkholderia* spp. + TX, Canadian thistle fungus (CBH Canadian Bioherbicide®) + TX, *Candida butyri* + TX, *Candida famata* + TX, *Candida fructus* + TX, *Candida glabrata* + TX, *Candida guilliermondii* + TX, *Candida melibiosica* + TX, *Candida oleophila* strain O + TX, *Candida parapsilosis* + TX, *Candida pelliculosa* + TX, *Candida pulcherrima* + TX, *Candida reukaufii* + TX, *Candida saitoana* (Bio-Coat® + TX, Biocure®) + TX, *Candida sake* + TX, *Candida* spp. + TX, *Candida tenuis* + TX, *Cedecea dravisae* + TX, *Cellulomonas flavigena* + TX, *Chaetomium cochliodes* (Nova-Cide®) + TX, *Chaetomium globosum* (Nova-Cide®) + TX, *Chromobacterium subtsugae* strain PRAA4-1T (Grandevo®) + TX, *Cladosporium cladosporioides* + TX, *Cladosporium oxysporum* + TX, *Cladosporium chlorocephalum* + TX, *Cladosporium* spp. + TX, *Cladosporium tenuissimum* + TX, *Clonostachys rosea* (EndoFine®) + TX, *Colletotrichum acutatum* + TX, *Coniothyrium minitans* (Cotans WG®) + TX, *Coniothyrium* spp. + TX, *Cryptococcus albidus* (YIELDPLUS®) + TX, *Cryptococcus humicola* + TX, *Cryptococcus infirmominiatus* + TX, *Cryptococcus laurentii* + TX, *Cryptophlebia leucotreta granulovirus* (Cryptex®) + TX, *Cupriavidus campinensis* + TX, *Cydia pomonella granulovirus* (CYD-X®) + TX, *Cydia pomonella granulovirus* (Madex® + TX, Madex Plus® + TX, Madex Max/ Carpovirusine®) + TX, *Cylindrobasidium laeve* (Stumpout®) + TX, *Cylindrocladium* + TX, *Debaryomyces hansenii* + TX, *Drechslera hawaiiensis* + TX, *Enterobacter cloacae* + TX, *Enterobacteriaceae* + TX, *Entomophthora virulenta* (Vektor®) + TX, *Epicoccum nigrum* + TX, *Epicoccum purpurascens* + TX, *Epicoccum* spp. + TX, *Filobasidium floriforme* + TX, *Fusarium acuminatum* + TX, *Fusarium chlamydosporum* + TX, *Fusarium oxysporum* (Fusaclean® / Biofox C®) + TX, *Fusarium proliferatum* + TX, *Fusarium* spp. + TX, *Galactomyces geotrichum* + TX, *Gliocladium catenulatum* (Primastop® + TX, Prestop®) + TX, *Gliocladium roseum* + TX, *Gliocladium* spp. (SoilGard®) + TX, *Gliocladium virens* (Soilgard®) + TX, *Granulovirus* (Granupom®) + TX, *Halobacillus halophilus* + TX, *Halobacillus litoralis* + TX, *Halobacillus trueperi* + TX, *Halomonas* spp. + TX, *Halomonas subglaciescola* + TX, *Halovibrio variabilis* + TX, *Hanseniaspora uvarum* + TX, *Helicoverpa armigera nucleopolyhedrovirus* (Helicovex®) + TX, *Helicoverpa zea nuclear polyhedrosis virus* (Gemstar®) + TX, Isoflavone – formononetin (Myconate®) + TX, *Kloeckera apiculata* + TX, *Kloeckera* spp. + TX, *Lagenidium giganteum* (Laginex®) + TX, *Lecanicillium longisporum* (Vertiblast®) + TX, *Lecanicillium muscarium* (Vertikil®) + TX, *Lymantria Dispar nucleopolyhedrosis virus* (Disparvirus®) + TX, *Marinococcus halophilus* + TX, *Meira geulakonigii* + TX, *Metarhizium anisopliae*

(Met52®) + TX, *Metarhizium anisopliae* (Destruxin WP®) + TX, *Metschnikowia fruticola* (Shemer®) + TX, *Metschnikowia pulcherrima* + TX, *Microdochium dimerum* (Antibot®) + TX, *Micromonospora coerulea* + TX, *Microsphaeropsis ochracea* + TX, *Muscodor albus* 620 (Muscudor®) + TX, *Muscodor roseus* strain A3-5 + TX, *Mycorrhizae* spp. (AMykor® + TX, Root Maximizer®) + TX, *Myrothecium verrucaria* strain AARC-0255 (DiTera®) + TX, BROS PLUS® + TX, *Ophiostoma piliferum* strain D97 (Sylvanex®) + TX, *Paecilomyces farinosus* + TX, *Paecilomyces fumosoroseus* (PFR-97® + TX, PreFeRal®) + TX, *Paecilomyces linacinus* (Biostat WP®) + TX, *Paecilomyces lilacinus* strain 251 (MeloCon WG®) + TX, *Paenibacillus polymyxa* + TX, *Pantoea agglomerans* (BlightBan C9-1®) + TX, *Pantoea* spp. + TX, *Pasteuria* spp. (Econem®) + TX, *Pasteuria nishizawae* + TX, *Penicillium aurantiogriseum* + TX, *Penicillium billai* (Jumpstart® + TX, TagTeam®) + TX, *Penicillium brevicompactum* + TX, *Penicillium frequentans* + TX, *Penicillium griseofulvum* + TX, *Penicillium purpurogenum* + TX, *Penicillium* spp. + TX, *Penicillium viridicatum* + TX, *Phlebiopsis gigantea* (Rotstop®) + TX, phosphate solubilizing bacteria (Phosphomeal®) + TX, *Phytophthora cryptogea* + TX, *Phytophthora palmivora* (Devine®) + TX, *Pichia anomala* + TX, *Pichia guillemontii* + TX, *Pichia membranaefaciens* + TX, *Pichia onychis* + TX, *Pichia stipites* + TX, *Pseudomonas aeruginosa* + TX, *Pseudomonas aureofaciens* (Spot-Less Biofungicide®) + TX, *Pseudomonas cepacia* + TX, *Pseudomonas chlororaphis* (AtEze®) + TX, *Pseudomonas corrugate* + TX, *Pseudomonas fluorescens* strain A506 (BlightBan A506®) + TX, *Pseudomonas putida* + TX, *Pseudomonas reactans* + TX, *Pseudomonas* spp. + TX, *Pseudomonas syringae* (Bio-Save®) + TX, *Pseudomonas viridiflava* + TX, *Pseudomonas fluorescens* (Zequanox®) + TX, *Pseudozyma flocculosa* strain PF-A22 UL (Sporodex L®) + TX, *Puccinia canaliculata* + TX, *Puccinia thlaspeos* (Wood Warrior®) + TX, *Pythium paroecandrum* + TX, *Pythium oligandrum* (Polygandron® + TX, Polyversum®) + TX, *Pythium periplocum* + TX, *Rhanella aquatilis* + TX, *Rhanella* spp. + TX, *Rhizobia* (Dormal® + TX, Vault®) + TX, *Rhizoctonia* + TX, *Rhodococcus globerulus* strain AQ719 + TX, *Rhodosporidium diobovatum* + TX, *Rhodosporidium toruloides* + TX, *Rhodotorula* spp. + TX, *Rhodotorula glutinis* + TX, *Rhodotorula graminis* + TX, *Rhodotorula mucilagnosa* + TX, *Rhodotorula rubra* + TX, *Saccharomyces cerevisiae* + TX, *Salinococcus roseus* + TX, *Sclerotinia minor* + TX, *Sclerotinia minor* (SARRITOR®) + TX, *Scytalidium* spp. + TX, *Scytalidium uredinicola* + TX, *Spodoptera exigua nuclear polyhedrosis virus* (Spod-X® + TX, Spexit®) + TX, *Serratia marcescens* + TX, *Serratia plymuthica* + TX, *Serratia* spp. + TX, *Sordaria fimicola* + TX, *Spodoptera littoralis nucleopolyhedrovirus* (Littovir®) + TX, *Sporobolomyces roseus* + TX, *Stenotrophomonas maltophilia* + TX, *Streptomyces ahygroscopicus* + TX, *Streptomyces albaduncus* + TX, *Streptomyces exfoliates* + TX, *Streptomyces galbus* + TX, *Streptomyces griseoplanus* + TX, *Streptomyces griseoviridis* (Mycostop®) + TX, *Streptomyces lydicus* (Actinovate®) + TX, *Streptomyces lydicus* WYEC-108 (ActinoGrow®) + TX, *Streptomyces violaceus* + TX, *Tilletiopsis minor* + TX, *Tilletiopsis* spp. + TX, *Trichoderma asperellum* (T34 Biocontrol®) + TX, *Trichoderma gamsii* (Tenet®) + TX, *Trichoderma atroviride* (Plantmate®) + TX, *Trichoderma hamatum* TH 382 + TX, *Trichoderma harzianum rifai* (Mycostar®) + TX, *Trichoderma harzianum* T-22 (Trianum-P® + TX, PlantShield HC® + TX, RootShield® + TX, Trianum-G®) + TX, *Trichoderma harzianum* T-39 (Trichodex®) + TX, *Trichoderma inhamatum* + TX, *Trichoderma koningii* + TX, *Trichoderma* spp. LC 52 (Sentinel®) + TX,

- Trichoderma lignorum* + TX, *Trichoderma longibrachiatum* + TX, *Trichoderma polysporum* (Binab T®) + TX, *Trichoderma taxi* + TX, *Trichoderma virens* + TX, *Trichoderma virens* (formerly *Gliocladium virens* GL-21) (SoilGuard®) + TX, *Trichoderma viride* + TX, *Trichoderma viride* strain ICC 080 (Remedier®) + TX, *Trichosporon pullulans* + TX, *Trichosporon* spp. + TX, *Trichothecium* spp. + TX, *Trichothecium roseum* + TX, *Typhula phacorrhiza* strain 94670 + TX, *Typhula phacorrhiza* strain 94671 + TX, *Ulocladium atrum* + TX, *Ulocladium oudemansii* (Botry-Zen®) + TX, *Ustilago maydis* + TX, various bacteria and supplementary micronutrients (Natural II®) + TX, various fungi (Millennium Microbes®) + TX, *Verticillium chlamydosporium* + TX, *Verticillium lecanii* (Mycotal® + TX, Vertalec®) + TX, Vip3Aa20 (VIPtera®) + TX, *Virgibacillus marismortui* + TX, *Xanthomonas campestris* pv. *Poae* (Camperico®) + TX, *Xenorhabdus bovienii* + TX, *Xenorhabdus nematophilus*;
- Plant extracts including: pine oil (Retenol®) + TX, azadirachtin (Plasma Neem Oil® + TX, AzaGuard® + TX, MeemAzal® + TX, Molt-X® + TX, Botanical IGR (Neemazad® + TX, Neemix®) + TX, canola oil (Lilly Miller Vegol®) + TX, *Chenopodium ambrosioides* near *ambrosioides* (Requiem®) + TX, *Chrysanthemum* extract (Crisant®) + TX, extract of neem oil (Trilogy®) + TX, essentials oils of *Labiatae* (Botania®) + TX, extracts of clove rosemary peppermint and thyme oil (Garden insect killer®) + TX, Glycinebetaine (Greenstim®) + TX, garlic + TX, lemongrass oil (GreenMatch®) + TX, neem oil + TX, *Nepeta cataria* (Catnip oil) + TX, *Nepeta catarina* + TX, nicotine + TX, oregano oil (MossBuster®) + TX, *Pedaliaceae* oil (Nematon®) + TX, pyrethrum + TX, *Quillaja saponaria* (NemaQ®) + TX, *Reynoutria sachalinensis* (Regalia® + TX, Sakalia®) + TX, rotenone (Eco Roten®) + TX, *Rutaceae* plant extract (Soleo®) + TX, soybean oil (Ortho ecosense®) + TX, tea tree oil (Timorex Gold®) + TX, thymus oil + TX, AGNIQUE® MMF + TX, BugOil® + TX, mixture of rosemary sesame peppermint thyme and cinnamon extracts (EF 300®) + TX, mixture of clove rosemary and peppermint extract (EF 400®) + TX, mixture of clove peppermint garlic oil and mint (Soil Shot®) + TX, kaolin (Screen®) + TX, storage glucan of brown algae (Laminarin®);
- pheromones including: blackheaded fireworm pheromone (3M Sprayable Blackheaded Fireworm Pheromone®) + TX, Codling Moth Pheromone (Paramount dispenser-(CM)/ Isomate C-Plus®) + TX, Grape Berry Moth Pheromone (3M MEC-GBM Sprayable Pheromone®) + TX, Leafroller pheromone (3M MEC – LR Sprayable Pheromone®) + TX, Muscamone (Snip7 Fly Bait® + TX, Starbar Premium Fly Bait®) + TX, Oriental Fruit Moth Pheromone (3M oriental fruit moth sprayable pheromone®) + TX, Peachtree Borer Pheromone (Isomate-P®) + TX, Tomato Pinworm Pheromone (3M Sprayable pheromone®) + TX, Entostat powder (extract from palm tree) (Exosex CM®) + TX, (E + TX,Z + TX,Z)-3 + TX,8 + TX,11 Tetradecatrienyl acetate + TX, (Z + TX,Z + TX,E)-7 + TX,11 + TX,13-Hexadecatrienal + TX, (E + TX,Z)-7 + TX,9-Dodecadien-1-yl acetate + TX, 2-Methyl-1-butanol + TX, Calcium acetate + TX, Scenturion® + TX, Biolure® + TX, Check-Mate® + TX, Lavandulyl senecioate;
- Microbials including: *Aphelinus abdominalis* + TX, *Aphidius ervi* (Aphelinus-System®) + TX, *Acerophagus papaya* + TX, *Adalia bipunctata* (Adalia-System®) + TX, *Adalia bipunctata* (Adaline®) + TX, *Adalia bipunctata* (Aphidalia®) + TX, *Agonaspis citricola* + TX, *Agonaspis fuscicollis* + TX, *Amblyseius andersoni* (Anderline® + TX, Andersoni-System®) + TX, *Amblyseius californicus* (Amblyline® + TX, Spical®) + TX, *Amblyseius cucumeris* (Thripex® + TX, Bugline cucumeris®) + TX,

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

- + TX, *Micromus angulatus* (Milacewing®) + TX, *Microterys flavus* + TX, *Muscidifurax raptorellus* and *Spalangia cameroni* (Biopar®) + TX, *Neodryinus typhlocybae* + TX, *Neoseiulus californicus* + TX, *Neoseiulus cucumeris* (THRYPEX®) + TX, *Neoseiulus fallacis* + TX, *Nesideocoris tenuis* (NesidioBug® + TX, Nesibug®) + TX, *Ophyra aenescens* (Biofly®) + TX, *Orius insidiosus* (Thripor-l® + TX, Oriline i®) + TX, *Orius laevigatus* (Thripor-L® + TX, Oriline l®) + TX, *Orius majusculus* (Oriline m®) + TX, *Orius strigicollis* (Thripor-S®) + TX, *Pauesia juniperorum* + TX, *Pediobius foveolatus* + TX, *Phasmarhabditis hermaphrodita* (Nemaslug®) + TX, *Phymastichus coffea* + TX, *Phytoseiulus macropilus* + TX, *Phytoseiulus persimilis* (Spidex® + TX, Phytoline p®) + TX, *Podisus maculiventris* (Podisus®) + TX, *Pseudacteon curvatus* + TX, *Pseudacteon obtusus* + TX, *Pseudacteon tricusps* + TX, *Pseudaphycus maculipennis* + TX, *Pseudleptomastix mexicana* + TX, *Psyllaephagus pilosus* + TX, *Psytalia concolor* (complex) + TX, *Quadrastichus* spp. + TX, *Rhyzobius lophanthae* + TX, *Rodolia cardinalis* + TX, *Rumina decollate* + TX, *Semielacher petiolatus* + TX, *Sitobion avenae* (Ervibank®) + TX, *Steinernema carpocapsae* (Nematac C® + TX, Millenium® + TX, BioNem C® + TX, NemAttack® + TX, Nemastar® + TX, Capsanem®) + TX, *Steinernema feltiae* (NemaShield® + TX, Nemasys F® + TX, BioNem F® + TX, Steinernema-System® + TX, NemAttack® + TX, Nemaplus® + TX, Exhibitline sf® + TX, Scia-rid® + TX, Entonem®) + TX, *Steinernema kraussei* (Nemasys L® + TX, BioNem L® + TX, Exhibitline srb®) + TX, *Steinernema riobrave* (BioVector® + TX, BioVektor®) + TX, *Steinernema scapterisci* (Nematac S®) + TX, *Steinernema* spp. + TX, *Steinemematid* spp. (Guardian Nematodes®) + TX, *Stethorus punctillum* (Stethorus®) + TX, *Tamarixia radiata* + TX, *Tetrastichus setifer* + TX, *Thripobius semiluteus* + TX, *Torymus sinensis* + TX, *Trichogramma brassicae* (Tricholine b®) + TX, *Trichogramma brassicae* (Tricho-Strip®) + TX, *Trichogramma evanescens* + TX, *Trichogramma minutum* + TX, *Trichogramma ostrinae* + TX, *Trichogramma platneri* + TX, *Trichogramma pretiosum* + TX, *Xanthopimpla stemmator*;
- other biologicals including: abscisic acid + TX, bioSea® + TX, *Chondrostereum purpureum* (Chontrol Paste®) + TX, *Colletotrichum gloeosporioides* (Collego®) + TX, Copper Octanoate (Cueva®) + TX, Delta traps (Trapline d®) + TX, *Erwinia amylovora* (Harpin) (ProAct® + TX, Ni-HIBIT Gold CST®) + TX, Ferri-phosphate (Ferramol®) + TX, Funnel traps (Trapline y®) + TX, Gallex® + TX, Grower's Secret® + TX, Homo-brassonolide + TX, Iron Phosphate (Lilly Miller Worry Free Ferramol Slug & Snail Bait®) + TX, MCP hail trap (Trapline f®) + TX, *Microctonus hyperodae* + TX, *Mycroleptodiscus terrestris* (Des-X®) + TX, BioGain® + TX, Aminomite® + TX, Zenox® + TX, Pheromone trap (Thripline ams®) + TX, potassium bicarbonate (MilStop®) + TX, potassium salts of fatty acids (Sanova®) + TX, potassium silicate solution (Sil-Matrix®) + TX, potassium iodide + potassiumthiocyanate (Enzicur®) + TX, SuffOil-X® + TX, Spider venom + TX, *Nosema locustae* (Semaspore Organic Grasshopper Control®) + TX, Sticky traps (Trapline YF® + TX, Rebell Amarillo®) + TX and Traps (Takitrapline y + b®) + TX; and
- a safener, such as benoxacor + TX, cloquintocet (including cloquintocet-mexyl) + TX, cyprosulfamide + TX, dichlormid + TX, fenclorazole (including fenclorazole-ethyl) + TX, fenclorim + TX, fluxofenim + TX, furilazole + TX, isoxadifen (including isoxadifen-ethyl) + TX, mefenpyr (including mefenpyr-diethyl) + TX, metcamifen + TX and oxabetrinil + TX.

The references in brackets behind the active ingredients, e.g. [3878-19-1] refer to the Chemical Abstracts Registry number. The above described mixing partners are known. Where the active ingredients are included in "The Pesticide Manual" [The Pesticide Manual - A World Compendium; Thirteenth Edition; Editor: C. D. S. Tomlin; The British Crop Protection Council], they are described therein under the entry number given in round brackets hereinabove for the particular compound; for example, the compound "abamectin" is described under entry number (1). Where "[CCN]" is added hereinabove to the particular compound, the compound in question is included in the "Compendium of Pesticide Common Names", which is accessible on the internet [A. Wood; Compendium of Pesticide Common Names, Copyright © 1995-2004]; for example, the compound "acetoprole" is described under the internet address <http://www.alanwood.net/pesticides/acetoprole.html>.

Most of the active ingredients described above are referred to hereinabove by a so-called "common name", the relevant "ISO common name" or another "common name" being used in individual cases. If the designation is not a "common name", the nature of the designation used instead is given in round brackets for the particular compound; in that case, the IUPAC name, the IUPAC/Chemical Abstracts name, a "chemical name", a "traditional name", a "compound name" or a "development code" is used or, if neither one of those designations nor a "common name" is used, an "alternative name" is employed. "CAS Reg. No" means the Chemical Abstracts Registry Number.

The active ingredient mixture of the compounds of formula I selected from Tables A-1 to A-12, Tables C-1 to C-12 and Table P with active ingredients described above comprises a compound selected from Tables A-1 to A-12, Tables C-1 to C-12 and Table P and an active ingredient as described above preferably in a mixing ratio of from 100:1 to 1:6000, especially from 50:1 to 1:50, more especially in a ratio of from 20:1 to 1:20, even more especially from 10:1 to 1:10, very especially from 5:1 and 1:5, special preference being given to a ratio of from 2:1 to 1:2, and a ratio of from 4:1 to 2:1 being likewise preferred, above all in a ratio of 1:1, or 5:1, or 5:2, or 5:3, or 5:4, or 4:1, or 4:2, or 4:3, or 3:1, or 3:2, or 2:1, or 1:5, or 2:5, or 3:5, or 4:5, or 1:4, or 2:4, or 3:4, or 1:3, or 2:3, or 1:2, or 1:600, or 1:300, or 1:150, or 1:35, or 2:35, or 4:35, or 1:75, or 2:75, or 4:75, or 1:6000, or 1:3000, or 1:1500, or 1:350, or 2:350, or 4:350, or 1:750, or 2:750, or 4:750. Those mixing ratios are by weight.

The mixtures as described above can be used in a method for controlling pests, which comprises applying a composition comprising a mixture as described above to the pests or their environment, with the exception of a method for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body.

The mixtures comprising a compound of formula I selected from Tables A-1 to A-12, Tables C-1 to C-12 and Table P and one or more active ingredients as described above can be applied, for example, in a single "ready-mix" form, in a combined spray mixture composed from separate formulations of the

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single active ingredient components, such as a "tank-mix", and in a combined use of the single active ingredients when applied in a sequential manner, i.e. one after the other with a reasonably short period, such as a few hours or days. The order of applying the compounds of formula I selected from Tables A-1 to A-12, Tables C-1 to C-12 and Table P and the active ingredients as described above is not essential for working the present invention.

The compositions according to the invention can also comprise further solid or liquid auxiliaries, such as stabilizers, for example unepoxidized or epoxidized vegetable oils (for example epoxidized coconut oil, rapeseed oil or soya oil), antifoams, for example silicone oil, preservatives, viscosity regulators, binders and/or tackifiers, fertilizers or other active ingredients for achieving specific effects, for example bactericides, fungicides, nematocides, plant activators, molluscicides or herbicides.

The compositions according to the invention are prepared in a manner known per se, in the absence of auxiliaries for example by grinding, screening and/or compressing a solid active ingredient and in the presence of at least one auxiliary for example by intimately mixing and/or grinding the active ingredient with the auxiliary (auxiliaries). These processes for the preparation of the compositions and the use of the compounds I for the preparation of these compositions are also a subject of the invention.

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 generally 1 to 2000 g of active ingredient per hectare, in particular 10 to 1000 g/ha, preferably 10 to 600 g/ha.

A preferred method of application in the field of crop protection is application to the foliage of the plants (foliar application), it being possible to select frequency and rate of application to match the danger of infestation with the pest in question. Alternatively, the active ingredient can reach the plants via the root system (systemic action), by drenching the locus of the plants with a liquid composition or by incorporating the active ingredient in solid form into the locus of the plants, for example into the soil, for example in the form of granules (soil application). In the case of paddy rice crops, such granules can be metered into the flooded paddy-field.

The compounds of the invention and compositions thereof are also be suitable for the protection of plant propagation material, for example seeds, such as fruit, tubers or kernels, or nursery plants, against pests of the abovementioned type. The propagation material can be treated with the compound prior to planting, for example seed can be treated prior to sowing. Alternatively, the

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compound can be applied to seed kernels (coating), either by soaking the kernels in a liquid composition or by applying a layer of a solid composition. It is also possible to apply the compositions when the propagation material is planted to the site of application, for example into the seed furrow during drilling. These treatment methods for plant propagation material and the plant propagation material thus treated are further subjects of the invention. Typical treatment rates would depend on the plant and pest/fungi to be controlled and are generally between 1 to 200 grams per 100 kg of seeds, preferably between 5 to 150 grams per 100 kg of seeds, such as between 10 to 100 grams per 100 kg of seeds.

The term seed embraces seeds and plant propagules of all kinds including but not limited to true seeds, seed pieces, suckers, corns, bulbs, fruit, tubers, grains, rhizomes, cuttings, cut shoots and the like and means in a preferred embodiment true seeds.

The present invention also comprises seeds coated or treated with or containing a compound of formula I. The term "coated or treated with and/or containing" generally signifies that the active ingredient is for the most part on the surface of the seed at the time of application, although a greater or lesser part of the ingredient may penetrate into the seed material, depending on the method of application. When the said seed product is (re)planted, it may absorb the active ingredient. In an embodiment, the present invention makes available a plant propagation material adhered thereto with a compound of formula (I). Further, it is hereby made available, a composition comprising a plant propagation material treated with a compound of formula (I).

Seed treatment comprises all suitable seed treatment techniques known in the art, such as seed dressing, seed coating, seed dusting, seed soaking and seed pelleting. The seed treatment application of the compound formula (I) can be carried out by any known methods, such as spraying or by dusting the seeds before sowing or during the sowing/planting of the seeds.

Biological 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, 24 ppm, 12.5 ppm, 6 ppm, 3 ppm, 1.5 ppm, 0.8 ppm or 0.2 ppm.

Example B1: Activity against *Bemisia tabaci* (Cotton white fly): Feeding/contact activity

Cotton leaf discs were placed on agar in 24-well microtiter plates and sprayed with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions. After drying the leaf discs were infested with adult white flies. The samples were checked for mortality 6 days after incubation.

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The following compounds resulted in at least 80% mortality at an application rate of 200 ppm: P1, P2, P10, P11, P14.

Example B2: Activity against *Diabrotica balteata* (Corn root worm)

5 Maize sprouts placed onto an agar layer in 24-well microtiter plates were treated with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions by spraying. After drying, the plates were infested with L2 larvae (6 to 10 per well). The samples were assessed for mortality and growth inhibition in comparison to untreated samples 4 days after infestation.

10 The following compounds gave an effect of at least 80% in at least one of the two categories (mortality or growth inhibition) at an application rate of 200 ppm: P1, P2, P10, P11, P12, P13, P14, P15.

Example B3: Activity against *Euschistus heros* (Neotropical Brown Stink Bug)

15 Soybean leaves on agar in 24-well microtiter plates were sprayed with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions. After drying the leaves were infested with N2 nymphs. The samples were assessed for mortality and growth inhibition in comparison to untreated samples 5 days after infestation.

The following compounds gave an effect of at least 80% in at least one of the two categories (mortality or growth inhibition) at an application rate of 200 ppm: P1, P2, P11, P13, P15.

20 Example B4: Activity against *Frankliniella occidentalis* (Western flower thrips): Feeding/contact activity

Sunflower leaf discs were placed on agar in 24-well microtiter plates and sprayed with aqueous test solutions prepared from 10'000 DMSO stock solutions. After drying the leaf discs were infested with a *Frankliniella* population of mixed ages. The samples were assessed for mortality 7 days after infestation.

25 The following compounds resulted in at least 80% mortality at an application rate of 200 ppm: P2.

Example B5: Activity against *Plutella xylostella* (Diamond back moth)

30 24-well microtiter plates with artificial diet were treated with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions by pipetting. After drying, *Plutella* eggs were pipetted through a plastic stencil onto a gel blotting paper and the plate was closed with it. The samples were assessed for mortality and growth inhibition in comparison to untreated samples 8 days after infestation.

The following compounds gave an effect of at least 80% in at least one of the two categories (mortality or growth inhibition) at an application rate of 200 ppm: P1, P2, P10, P11, P12, P13, P14, P15.

35 Example B6: Activity against *Myzus persicae* (Green peach aphid): Feeding/Contact activity

Sunflower leaf discs were placed onto agar in a 24-well microtiter plate and sprayed with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions. After drying, the leaf discs were infested with an aphid population of mixed ages. The samples were assessed for mortality 6 days after infestation.

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The following compounds resulted in at least 80% mortality at an application rate of 200 ppm: P1, P2, P10, P11, P12, P13, P14, P15.

Example B7: Activity against *Spodoptera littoralis* (Egyptian cotton leaf worm)

- 5 Cotton leaf discs were placed onto agar in 24-well microtiter plates and sprayed with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions. After drying the leaf discs were infested with five L1 larvae. The samples were assessed for mortality, anti-feeding effect, and growth inhibition in comparison to untreated samples 3 days after infestation. Control of *Spodoptera littoralis* by a test sample is given when at least one of the categories mortality, anti-feedant effect, and growth inhibition
- 10 is higher than the untreated sample.

The following compounds resulted in at least 80% control at an application rate of 200 ppm: P1, P2, P10, P11, P12, P13, P14, P15.

Example B8: Activity against *Myzus persicae* (Green peach aphid): Systemic activity

- 15 Roots of pea seedlings infested with an aphid population of mixed ages were placed directly into aqueous test solutions prepared from 10'000 DMSO stock solutions. The samples were assessed for mortality 6 days after placing seedlings into test solutions.

The following compounds resulted in at least 80% mortality at a test rate of 24 ppm: P11.

20 Example B9: Activity against *Chilo suppressalis* (Striped rice stemborer)

- 24-well microtiter plates with artificial diet were treated with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions by pipetting. After drying, the plates were infested with L2 larvae (6-8 per well). The samples were assessed for mortality, anti-feeding effect, and growth inhibition in comparison to untreated samples 6 days after infestation. Control of *Chilo suppressalis* by a test
- 25 sample is given when at least one of the categories mortality, anti-feedant effect, and growth inhibition is higher than the untreated sample.

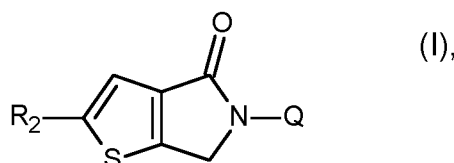
The following compounds resulted in at least 80% control at an application rate of 200 ppm: P2, P14, P15.

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CLAIMS

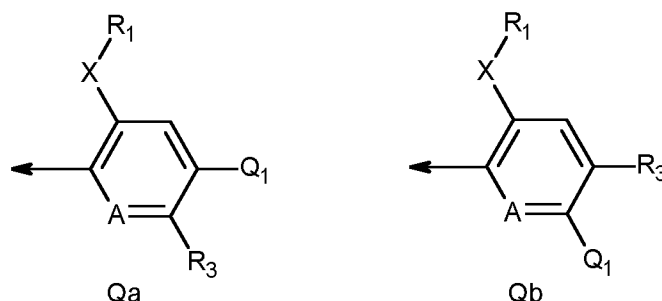
1. A compound of formula (I)



5 wherein

R₂ is C₁-C₆haloalkyl;

Q is a radical selected from the group consisting of formula Qa and Qb



wherein the arrow denotes the point of attachment to the nitrogen atom of the bicyclic ring;

10 and wherein A represents CH or N;

X is S, SO, or SO₂;

R₁ is C₁-C₄alkyl, or C₃-C₆cycloalkyl-C₁-C₄alkyl;

Q₁ is hydrogen, halogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano, C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)₂, -

15 N(R₄)C(=O)R₅, -N(R₄)CON(R₄)₂, (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or

Q₁ is a five- to six-membered aromatic ring system, linked via a ring carbon atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkoxy, C₁-C₄haloalkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl and C₁-C₄alkylsulfonyl; and said ring system can contain 1, 2 or 3 ring heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, where said ring system may not contain more than one ring oxygen atom and may not contain more than one ring sulfur atom; or

Q₁ is a five-membered aromatic ring system linked via a ring nitrogen atom to the ring which contains the substituent A, said ring system is unsubstituted or is mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkoxy, C₁-C₄haloalkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl and C₁-C₄alkylsulfonyl; and said ring system contains 1, 2 or 3 ring heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, where said ring system contains at least one ring nitrogen atom and may not contain more than one ring oxygen atom and may not contain more than one ring sulfur atom;

30 R₃ is hydrogen, halogen or C₁-C₄alkyl;

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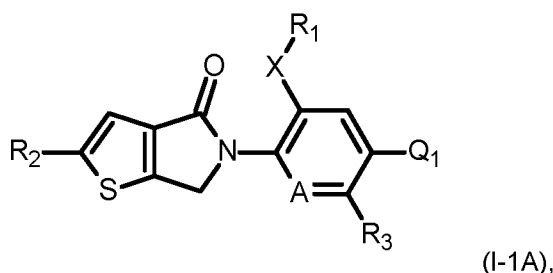
each R_4 independently is hydrogen, C_1 - C_4 alkyl or C_3 - C_6 cycloalkyl; and

R_5 is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl or C_3 - C_6 cycloalkyl; or

an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I.

5

2. A compound of formula I according to claim 1, represented by the compounds of formula I-1A



wherein A, R_1 , R_2 , R_3 , X, Q_1 , R_4 and R_5 are as defined under formula I in claim 1; or

an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-1A.

10

3. A compound of formula I-1A according to claim 2, wherein Q_1 is selected from the group consisting of hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 2-pyridyloxy, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl and pyrimidin-2-yl;

15

4. A compound of formula I-1A according to claim 2,

20

wherein

A is CH or N;

R_1 is C_1 - C_4 alkyl or cyclopropyl- C_1 - C_4 alkyl;

R_2 is C_1 - C_2 haloalkyl;

R_3 is hydrogen or C_1 - C_4 alkyl;

25

X is S or SO₂;

Q_1 is hydrogen, C_1 - C_6 haloalkyl, C_3 - C_6 cycloalkyl, C_3 - C_6 cycloalkyl monosubstituted by cyano,

C_1 - C_6 cyanoalkyl, C_1 - C_6 cyanoalkoxy, C_3 - C_6 cyanocycloalkyl- C_1 - C_4 alkoxy, C_1 - C_6 haloalkoxy, -

N(R_4)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy; in which each R_4 independently is hydrogen or C_1 - C_4 alkyl; and R_5 is C_1 - C_6 alkyl or C_3 - C_6 cycloalkyl.

30

5. A compound of formula I-1A according to claim 4, wherein

A is CH or N;

R_1 is ethyl or cyclopropylmethyl;

R_2 is CF₂CF₃ or CF₃;

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R₃ is hydrogen or methyl;

X is S or SO₂; and

Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-

5 difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, or 2-pyridyloxy.

6. A compound of formula I-1A according to claim 2, wherein

A is CH or N, preferably A is N;

R₁ is ethyl or cyclopropylmethyl; preferably R₁ is ethyl;

10 R₂ is C₁-C₂haloalkyl; preferably R₂ is CF₂CF₃ or CF₃;

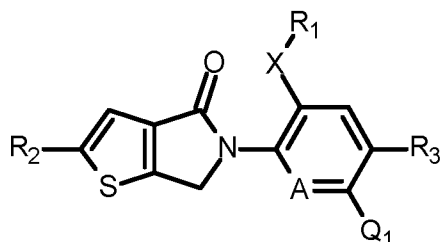
X is S or SO₂; preferably X is SO₂;

R₃ is hydrogen; and

Q₁ is hydrogen, trifluoromethyl, difluoroethyl, cyclopropyl, cyanocyclopropyl, cyanoisopropyl, cyanoisopropoxy, cyanocyclopropylmethoxy, trifluoroethoxy, difluoropropoxy, (oxazolidin-2-one)-3-yl,

15 2-pyridyloxy, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl.

7. A compound of formula I according to claim 1, represented by the compounds of formula I-2A



20 (I-2A),

wherein A, R₁, R₂, R₃, X, Q₁, R₄ and R₅ are as defined under formula in claim 1; or

an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-2A.

25 8. A compound of formula I-2A according to claim 7, wherein Q₁ is selected from the group consisting of cyclopropyl, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, 3-chloro-pyrazol-1-yl, 3-trifluoromethyl-pyrazol-1-yl, 1,2,4-triazol-1-yl and pyrimidin-2-yl.

30 9. A compound of formula I-2A according to claim 7, wherein

A is CH or N;

R₁ is C₁-C₄alkyl or cyclopropyl-C₁-C₄alkyl;

R₂ is C₁-C₂haloalkyl;

R₃ is hydrogen or C₁-C₄alkyl;

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X is S or SO₂; and

Q₁ is C₃-C₆cycloalkyl, -N(R₄)COR₅, or (oxazolidin-2-one)-3-yl; in which each R₄ independently is hydrogen or C₁-C₄alkyl; and R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl.

5 10. A compound of formula I-2A according to claim 9, wherein

A is CH or N;

R₁ is ethyl or cyclopropylmethyl;

R₂ is CF₂CF₃ or CF₃;

R₃ is hydrogen or methyl;

10 X is S or SO₂; and

Q₁ is cyclopropyl, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), or (oxazolidin-2-one)-3-yl.

11. A compound of formula I-2A according to claim 7, wherein

15 A is CH or N, preferably A is N;

R₁ is ethyl or cyclopropylmethyl; preferably R₁ is ethyl;

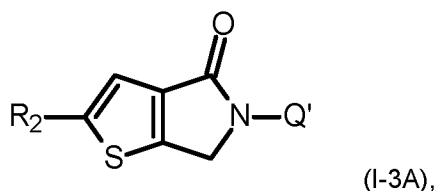
R₂ is C₁-C₂haloalkyl; preferably R₂ is CF₂CF₃ or CF₃;

X is S or SO₂; preferably X is SO₂;

R₃ is hydrogen; and

20 Q₁ is cyclopropyl, (oxazolidin-2-one)-3-yl, N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl, N-linked triazolyl, C-linked pyrimidinyl, or -N(R₄)COR₅, in which R₄ is independently either hydrogen or methyl and R₅ is either methyl, ethyl or cyclopropyl.

12. A compound of formula I according to claim 1, represented by the compounds of formula I-3A

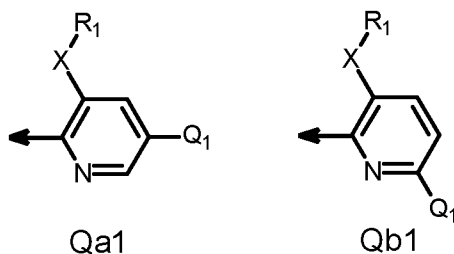


25

wherein

R₂ is C₁-C₄haloalkyl, preferably CF₃ or CF₂CF₃;

Q' is a radical selected from the group consisting of formula Qa1 and Qb1



30 wherein the arrow denotes the point of attachment to the nitrogen atom of the bicyclic ring;

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and wherein

X is S, SO, or SO₂, preferably S or SO₂, more preferably SO₂;

R₁ is C₁-C₄alkyl, preferably ethyl;

Q₁ is hydrogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano,

- 5 C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy; or

Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or

Q₁ is unsubstituted pyrimidinyl, preferably pyrimidin-2-yl; or

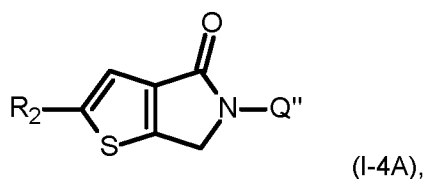
Q₁ is unsubstituted N-linked triazolyl, preferably 1,2,4-triazol-1-yl; or

Q₁ is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; preferably Q₁ is 3-chloro-pyrazol-1-yl or 3-trifluoromethyl-pyrazol-1-yl;

- 15 R₄ is C₁-C₄alkyl, preferably methyl; and

R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl, preferably R₅ is methyl, ethyl or cyclopropyl; or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-3A.

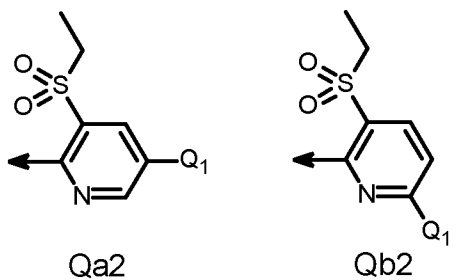
13. A compound of formula I according to claim 1, represented by the compounds of formula I-4A



wherein

R₂ is C₁-C₄haloalkyl, preferably CF₃ or CF₂CF₃;

Q'' is a radical selected from the group consisting of formula Qa2 and Qb2



- 25 wherein the arrow denotes the point of attachment to the nitrogen atom of the bicyclic ring; and wherein

Q₁ is hydrogen, C₁-C₆haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl monosubstituted by cyano, C₁-C₆cyanoalkyl, C₁-C₆cyanoalkoxy, C₃-C₆cyanocycloalkyl-C₁-C₄alkoxy, C₁-C₆haloalkoxy, -N(R₄)COR₅, (oxazolidin-2-one)-3-yl or 2-pyridyloxy;

- 30 preferably Q₁ is hydrogen, trifluoromethyl, 1,1-difluoroethyl, cyclopropyl, 1-cyanocyclopropyl, 1-cyano-1-methyl-ethyl, 1-cyano-1-methyl-ethoxy, (1-cyanocyclopropyl)methoxy, 2,2,2-trifluoroethoxy, 2,2-

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difluoropropoxy, -N(CH₃)COCH₃, -N(CH₃)COCH₂CH₃, -N(CH₃)CO(cyclopropyl), (oxazolidin-2-one)-3-yl, or 2-pyridyloxy; or

Q₁ is unsubstituted pyrimidinyl, preferably pyrimidin-2-yl; or

Q₁ is unsubstituted N-linked triazolyl, preferably 1,2,4-triazol-1-yl; or

- 5 Q₁ is N-linked pyrazolyl which can be mono-substituted by chloro or trifluoromethyl; preferably Q₁ is 3-chloro-pyrazol-1-yl or 3-trifluoromethyl-pyrazol-1-yl;

R₄ is C₁-C₄alkyl, preferably methyl; and

R₅ is C₁-C₆alkyl or C₃-C₆cycloalkyl, preferably methyl, ethyl or cyclopropyl; or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide of a compound of formula I-4A.

10

14. A compound of formula I according to claim 1 selected from the group consisting of:

1-[5-ethylsulfonyl-6-[4-oxo-2-(trifluoromethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]cyclopropane-carbonitrile (compound P1)

15 1-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-

pyridyl]cyclopropane-carbonitrile (compound P2);

2-[[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]oxy]-2-methyl-propanenitrile (compound P3);

5-[3-ethylsulfonyl-5-(2,2,2-trifluoroethoxy)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P4);

20 2-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]-2-methyl-propanenitrile (compound P5);

5-[5-(2,2-difluoropropoxy)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P6);

25 N-[5-ethylsulfonyl-6-[4-oxo-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-5-yl]-3-pyridyl]-N-methyl-acetamide (compound P7);

5-[5-(1,1-difluoroethyl)-3-ethylsulfonyl-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P8);

5-(5-acetyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P9);

30 5-(6-cyclopropyl-3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P10);

5-(3-ethylsulfonyl-6-pyrimidin-2-yl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P11);

35 5-(3-ethylsulfonyl-6-methoxy-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P12);

5-[3-ethylsulfonyl-6-(1,2,4-triazol-1-yl)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P13);

5-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P14); and

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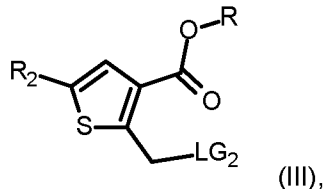
5-(3-ethylsulfonyl-2-pyridyl)-2-(1,1,2,2,2-pentafluoroethyl)-6H-thieno[2,3-c]pyrrol-4-one (compound P15).

15. A composition comprising an insecticidally, acaricidally, nematocidally or molluscicidally effective amount of a compound of formula (I), or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, as defined in any one of claims 1 – 14 and, optionally, an auxiliary or diluent.

16. A method of combating and controlling insects, acarines, nematodes or molluscs which comprises applying to a pest, to a locus of a pest, or to a plant susceptible to attack by a pest an insecticidally, acaricidally, nematocidally or molluscicidally effective amount of a compound of formula (I), or an agrochemically acceptable salt, stereoisomer, enantiomer, tautomer or N-oxide thereof, as defined in any one of claims 1 – 14 or a composition as defined in claim 15.

17. A method for the protection of plant propagation material from the attack by insects, acarines, nematodes or molluscs, which comprises treating the propagation material or the site, where the propagation material is planted, with a composition according to claim 15.

18. A compound of formula III



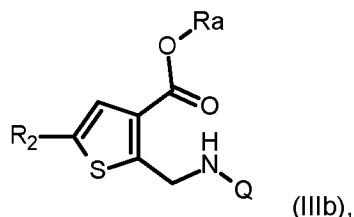
wherein

R₂ is as defined under formula I above;

LG₂ is a leaving group, for example bromo Br, chloro Cl or iodo I; and

R is C₁-C₆alkyl, benzyl or phenyl.

19. A compound of formula IIIb



wherein

R₂ and Q are as defined under formula I above; and

Ra is hydrogen, C₁-C₆alkyl, benzyl or phenyl.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2021/069946

A. CLASSIFICATION OF SUBJECT MATTER INV. C07D333/38 A01N43/26 C07D409/12 C07D495/04 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C07D A01N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2019/131575 A1 (SUMITOMO CHEMICAL CO [JP]) 4 July 2019 (2019-07-04) claims 1 and 12 -----	1-19
A	WO 2016/116338 A1 (SYNGENTA PARTICIPATIONS AG [CH]) 28 July 2016 (2016-07-28) claims 1 and 12 -----	1-19
☐ 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 8 October 2021		Date of mailing of the international search report 18/10/2021
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 Sahagún Krause, H

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2021/069946

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2019131575 A1	04-07-2019	BR 112020013023 A2 CN 111770923 A EP 3733667 A1 JP W02019131575 A1 US 2021059255 A1 WO 2019131575 A1	24-11-2020 13-10-2020 04-11-2020 14-01-2021 04-03-2021 04-07-2019
WO 2016116338 A1	28-07-2016	BR 112017015514 A2 CN 107207501 A EP 3247712 A1 JP 2018507184 A US 2017362224 A1 US 2019144445 A1 WO 2016116338 A1	02-05-2018 26-09-2017 29-11-2017 15-03-2018 21-12-2017 16-05-2019 28-07-2016