

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization

International Bureau



(10) International Publication Number

WO 2016/023954 A2

(43) International Publication Date
18 February 2016 (18.02.2016)

(51) International Patent Classification:
C07D 471/04 (2006.01)

(74) Agent: SYNGENTA INTERNATIONAL AG; Intellectual Property, WRO 1008-Z1-26, Schwarzwaldallee 215, CH-4058 Basel (CH).

(21) International Application Number:

PCT/EP2015/068577

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(22) International Filing Date:

12 August 2015 (12.08.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

14180611.7 12 August 2014 (12.08.2014) EP
14186946.1 30 September 2014 (30.09.2014) EP
14197164.8 10 December 2014 (10.12.2014) EP

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

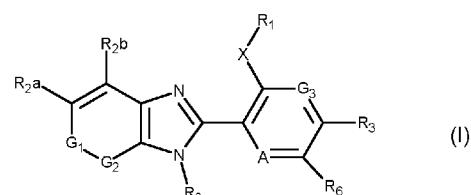
Declarations under Rule 4.17:

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

Published:

- without international search report and to be republished upon receipt of that report (Rule 48.2(g))

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



WO 2016/023954 A2

(57) Abstract: Compounds of formula (I), wherein the substituents are as defined in claim 1, and the agrochemically acceptable salts, stereoisomers, enantiomers, tautomers and N-oxides of those compounds, can be used as insecticides and can be prepared in a manner known per se.

-1-

Pesticidally active heterocyclic derivatives with sulphur containing substituents

The present invention relates to pesticidally active, in particular insecticidally active heterocyclic derivatives containing sulphur substituents, 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*).

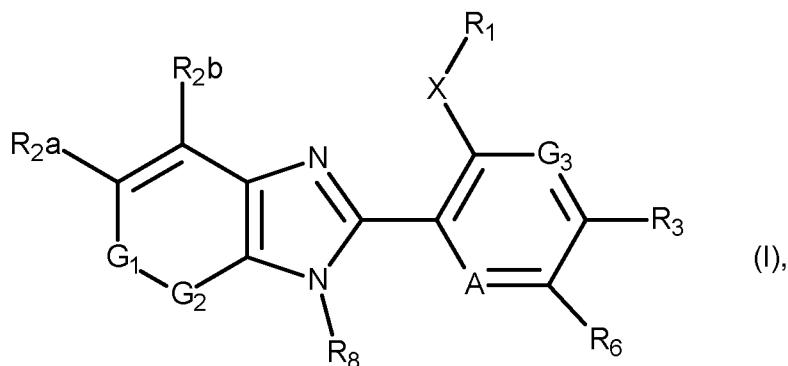
5

Heterocyclic compounds with pesticidal action are known and described, for example, in WO 2012/086848 and WO 2013/018928.

There have now been found novel pesticidally active heterocyclic derivatives with sulphur containing

10 phenyl and pyridyl substituents.

The present invention accordingly relates to compounds of formula I,



wherein

15 A represents CH, N or CR; wherein R is C₁-C₄alkyl, C₁-C₄haloalkyl, cyano, nitro or halogen;
 X is S, SO or SO₂;
 R₁ is C₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl or C₃-C₆cycloalkyl mono- or polysubstituted by substituents selected from the group consisting of halogen, C₁-C₄haloalkyl, cyano and C₁-C₄alkyl; or R₁ is C₃-C₆cycloalkyl-C₁-C₄alkyl mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄haloalkyl and C₁-C₄alkyl;
 20 or R₁ is C₂-C₆alkenyl, C₂-C₆haloalkenyl or C₂-C₆alkynyl;
 R_{2a} and R_{2b} are, independently from each other, hydrogen, halogen, cyano, C₁-C₆haloalkoxy, C₁-C₆haloalkyl or C₁-C₆haloalkyl substituted by one or two substituents selected from the group consisting of hydroxyl, methoxy and cyano; or
 25 R_{2a} and R_{2b} are, independently from each other, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl, O(C₁-C₄haloalkyl), or -C(O)C₁-C₄haloalkyl; or

-2-

R_2a and R_2b are, independently from each other, C_3 - C_6 cycloalkyl which can be mono - or polysubstituted by substituents selected from the group consisting of halogen, cyano, C_1 - C_4 haloalkyl and C_1 - C_4 alkyl;

R_3 is hydrogen, halogen, cyano, nitro, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 alkoxy C_1 - C_6 alkyl, C_1 - C_6 haloalkyl,

5 C_3 - C_6 cycloalkyl or C_3 - C_6 cycloalkyl- C_1 - C_4 alkyl; or

R_3 is C_3 - C_6 cycloalkyl mono- or polysubstituted by substituents selected from the group consisting of halogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl and cyano; or

R_3 is phenyl which can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro, C_2 - C_6 alkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl, C_2 - C_6 haloalkynyl, C_1 - C_4 alkoxy

10 C_1 - C_4 alkyl, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 haloalkoxy, C_1 - C_4 alkoxy, C_1 - C_4 haloalkylsulfanyl, C_1 - C_4 haloalkylsulfinyl, C_1 - C_4 haloalkylsulfonyl, C_1 - C_4 alkylsulfanyl, C_1 - C_4 alkylsulfinyl, C_1 - C_4 alkylsulfonyl and $-C(O)C_1$ - C_4 haloalkyl; or

R_3 is C_2 - C_6 alkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl or C_2 - C_6 haloalkynyl; or

R_3 is C_1 - C_6 haloalkylsulfanyl, C_1 - C_6 haloalkylsulfinyl, C_1 - C_6 haloalkylsulfonyl, C_1 - C_6 haloalkoxy,

15 $-C(O)C_1$ - C_4 haloalkyl, C_1 - C_6 alkylsulfanyl, C_1 - C_6 alkylsulfinyl or C_1 - C_6 alkylsulfonyl; or

R_3 is a five- to six-membered, aromatic, partially saturated or fully saturated ring system linked via a nitrogen atom to the ring which contains the substituent G_3 , said ring system can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro,

C_2 - C_6 alkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl, C_2 - C_6 haloalkynyl, C_1 - C_4 alkoxy C_1 - C_4 alkyl, C_1 - C_4 alkyl,

20 C_1 - C_4 haloalkyl, C_1 - C_4 haloalkoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkylsulfanyl, C_1 - C_4 alkylsulfinyl, C_1 - C_4 alkylsulfonyl and $-C(O)C_1$ - C_4 alkyl, C_1 - C_4 haloalkylsulfanyl, C_1 - C_4 haloalkylsulfinyl, C_1 - C_4 haloalkylsulfonyl and $-C(O)C_1$ - C_4 haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom; or

25 R_3 is a five-to six membered, aromatic, partially saturated or fully saturated ring system linked via a carbon atom to the ring which contains the substituent G_3 , said ring system can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro,

C_2 - C_6 alkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl, C_2 - C_6 haloalkynyl, C_1 - C_4 alkoxy C_1 - C_4 alkyl, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 haloalkoxy, C_1 - C_4 alkoxy, C_1 - C_4 alkylsulfanyl, C_1 - C_4 alkylsulfinyl, C_1 - C_4 alkylsulfonyl

30 and $-C(O)C_1$ - C_4 alkyl, C_1 - C_4 haloalkylsulfanyl, C_1 - C_4 haloalkylsulfinyl, C_1 - C_4 haloalkylsulfonyl and $-C(O)C_1$ - C_4 haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom;

R_8 is C_1 - C_4 alkyl which can be mono- or polysubstituted by substituents selected from the group

35 consisting of halogen and C_1 - C_2 alkylsulfinyl;

G_1 is NR_4 and G_2 is $C(Y)$; or

G_1 is $C(Y)$ and G_2 is NR_5 ;

Y is O or S;

G_3 is N or CR_9 ;

R₄ is C₁-C₆alkyl, C₁-C₆haloalkyl; or

R₄ is C₃-C₆cycloalkyl which can be mono- or polysubstituted by R₇; or

R₄ is C₃-C₆cycloalkyl-C₁-C₄alkyl which can be mono- or polysubstituted by R₁₀; or

R₄ is C₁-C₄alkyl substituted by cyano, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfonyl, C₁-C₄alkylsulfinyl, C₁-

5 C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfonyl, C₁-C₄haloalkylsulfinyl, C₁-C₄alkoxy,

C₁-C₄alkoxyC₁-C₄alkoxy, C₃-C₆ cycloalkyl or by phenyl, which itself can be mono - or polysubstituted by substituents selected from the group consisting of halogen, C₁-C₄alkyl, cyano, C₁-C₄haloalkyl and C₁-C₄alkoxy;

R₄ is C₂-C₆alkenyl substituted by R₁₁ or C₂-C₆alkynyl substituted by R₁₁; or

10 R₄ is C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₆haloalkoxy, C₁-C₆alkoxy, C₁-C₆alkylsulfanyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfinyl, C₁-C₆haloalkylsulfanyl, C₁-C₆haloalkylsulfinyl, C₁-C₆haloalkylsulfonyl, C₁-C₆haloalkylsulfinyl or hydroxyl; or

R₄ is a five- to six-membered, aromatic, partially saturated or fully saturated ring system, said ring system can be mono- or polysubstituted by substituents selected from the group consisting of halogen,

15 cyano, nitro, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfonyl, C₁-

C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not

20 contain more than one oxygen atom and not more than one sulfur atom;

R₅ is C₁-C₆alkyl, C₁-C₆haloalkyl; or

R₅ is C₃-C₆cycloalkyl which can be mono- or polysubstituted by R₇; or

R₅ is C₃-C₆cycloalkyl-C₁-C₄alkyl which can be mono- or polysubstituted by R₁₀; or

R₅ is C₁-C₄alkyl substituted by cyano, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfonyl, C₁-C₄alkylsulfinyl, C₁-

25 C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfonyl, C₁-C₄haloalkylsulfinyl, C₁-C₄ alkoxy,

C₁-C₄alkoxyC₁-C₄alkoxy, C₃-C₆ cycloalkyl or by phenyl, which itself can be mono - or polysubstituted by substituents selected from the group consisting of halogen, C₁-C₄alkyl, cyano, C₁-C₄haloalkyl and C₁-C₄alkoxy; or

R₅ is C₂-C₆alkenyl substituted by R₁₁ or C₂-C₆alkynyl substituted by R₁₁; or

30 R₅ is C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₆haloalkoxy, C₁-C₆alkoxy, C₁-C₆alkylsulfanyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfinyl, C₁-C₆haloalkylsulfanyl, C₁-C₆haloalkylsulfonyl, C₁-C₆haloalkylsulfinyl or hydroxyl; or

R₅ is a five- to six-membered, aromatic, partially saturated or fully saturated ring system, said ring system can be mono- or polysubstituted by substituents selected from the group consisting of halogen,

35 cyano, nitro, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₄alkoxyC₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfonyl, C₁-

C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-

C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms

-4-

selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom;

R₆ and R₉, independently from each other, are hydrogen, halogen, nitro, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₆ cycloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxyC₁-C₄alkyl, or C₁-C₄haloalkyl;

5 R₇ and R₁₀, independently from each other, are halogen, nitro, cyano, C₁-C₄alkoxy, C₁-C₄haloalkoxy, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl;

R₁₁ is nitro, cyano, C₁-C₄alkoxy, C₁-C₄ alkoxy C₁-C₄ alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfonyl, C₁-C₄alkylsulfinyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfonyl, C₁-C₄haloalkylsulfinyl or phenyl which itself can be mono - or polysubstituted by substituents selected from the group consisting of halogen,

10 C₁-C₄alkyl, cyano, C₁-C₄haloalkyl and C₁-C₄alkoxy; and 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,

15 sulfuric acid, nitric 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

20 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,

25 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.

The alkyl groups occurring in the definitions of the substituents can be straight-chain or branched and are, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, pentyl, hexyl, nonyl, decyl and their branched isomers. Alkylsulfanyl, alkylsulfinyl, alkylsulfonyl, alkoxy, alkenyl and alkynyl radicals are derived from the alkyl radicals mentioned. The alkenyl and alkynyl groups can be mono- or polyunsaturated.

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

Haloalkyl groups preferably have a chain length of from 1 to 6 carbon atoms. Haloalkyl is, for example, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, 2,2,2-

-5-

trifluoroethyl, 2-fluoroethyl, 2-chloroethyl, pentafluoroethyl, 1,1-difluoro-2,2,2-trichloroethyl, 2,2,3,3-tetrafluoroethyl and 2,2,2-trichloroethyl.

Alkoxy is, for example, methoxy, ethoxy, propoxy, i-propoxy, n-butoxy, isobutoxy, sec-butoxy and tert-

5 butoxy and also the isomeric pentyloxy and hexyloxy radicals.

Alkoxyalkyl groups preferably have a chain length of 1 to 6 carbon atoms containing one or more oxygen atoms. Alkoxyalkyl is, for example, methoxymethyl, methoxyethyl, ethoxymethyl, ethoxyethyl, n-propoxymethyl, n-propoxyethyl, isopropoxymethyl, isopropoxyethyl or a dialkoxyalkyl derivative such 10 as for example $-\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_3$.

Alkoxycarbonyl is for example methoxycarbonyl (which is C_1 alkoxycarbonyl), ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, tert-butoxycarbonyl, n-pentoxycarbonyl or hexoxycarbonyl.

15

The cycloalkyl groups preferably have from 3 to 6 ring carbon atoms, for example cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

As used herein, the term " $\text{C}_2\text{-C}_6$ alkynyl" refers to a straight or branched hydrocarbon chain radical

20 group consisting solely of carbon and hydrogen atoms, containing at least one triple bond, having from two to six carbon atoms, and which is attached to the rest of the molecule by a single bond. The term " $\text{C}_2\text{-C}_4$ alkynyl" and " $\text{C}_2\text{-C}_3$ alkynyl" are to be construed accordingly. Examples of $\text{C}_2\text{-C}_6$ alkynyl include, but are not limited to, ethynyl, prop-1-ynyl, but-1-ynyl, but-2-ynyl.

25 As used herein, the term " $\text{C}_2\text{-C}_6$ alkenyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one double bond, having from two to six carbon atoms, and which is attached to the rest of the molecule by a single bond. The term " $\text{C}_2\text{-C}_4$ alkenyl" and " $\text{C}_2\text{-C}_3$ alkenyl" are to be construed accordingly. Examples of $\text{C}_2\text{-C}_6$ alkenyl include, but are not limited to, prop-1-enyl, but-1-enyl, but-2-enyl.

30 Alkylsulfanyl is for example methylsulfanyl, ethylsulfanyl, propylsulfanyl, isopropylsulfanyl, butylsulfanyl, pentylsulfanyl, and hexylsulfanyl.

Alkylsulfinyl is for example methylsulfinyl, ethylsulfinyl, propylsulfinyl, isopropylsulfinyl, a butylsulfinyl, pentylsulfinyl, and hexylsulfinyl.

Alkylsulfonyl is for example methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl,

35 butylsulfonyl, pentylsulfonyl, and hexylsulfonyl.

-6-

Haloalkylsulfanyl is for example trifluoromethylsulfanyl, 2, 2, 2-trifluoroethylsulfanyl, and pentafluoroethylsulfanyl.

Haloalkylsulfinyl is for example trifluoromethylsulfinyl, 2, 2, 2-trifluoroethylsulfinyl, or pentafluoroethylsulfinyl.

5 Haloalkylsulfonyl is for example trifluoromethylsulfonyl, 2, 2, 2-trifluoroethylsulfonyl, and pentafluoroethylsulfonyl.

In the context of this invention, examples of a five- to six-membered, aromatic, partially saturated or fully saturated ring system are, but are not limited to, phenyl, pyrrolyl; pyrazolyl; isoxazolyl; furanyl; thienyl; imidazolyl; oxazolyl; thiazolyl; isothiazolyl; triazolyl; oxadiazolyl; thiadiazolyl; tetrazolyl; furyl;

10 pyridyl; pyrimidyl; pyrazinyl; pyridazinyl; triazinyl, pyranyl; pyrrolidinyl, piperidinyl; pyrrolidinyl-2-one; piperidinyl-2-one; (1H-pyrrol-1-yl)-; (1H-pyrrol-2-yl)-; (1H-pyrrol-3-yl)-; (1H-pyrazol-1-yl)-; (1H-pyrazol-3-yl)-; (3H-pyrazol-3-yl)-; (1H-pyrazol-4-yl)-; (3-isoxazolyl)-; (5-isoxazolyl)-; (2-furanyl)-; (3-furanyl)-; (2-thienyl)-; (3-thienyl)-; (1H-imidazol-2-yl)-; (1H-imidazol-4-yl)-; (1H-imidazol-5-yl)-; (2-oxazol-2-yl)-; (oxazol-4-yl)-; (oxazol-5-yl)-; (thiazol-2-yl)-; (thiazol-4-yl)-; (thiazol-5-yl)-; (isothiazol-3-yl)-; (isothiazol-5-yl)-; (1H-1,2,3-triazol-1-yl)-; (1H-1,2,4-triazol-3-yl)-; (4H-1,2,4-triazol-4-yl)-; (1H-1,2,4-triazol-1-yl)- (1,2,3-oxadiazol-2-yl)-; (1,2,4-oxadiazol-3-yl)-; (1,2,4-oxadiazol-4-yl)-; (1,2,4-oxadiazol-5-yl)-; (1,2,3-thiadiazol-2-yl)-; (1,2,4-thiadiazol-3-yl)-; (1,2,4-thiadiazol-4-yl)-; (1,3,4-thiadiazol-5-yl)-; (1H-tetrazol-1-yl)-; (1H-tetrazol-5-yl)-; (2H-tetrazol-5-yl)-; (2-pyridyl)-; (3-pyridyl)-; (4-pyridyl)-; (2-pyrimidinyl)-; (4-pyrimidinyl)-; (5-pyrimidinyl)-; (2-pyrazinyl)-; (3-pyridazinyl)-; (4-pyridazinyl)-; (1,3,5-triazin-2-yl)-; (1,2,4-triazin-5-yl)-; (1,2,4-triazin-6-yl)-; (1,2,4-triazin-3-yl)- and (furazan-3-yl)-.

In the context of this invention “mono- to polysubstituted” in the definition of the substituents, means typically, depending on the chemical structure of the substituents, monosubstituted to seven-times substituted, preferably monosubstituted to five-times substituted, more preferably mono-, di- or tri-

25 substituted.

In the context of this invention pyrimidinyl or pyridinyl as R₃ may be both linked via any carbon atom to the ring which contains the substituent G₃.

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

Compounds of formula I are preferred, wherein

G₁ is NR₄ and G₂ is C(O); and R₄ is as defined under formula I above.

35

Compounds of formula I are preferred, wherein

R₃ is hydrogen, halogen, cyano, nitro, C₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl, C₃-C₆halocycloalkyl which can be mono- or polysubstituted by substituents selected from the group consisting of halogen and cyano; or

R₃ is C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl; or

5 R₃ is phenyl which can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; or

R₃ is C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl, C₁-C₄haloalkoxy, -C(O)C₁-C₄haloalkyl, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, or C₁-C₄alkylsulfonyl; or

10 R₃ is pyrimidinyl or pyridinyl which both can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; or

R₃ is a five- to six-membered, aromatic, partially saturated or fully saturated ring system linked via a nitrogen atom to the ring which contains the substituent G₃, said ring system can be mono- or

15 polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, C₁-C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one

20 oxygen atom and not more than one sulfur atom;

G₁ is NR₄ and G₂ is C(O); or

G₁ is C(O) and G₂ is NR₅; and

R₇ and R₁₀, independently from each other, are halogen, nitro, cyano, C₁-C₄haloalkoxy, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄haloalkyl.

25

Compounds of formula I are also preferred, wherein R₃ is hydrogen, halogen, cyano, nitro, C₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl, C₃-C₆halocycloalkyl which can be mono- or polysubstituted by substituents selected from the group consisting of halogen and cyano; or

R₃ is C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl; or

30 R₃ is phenyl which can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; or

R₃ is C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl, C₁-C₄haloalkoxy, -C(O)C₁-C₄haloalkyl, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, or C₁-C₄alkylsulfonyl; or

35 R₃ is pyrimidinyl or pyridinyl which both can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; or

R₃ is a five- to six-membered, aromatic, partially saturated or fully saturated ring system linked via a nitrogen atom to the ring which contains the substituent G₃, said ring system can be mono- or

-8-

polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, C₁-C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and -C(O)C₁-C₄haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group

5 consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom; and

R₄ and R₅ are, independently from each other, C₁-C₆alkyl, C₁-C₆haloalkyl, or are C₃-C₆cycloalkyl which can be mono- or poly substituted by R₇; or are C₃-C₆cycloalkyl-C₁-C₄alkyl which can be mono- or polysubstituted by R₁₀; or

10 R₄ and R₅ are, independently from each other, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₆haloalkoxy, C₁-C₆alkoxy, C₁-C₆haloalkylsulfanyl, C₁-C₄haloalkylsulfonyl, C₁-C₆haloalkylsulfinyl or hydroxyl.

Also preferred are compounds of formula I, wherein

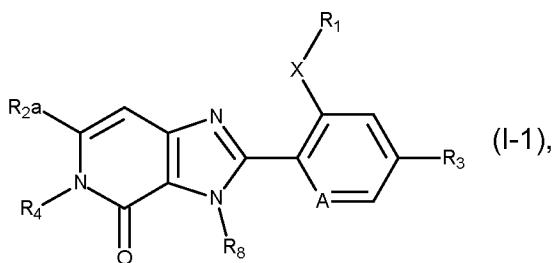
15 R₄ and R₅ are, independently from each other, C₁-C₆alkyl, C₁-C₆haloalkyl, or are C₃-C₆cycloalkyl which can be mono- or poly substituted by R₇; or are C₃-C₆cycloalkyl-C₁-C₄alkyl which can be mono- or polysubstituted by R₁₀; or

R₄ and R₅ are, independently from each other, C₁-C₆alkyl substituted by phenyl;

R₄ and R₅ are, independently from each other, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl,

20 C₂-C₆haloalkynyl, C₁-C₆haloalkoxy, C₁-C₆alkoxy, C₁-C₆haloalkylsulfanyl, C₁-C₄haloalkylsulfonyl, C₁-C₆haloalkylsulfinyl or hydroxyl.

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



25

wherein the substituents X, A, R₁, R_{2a}, R₃, R₄, R₈ are as defined under formula I above.

Preferred are compounds of formula I-1, wherein

A is C-H or N;

30 R₁ is C₁-C₄ alkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl or C₃-C₆cycloalkyl;

R_{2a} is halogen, C₁-C₄haloalkyl, cyano or C₃-C₆cycloalkyl which can be mono - or polysubstituted by substituents selected from the group consisting of halogen, cyano and C₁-C₄alkyl;

R₄ is C₁-C₄alkyl or C₁-C₄haloalkyl;

R₃ is hydrogen, halogen or C₁-C₄haloalkyl; and X and R₈ is as defined under formula I above.

-9-

Further preferred are compounds of formula I-1, wherein

A is as C-H or N;

R₁ is methyl, ethyl, n-propyl, i-propyl or cyclopropylmethyl;

5 R_{2a} is halogen, trifluoromethyl, cyano or cyclopropyl which can be monosubstituted by cyano;

R₃ is hydrogen or trifluoromethyl;

R₄ is methyl or ethyl; and X and R₈ are as defined under formula I above.

Further preferred are compounds of formula I-1, wherein

10 A is C-H or N;

R₁ is ethyl;

R_{2a} is trifluoromethyl;

R₃ is hydrogen or trifluoromethyl;

R₄ is methyl; and X and R₈ are as defined under formula I above.

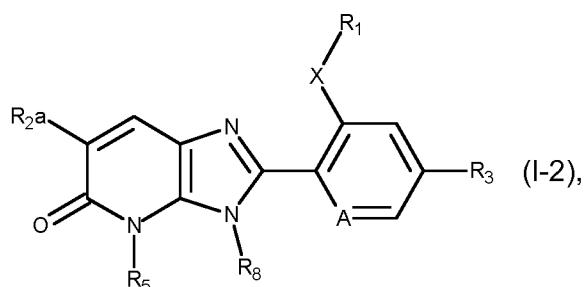
15

In all of the preferred embodiments of formula I-1 above, X is preferably S or SO₂ and independently,

R₈ is methyl.

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

20



wherein the substituents X, A, R₁, R_{2a}, R₃, R₅, R₈ are as defined under formula I above.

25 Preferred are compounds of formula I-2, wherein

A is C-H or N;

R₁ is C₁-C₄ alkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl or C₃-C₆cycloalkyl;

R_{2a} is halogen, C₁-C₄haloalkyl, cyano or C₃-C₆cycloalkyl which can be mono - or polysubstituted by substituents selected from the group consisting of halogen, cyano and C₁-C₄alkyl;

30 R₃ is hydrogen, halogen or C₁-C₄haloalkyl;

R₅ is C₁-C₄alkyl or C₁-C₄haloalkyl; and X and R₈ are as defined under formula I above.

Further preferred are compounds of formula I-2, wherein

-10-

A is as C-H or N;

R₁ is methyl, ethyl, n-propyl, i-propyl or cyclopropylmethyl;

R_{2a} is halogen, trifluoromethyl, cyano or cyclopropyl which can be monosubstituted by cyano;

R₃ is hydrogen or trifluoromethyl;

5 R₅ is methyl or ethyl; and X and R₈ are as defined under formula I above.

Further preferred are compounds of formula I-2, wherein

A is C-H or N;

R₁ is ethyl;

10 R_{2a} is trifluoromethyl;

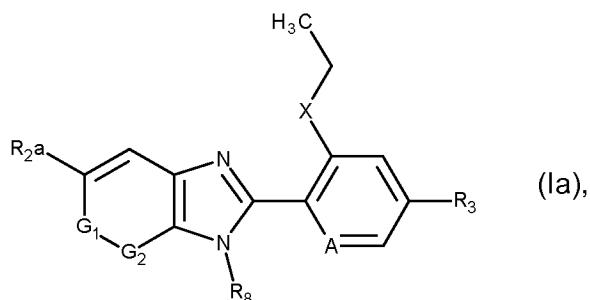
R₃ is hydrogen or trifluoromethyl;

R₅ is methyl; and X and R₈ are defined under formula I above.

In all of the preferred embodiments of formula I-2 above, X is preferably S or SO₂ and independently,

15 R₈ is methyl.

An especially preferred group of compounds of formula I is represented by the compounds of formula Ia



20 wherein

R_{2a} is C₁-C₄haloalkyl;

R₃ is hydrogen, C₁-C₄haloalkyl or phenyl which can be substituted by halogen;

A is C-H or N;

X is S or SO₂;

25 G₁ is NR₄ and G₂ is C(O); or

G₁ is C(O) and G₂ is NR₅;

R₄ is C₁-C₄alkyl;

R₅ is C₁-C₄alkyl; and

R₈ is C₁-C₄alkyl.

30

In especially preferred compounds of formula I,

R₁ is C₁-C₄alkyl;

-11-

R_{2a} is C₁-C₄haloalkyl;

R_{2b} is hydrogen;

R₃ is C₁-C₄haloalkyl;

G₁ is NR₄ and G₂ is C(O);

5 R₄ is C₁-C₆alkyl or C₂-C₆alkenyl, or R₄ is C₁-C₆alkyl substituted by phenyl; in particular R₄ is C₁-C₆alkyl, C₂-C₆alkenyl or benzyl;

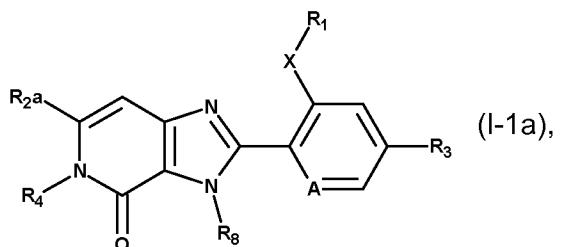
G₃ is CR₆;

R₆ is hydrogen;

X is SO₂; and

10 A is N.

A further preferred group of compounds of formula I is represented by the compounds of formula I-1a:



15 wherein

A is N or CH;

R₁ is C₁-C₄alkyl; preferably ethyl;

R_{2a} is C₁-C₄haloalkyl; preferably trifluoromethyl;

R₃ is hydrogen, halogen, C₂-C₆alkenyl, C₁-C₄haloalkyl or C₃-C₆cycloalkyl, preferably hydrogen, bromo,

20 prop-1-enyl, trifluoromethyl, pentafluoroethyl or cyclopropyl; or

R₃ is phenyl which can be mono- or di-substituted by substituents selected from the group consisting of cyano, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₄haloalkoxy and C₁-C₄haloalkyl; preferably phenyl which can be mono- or di-substituted by substituents selected from the group consisting of cyano, fluoro, chloro, methyl, ethyl, methoxy, trifluoromethoxy and trifluoromethyl; or

25 R₃ is pyrazolyl, which can be mono-substituted by C₁-C₄haloalkyl; preferably pyrazolyl, which can be mono-substituted by trifluoromethyl; or

R₃ is pyridinyl which can be mono- or di-substituted by substituents selected from the group consisting of C₁-C₄alkyl, C₁-C₄haloalkyl and halogen; preferably pyridinyl which can be mono- or di-substituted by substituents selected from the group consisting of fluoro and trifluoromethyl; or

30 R₃ is pyrimidinyl which can be mono-substituted by C₁-C₄alkoxy; preferably pyrimidinyl which can be mono-substituted by methoxy;

R₄ is C₁-C₆alkyl; preferably methyl, ethyl, propyl or butyl; or

R₄ is C₁-C₆haloalkyl; preferably 1,1,1-trifluoroethyl;

-12-

R₄ is C₁-C₄alkyl mono-substituted by cyano, C₁-C₄alkylsulfanyl, phenyl, C₁-C₄alkoxy, C₁-C₄alkoxy C₁-C₄alkoxy or C₃-C₆cycloalkyl; preferably R₄ is C₁-C₄alkyl which can be mono-substituted by cyano, phenyl, methoxy, methylthio or cyclohexyl; or

R_4 is C_2 - C_6 alkenyl or C_2 - C_6 alkynyl; preferably allyl, prop-1-enyl or but-2-ynyl; or

5 R₄ is C₂-C₆alkenyl substituted by phenyl;

R₄ is benzyl which can be mono-substituted by C₁-C₄alkoxy; preferably benzyl which can be mono-substituted by methoxy;

R_8 is C_1 - C_4 alkyl; preferably methyl; and

X is S or SO_2 .

10

Preferred compounds of formula I-1a are those, wherein

A is N or CH;

R₁ is C₁-C₄alkyl; preferably ethyl;

R_{2a} is C_1 - C_4 haloalkyl; preferably trifluoromethyl;

15

R_3 is hydrogen, halogen, C_2 - C_4 alkenyl, C_1 - C_4 haloalkyl, C_3 - C_6 cycloalkyl, or is phenyl which can be mono- or di-substituted by substituents selected from the group consisting of halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 alkoxy and C_1 - C_4 haloalkyl; or is pyrazolyl, which can be mono-substituted by C_1 - C_4 alkyl; or is pyridinyl, which can be which can be mono- or di-substituted by substituents selected from the group consisting of halogen, C_1 - C_4 alkyl, C_1 - C_4 alkoxy and C_1 - C_4 haloalkyl;

20

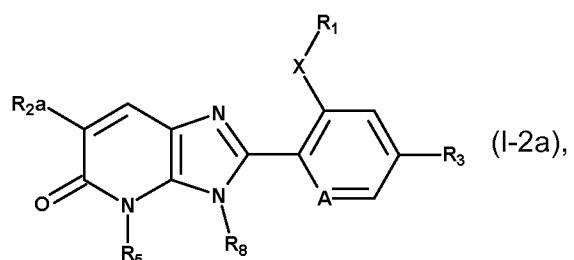
R_4 is C_1 - C_6 alkyl which can be substituted by cyano, phenyl or C_3 - C_6 cycloalkyl; wherein the phenyl group itself can be mono-substituted by C_1 - C_4 alkoxy; or is C_2 - C_6 alkynyl, C_1 - C_4 alkoxy- C_1 - C_4 alkoxy, C_4 alkoxy- C_1 - C_4 alkyl or C_1 - C_4 alkylsulfanyl- C_1 - C_4 alkyl;

R_8 is C_1 - C_4 alkyl; preferably methyl; and

X is S or SO₂.

25

Further preferred are compounds of formula I represented by the compounds of formula I-2a



wherein

30 A is N or CH; preferably N;

R₁ is C₁-C₄alkyl; preferably ethyl;

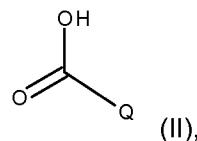
R_{2a} is hydrogen, halogen or C_1 - C_4 haloalkyl; preferably hydrogen, bromo or trifluoromethyl;

R₃ is C₁-C₄haloalkyl, phenyl or phenyl substituted by C₁-C₄haloalkyl; preferably trifluoromethyl or phenyl substituted by trifluoromethyl;

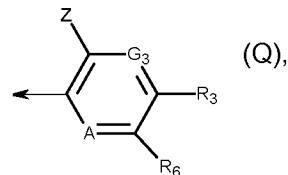
-13-

R_5 is C_1 - C_4 alkyl, preferably methyl; R_8 is C_1 - C_4 alkyl, preferably methyl; and X is S or SO_2 .

The process according to the invention for preparing compounds of formula (I) is carried out by
 5 methods known to those skilled in the art, or described for example in WO 2009/131237, WO 2011/043404, WO 2011/040629, WO 2010/125985, WO 2012/086848, WO 2013/018928, WO 2013/191113, WO 2013/180193 and WO 2013/180194, and involves reaction of a compound of formula II,

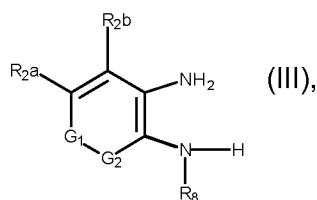


10 wherein Q is the group



wherein Z is $X-R_1$ or a leaving group, for example a halogen, and wherein X , R_1 , R_3 , R_6 , G_3 and A are as described under formula I above, and wherein the arrow in the radical Q shows the point of attachment to the carbon atom of the carboxyl group in the compound of formula II,

15 with a compound of formula III,

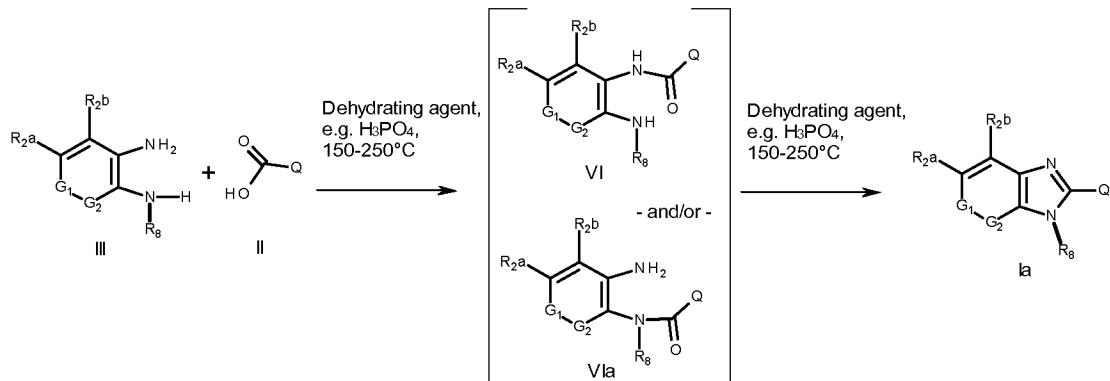


wherein R_8 , R_{2a} , R_{2b} , G_1 and G_2 are as described under formula I above, in the presence of a dehydrating agent, such as for example polyphosphoric acid at temperature between 150°C to 250°C, to yield compounds of formula Ia, wherein the substituents are as described above and under formula I.

20 Such processes are well known and have been described for example in WO 2008/128968 or WO 2006/003440. The process is summarized in scheme 1 for compounds of formula Ia:

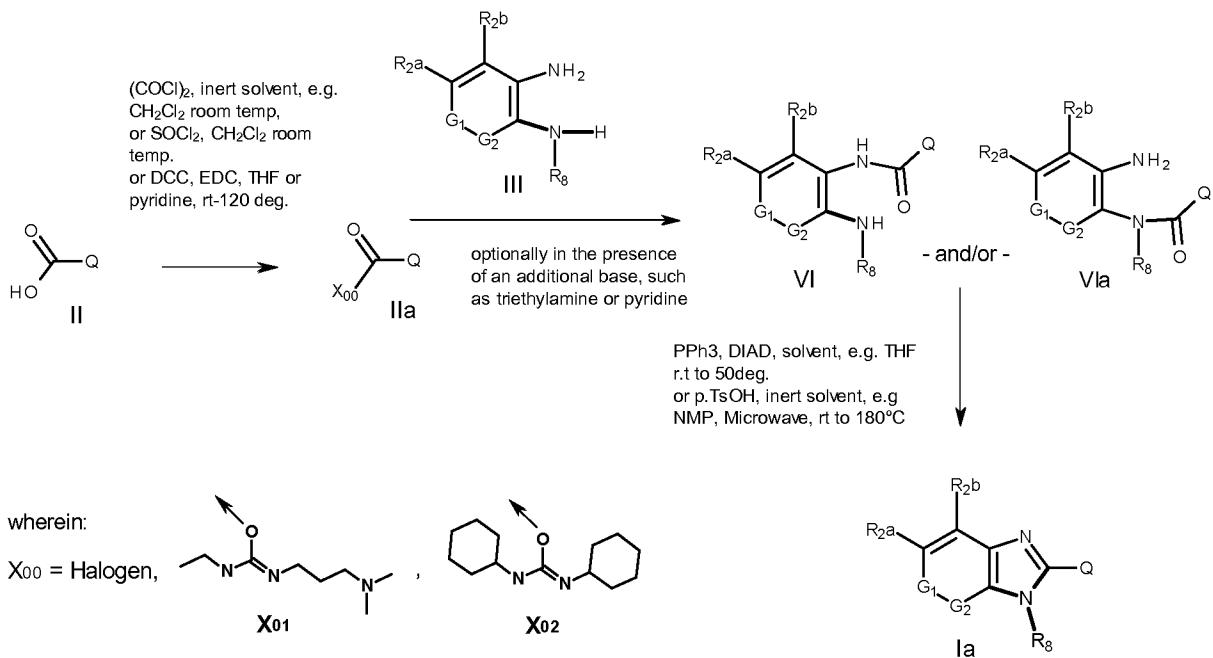
Scheme 1

-14-



As can be seen in scheme 1, the formation of compounds of formula Ia occurs through the intermediacy of a compound of formula VI (and/or its position isomer VIa). Intermediate VI or intermediate VIa may form as a pure entity, or intermediates VI and VIa may arise as a mixture of regioisomeric acylation products. It is in many cases advantageous to thus prepare compounds of formula (I) through such intermediates VI/VIa, which may be isolated and optionally purified. This is illustrated for compounds of formula Ia in scheme 2:

Scheme 2



10

Compounds of the formula VI and/or VIa (or a mixture thereof), or a salt thereof, wherein Q is as defined above, and wherein R_8 , R_{2a} , R_{2b} , G_1 and G_2 are as described under formula I above, may be prepared by

15 i) activation of compound of formula II, wherein Q is as defined above, by methods known to those skilled in the art and described in, for example, *Tetrahedron*, 2005, 61 (46), 10827-10852, to form an activated species IIa, wherein Q is as defined above and wherein X_{00} is halogen, preferably chlorine.

-15-

For example, compounds IIa where X_{00} is halogen, preferably chlorine, are formed by treatment of II with, for example, oxallyl chloride (COCl)₂ or thionyl chloride SOCl_2 in the presence of catalytic quantities of N,N-dimethylformamide DMF in inert solvents such as methylene chloride CH_2Cl_2 or tetrahydrofuran THF at temperatures between 20 to 100°C, preferably 25°C. Alternatively, treatment of 5 compounds of formula II with, for example, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide EDC or dicyclohexyl carbodiimide DCC will generate an activated species IIa, wherein X_{00} is X_{01} or X_{02} respectively, in an inert solvent, such as pyridine or tetrahydrofuran THF, optionally in the presence of a base, such as triethylamine, at temperatures between 25-180°C; followed by

ii) treatment of the activated species IIa with a compound of formula III (or a salt thereof), wherein R_8 ,

10 R_{2a} , R_{2b} , G_1 and G_2 are as described under formula I above, optionally in the presence of a base, such as triethylamine or pyridine, in an inert solvents such as dichloromethane, tetrahydrofuran, dioxane or toluene, at temperatures between 0 and 80°C, to form the compounds of formula VI and/or VIa (or a mixture thereof).

Compounds of formula VI and/or VIa (or a mixture thereof) may further be converted into compounds

15 of formula Ia, wherein Q is as defined above, and wherein R_8 , R_{2a} , R_{2b} , G_1 and G_2 are as described under formula I above, by dehydration, eg. by heating the compounds VI and/or VIa (or a mixture thereof) in the presence of an acid catalyst, such as for example methane sulfonic acid, or *para*-toluene sulfonic acid TsOH, in an inert solvent such as N-methyl pyrrolidine NMP at temperatures between 25-180°C, preferably 100-170°C, optionally under microwave conditions. Such processes 20 have been described previously, for example, in WO 2010/125985.

Compounds of formula Ia2wherein Q is as defined above, and wherein Z is a leaving group, for example halogen, preferably fluorine or chlorine, and wherein R_8 , R_{2a} , R_{2b} , G_1 and G_2 are as described under formula I above, can be reacted with compounds of formula V

25 $R_1\text{-SH}$ (V),

or a salt thereof, wherein R_1 is as defined in formula I, optionally in the presence of a suitable base, such as alkali metal carbonates, for example sodium carbonate and potassium carbonate, or alkali metal hydrides such as sodium hydride, or alkali metal hydroxides such as sodium hydroxide and 30 potassium hydroxide, in an inert solvent at temperatures preferably between 25-120°C, to generate compounds of formula Ib, a subgroup of formula I above, wherein R_1 is as described under formula I above, and in which R_3 , R_6 , G_3 , A, R_8 , R_{2a} , R_{2b} , G_1 and G_2 are as described under formula I above.

Examples of solvent to be used include ethers such as THF, ethylene glycol dimethyl ether, tert-butylmethyl ether, and 1,4-dioxane, aromatic hydrocarbons such as toluene and xylene, nitriles such

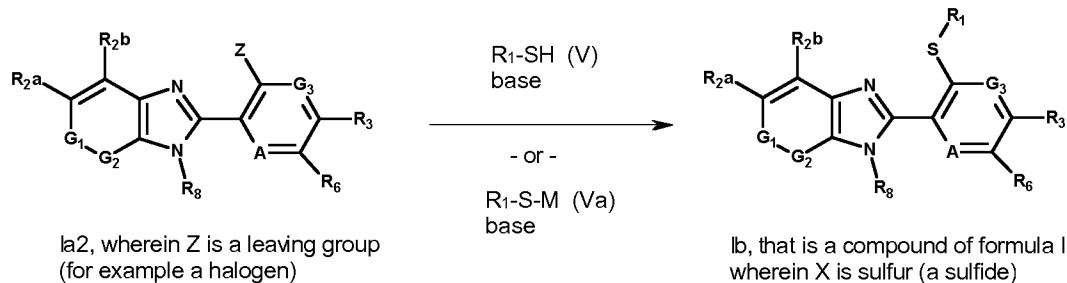
35 as acetonitrile or polar aprotic solvents such as N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl-2-pyrrolidone or dimethyl sulfoxide. Similar chemistry has been previously described, as for example in WO2013/018928. Examples of salts of the compound of formula V include compounds of the formula Va

R₁-S-M (Va),

wherein R₁ is as defined above and wherein M is, for example, sodium or potassium. This is illustrated

5 for compounds of formula Ib in scheme 3:

Scheme 3

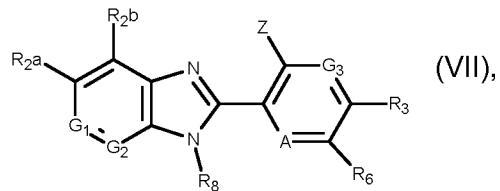


10 Alternatively, this reaction can be carried out in the presence of a palladium catalyst, such as tris(dibenzylideneacetone)dipalladium(0), in the presence of a phosphor ligand, such as xanthphos, in an inert solvent, for example, xylene at temperatures between 100-160°C, preferably 140°C, as described by Perrio et al. in Tetrahedron 2005, 61, 5253-5259.

15 The subgroup of compounds of formula I, wherein X is SO (sulfoxide) and/or SO₂ (sulfone), may be obtained by means of an oxidation reaction of the corresponding sulfide compounds of formula I, wherein X is S (i.e. a compound of formula Ib above), involving reagents such as, for example, m-chloroperoxybenzoic acid (mCPBA), hydrogen peroxide, oxone, sodium periodate, sodium hypochlorite or tert-butyl hypochlorite amongst other oxidants. The oxidation reaction is generally 20 conducted in the presence of a solvent. Examples of the solvent to be used in the reaction include aliphatic halogenated hydrocarbons such as dichloromethane and chloroform; alcohols such as methanol and ethanol; acetic acid; water; and mixtures thereof. The amount of the oxidant to be used in the reaction is generally 1 to 3 moles, preferably 1 to 1.2 moles, relative to 1 mole of the sulfide compounds Ib to produce the sulfoxide compounds I (wherein X=SO), and preferably 2 to 2.2 moles of 25 oxidant, relative to 1 mole of the sulfide compounds Ib to produce the sulfone compounds I (wherein X=SO₂). Such oxidation reactions are disclosed, for example, in WO 2013/018928.

30 Compounds of formula Ic, a subgroup of formula Ia above, wherein G₁ is NR₄ and G₂ is C(O), and wherein Z is X-R₁ or a leaving group, for example halogen, preferably fluorine or chlorine, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, could be prepared from compounds of formula (VII)

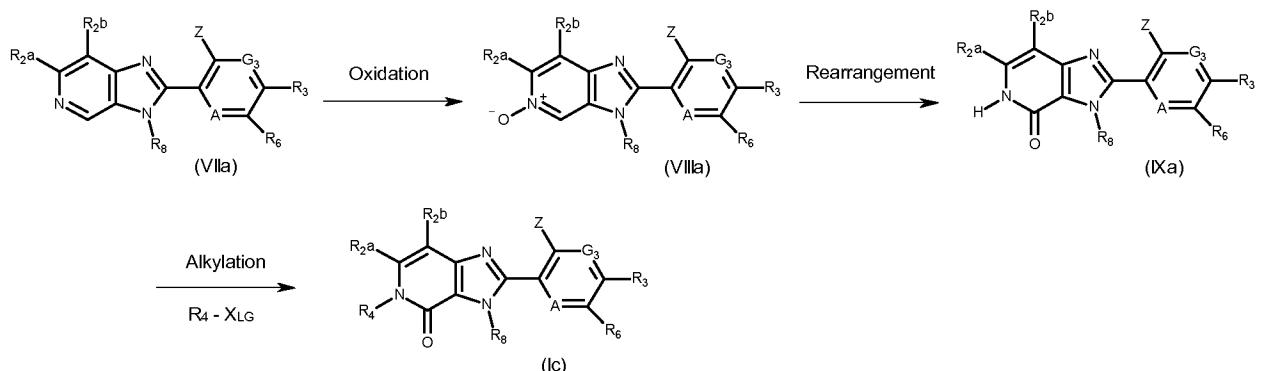
-17-



wherein G_1 is nitrogen and G_2 is CH (linked by a double bond; thus defining compound VIIa), and in which Z is $X-R_1$ or a leaving group, for example halogen, and wherein X , R_1 , R_{2a} , R_{2b} , R_3 , R_6 , R_8 , G_3 and A are as described under formula I above, via formation of an N-oxide of formula VIIia, followed by rearrangement to a compound of formula IXa and alkylation of compound IXa with a reagent of formula R_4-X_{LG} . This is illustrated for compounds of formula Ic, from compounds of formula VII wherein G_1 is N and G_2 is CH (that is a compound of formula VIIa), in scheme 4:

Scheme 4

10



N-oxide compounds of formula (VIIia), wherein Z is $X-R_1$ or a leaving group, for example halogen, and wherein X , R_1 , R_3 , R_6 , G_3 , A , R_8 , R_{2a} and R_{2b} are as described under formula I above, may be

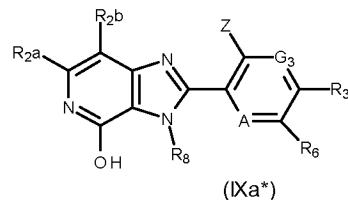
15 prepared from a compound of formula (VIIa), wherein Z is $X-R_1$ or a leaving group, for example halogen, and wherein X , R_1 , R_3 , R_6 , G_3 , A , R_8 , R_{2a} and R_{2b} are as described under formula I above, via oxidation by reaction with a suitable oxidizing agent, such as meta-perbenzoic acid or hydrogen peroxide in the appropriate inert solvent, such as for example dichloromethane or chloroform. Such oxidations are known from the literature, for example from WO 2013/018928, WO 2010/073128 or

20 Synthetic Communications 2013, 43(8), 1092-1100.

Compounds of formula (IXa) may be prepared from a compound of formula (VIIia), wherein for both compounds Z is $X-R_1$ or a leaving group, for example halogen, and wherein X , R_1 , R_3 , R_6 , G_3 , A , R_8 , R_{2a} and R_{2b} are as described under formula I above, via rearrangement, for example mediated by anhydride reagents, such as trifluoroacetic anhydride, in the appropriate solvent, such as N,N-dimethylformamide. Such rearrangement reactions are well known from the literature, for example from Journal of Organic Chemistry 196), 26, 428-430 or Journal of Heterocyclic Chemistry 1976, 13(6), 1197-2000.

-18-

Compounds of formula (IXa), wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, may exist in a tautomeric form (IXa*), or in a mixture thereof.

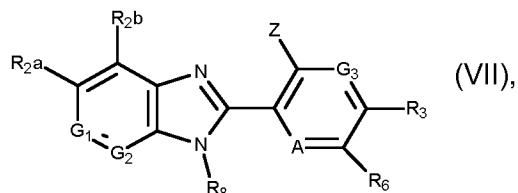


5

Compounds of formula (Ic), wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, and in which R₄ is as defined under formula I above, may be prepared from a compound of formula (IXa), wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, via alkylation with a reagent R₄-X_{LG}, wherein R₄ is as described in compounds of formula I and X_{LG} is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as cesium carbonate or sodium hydride in an appropriate solvent such as N,N-dimethylformamide, N,N-dimethylacetamide or acetonitrile. Such alkylation is well known from the literature, for example from European Journal of Organic Chemistry 2002 (11), 1763-1769.

10

Compounds of formula Id, a subgroup of formula Ia above, wherein G₂ is NR₅ and G₁ is C(O), and wherein Z is X-R₁ or a leaving group, for example halogen, preferably fluorine or chlorine, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, could be prepared from compounds of formula (VII)

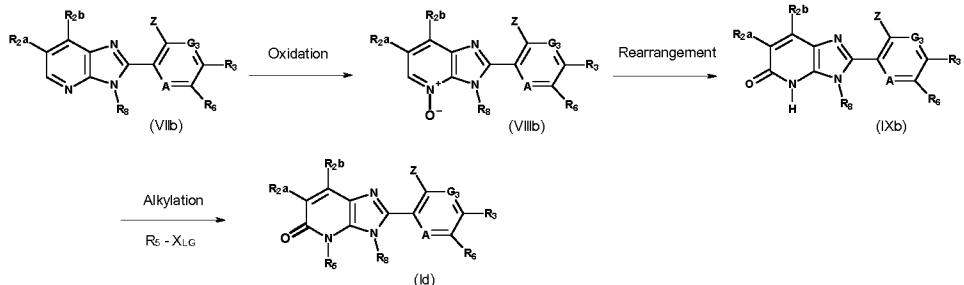


20

wherein G₂ is nitrogen and G₁ is CH (linked by a double bond; thus defining compound VIIb), and in which Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R_{2a}, R_{2b}, R₃, R₆, R₈, G₃ and A are as described under formula I above, via formation of an N-oxide of formula VIIb, followed by rearrangement to a compound of formula IXb and alkylation of compound IXb with a reagent of formula R₅-X_{LG}. This is illustrated for compounds of formula Id, from compounds of formula VII wherein G₂ is N and G₁ is CH (that is a compound of formula VIIb), in scheme 5:

Scheme 5

-19-

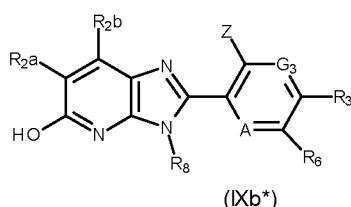


N-oxide compounds of formula (VIIIb), wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, may be prepared from a compound of formula (VIIb), wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, via oxidation by reaction with a suitable oxidizing agent, such as meta-perbenzoic acid or hydrogen peroxide in the appropriate inert solvent, such as for example dichloromethane or chloroform. Such oxidations are known from the literature, for example from WO 2013/018928, WO 2010/073128 or Synthetic Communications 2013, 43(8), 1092-1100.

5 Compounds of formula (IXb) may be prepared from a compound of formula (VIIIb), wherein for both compounds Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, via rearrangement, for example mediated by anhydride reagents, such as trifluoroacetic anhydride, in the appropriate solvent, such as N,N-dimethylformamide. Such rearrangement reactions are well known from the literature, for example from Journal of Organic Chemistry 196), 26, 428-430 or Journal of Heterocyclic Chemistry 1976, 13(6), 1197-2000.

10 Compounds of formula (IXb) may be prepared from a compound of formula (VIIIb), wherein for both compounds Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, via rearrangement, for example mediated by anhydride reagents, such as trifluoroacetic anhydride, in the appropriate solvent, such as N,N-dimethylformamide. Such rearrangement reactions are well known from the literature, for example from Journal of Organic Chemistry 196), 26, 428-430 or Journal of Heterocyclic Chemistry 1976, 13(6), 1197-2000.

15 Compounds of formula (IXb), wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, may exist in a tautomeric form (IXb*), or in a mixture thereof.



20 Compounds of formula (Id), wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, and in which R₅ is as defined under formula I above, may be prepared from a compound of formula (IXb), wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, via alkylation with a reagent $R_5 - X_{LG}$, wherein R₄ is as described in compounds of formula I and X_{LG} is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium hydride in an appropriate solvent such as N,N-dimethylformamide, N,N-dimethylacetamide or

-20-

acetonitrile. Such alkylation is well known from the literature, for example from European Journal of Organic Chemistry 2002 (11), 1763-1769.

Compounds of formula VIIb, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein

5 X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, have been described previously, for example in, WO2013/018928 or WO2012/086848.

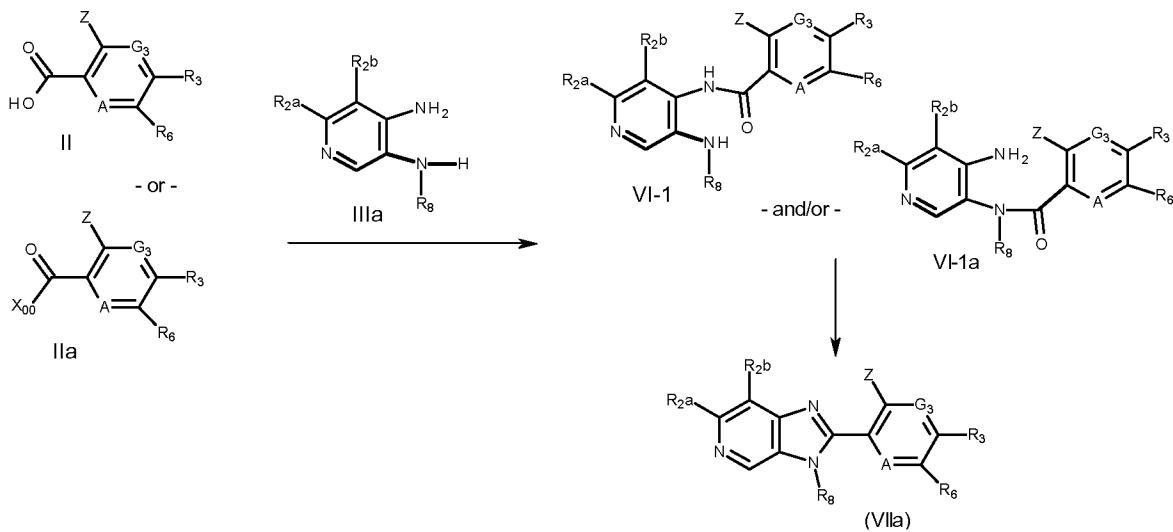
Compounds of formula VIIa, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein

10 X, R₁, R₃, R₆, G₃, A, R₈, R_{2a} and R_{2b} are as described under formula I above, may be prepared by

reaction between compounds of formula II respectively IIa, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃ and A are as described under formula I above, and in which X₀₀ is as described above, and compounds of formula IIIa, wherein R₈, R_{2a} and R_{2b} are as described under formula I above, under similar conditions as for the preparation of compounds of formula Ia from compounds of formula II/IIa and III described above (see scheme 1 and 2). This is

15 illustrated for compounds of formula VIIa in scheme 6:

Scheme 6



Analogously to descriptions in schemes 1 and 2, the formation of compounds of formula VIIa occurs

20 through the intermediacy of compounds of formula VI-1 and/or VI-1a (or a mixture thereof), or salts thereof, which optionally may be isolated and purified.

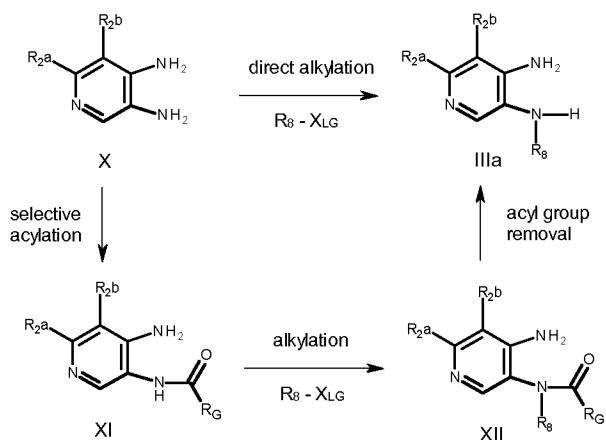
Compounds of the formula IIIa, wherein R₈, R_{2a} and R_{2b} are as described under formula I above, may be prepared from diamino compounds of formula X, wherein R_{2a} and R_{2b} are as described under

25 formula I above, by means of a direct alkylation with R₈-X_{LG}, wherein R₈ is as described under formula I above and wherein X_{LG} is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium

-21-

hydride, in a appropriate solvent such as for example N,N-dimethylformamide, N,N-dimethylacetamide or acetonitrile (scheme 7).

Scheme 7



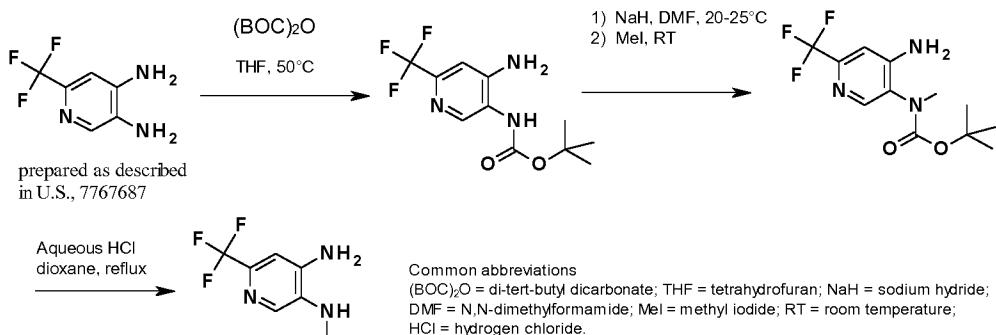
5

Alternatively, the sequence to prepare compounds of formula IIIa from compounds of formula X, may involve i. a selective acylation of compound X to form a compound of formula XI, wherein R_{2a} and R_{2b} are as described under formula I above and wherein the acylation agent is for example di-tert-butyl dicarbonate (leading to compound XI wherein R_G is tert-butoxy), in an ether solvent, such as for example, tetrahydrofuran or dioxane; ii. alkylation of compound XI with $\text{R}_8-\text{X}_{\text{LG}}$, wherein R_8 is as described under formula I above and wherein X_{LG} is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium hydride, in a appropriate solvent such as for example N,N-dimethylformamide, N,N-dimethylacetamide or acetonitrile, to generate a compound of formula XII, wherein R_8 , R_{2a} and R_{2b} are as described under formula I above and wherein R_G is for example tert-butoxy; and finally iii. deacylation of compound XII to form the compound of formula IIIa, wherein R_8 , R_{2a} and R_{2b} are as described under formula I above. When R_G is for example tert-butoxy, conditions for the acyl group removal include, for example, treatment of compound XII with hydrogen halide, in particular hydrogen chloride or hydrogen bromide, in solvents such as ethers (for example diethyl ether, tetrahydrofuran or dioxane) or acetic acid. Alternatively, compound XII may also be treated with, for example, trifluoroacetic acid, in optional presence of an inert solvent, such as for example dichloromethane or chloroform, to form a compound of formula IIIa.

This alternative approach to prepare compounds of formula IIIa is described in more details in scheme 8 for the particular situation where R_{2b} is H, R_{2a} is CF_3 , R_8 is CH_3 , and R_G is tert-butoxy:

Scheme 8

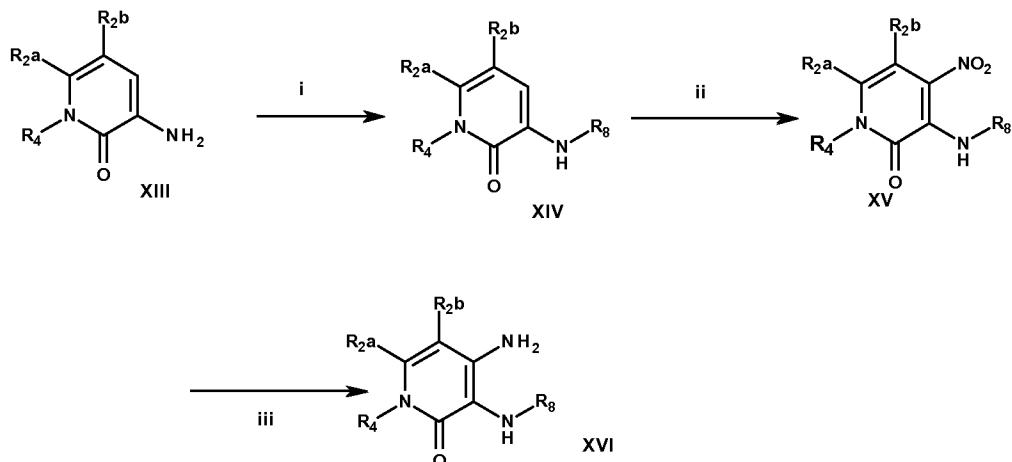
-22-



Diamino compounds of formula (X) are either known, commercially available or may be made by methods known to a person skilled in the art, for example in analogy to a preparation method described in US 7767687.

5 Alternatively, the sequence to prepare compounds of formula XVI wherein R_{2a}, R_{2b}, R₄ and R₈ are as described under formula I above, from compounds of formula XIII, may involve i. alkylation of compound XIII with R₈-X_{LG}, wherein R₈ is as described under formula I above and wherein X_{LG} is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium hydride, in an appropriate 10 solvent such as for example N,N-dimethylformamide, N,N-dimethylacetamide or acetonitrile, to generate a compound of formula XIV, wherein R₈, R_{2b}, R₄ and R_{2a} are as described under formula I above; ii. a reaction of nitration of compound XIV in classical conditions, for example, see for example, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Fourth Edition by Jerry March, 1992 (Publisher Wiley New York, N. Y.) p 523-525; and finally iii. a reaction of reduction of compound 15 XV in classical conditions, for example, see for example, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Fourth Edition by Jerry March, 1992 (Publisher Wiley New York, N. Y.) p 1216-1217. See scheme 9.

Scheme 9



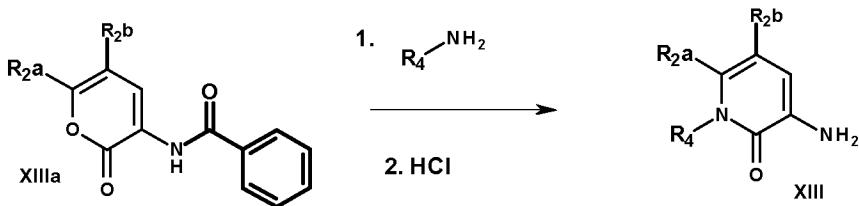
-23-

Compounds of formula XIII may be made by methods known to a person skilled in the art, for example Synthesis 2005, No. 8, pp 1269–1278 and Synthesis 2011, No. 7, pp 1149–1156.

Compounds of formula XIII may be prepared by methods known to a person skilled in the art. For example via the reaction of compound XIIIa with the appropriate amine (scheme 9a). Compounds of

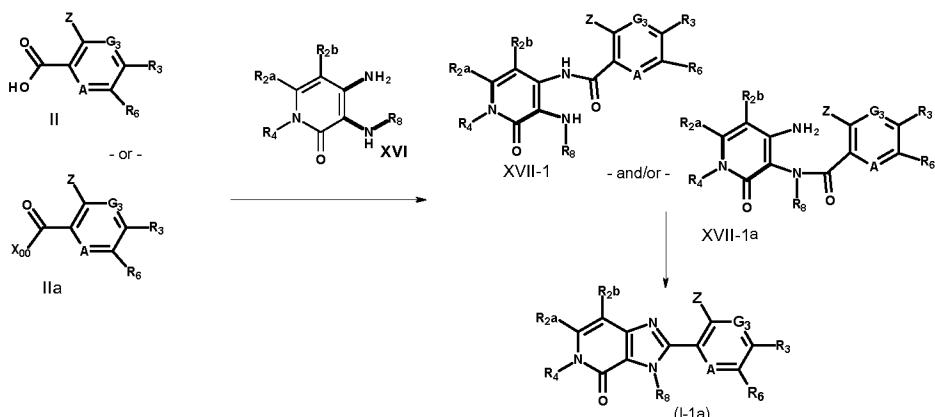
5 formula XIIIa may be made by methods known to a person skilled in the art. See, for example Synthesis 2005, No. 8, pages 1269–1278 and Synthesis 2011, No. 7, pages 1149–1156.

Scheme 9a



10 Compounds of formula I-1a, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R_{2b}, R₃, R₆, G₃, A, R₈ and R_{2a} are as described under formula I above, may be prepared by reaction between compounds of formula II respectively IIa, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R₃, R₆, G₃ and A are as described under formula I above, and in which X₀₀ is as described above, and compounds of formula XVI, wherein R₈ and R_{2a} are as described under formula I above, under similar conditions as for the preparation of compounds of formula Ia from compounds of formula II/IIa and III described above (see scheme 1 and 2). This is illustrated for compounds of formula XVI in scheme 10:

Scheme 10



20

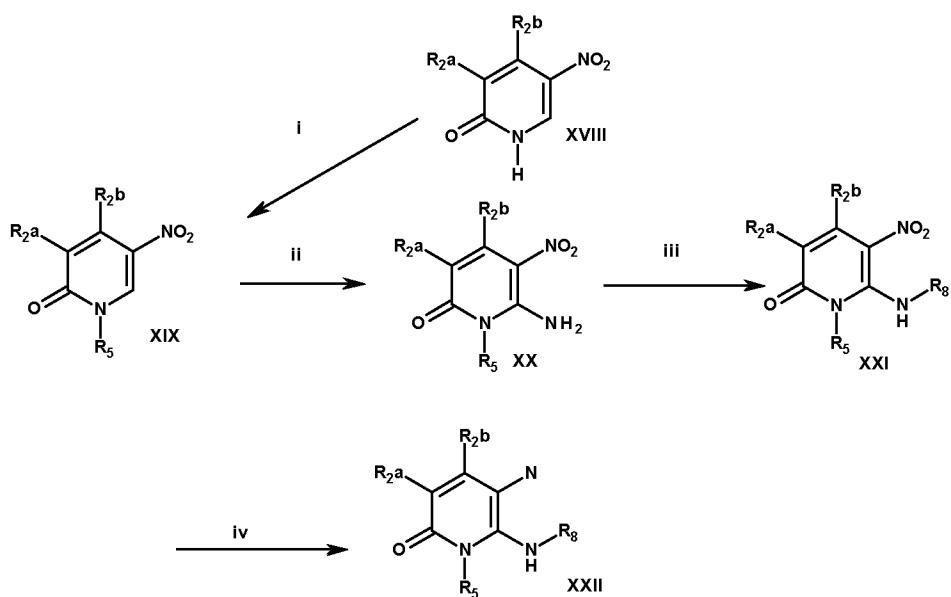
Alternatively, the sequence to prepare compounds of formula XXII wherein R_{2a}, R₄ and R₈ are as described under formula I above, from compounds of formula XVIII, may involve i. alkylation of

-24-

compound XVIII with R_5-X_{LG} , wherein R_5 is as described under formula I above and wherein X_{LG} is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as sodium carbonate, potassium carbonate or cesium carbonate, or sodium hydride, in an appropriate solvent such as for example N,N-dimethylformamide, N,N-dimethylacetamide or acetonitrile, to

5 generate a compound of formula XIX, wherein R_8 , R_4 and R_{2a} are as described under formula I above ;
 ii. a reaction of Vicarious nucleophilic substitution (VNS) reaction of compound XIX in classical conditions, for example, J. Org. Chem., Vol. 61, No. 2, 1996 p 442; iii. . alkylation of compound XX with R_8-XLG , wherein R_8 is as described under formula I above and wherein XLG is a leaving group, such as halogen, preferably iodine, bromine or chlorine, in presence of a base, such as sodium
 10 carbonate, potassium carbonate or cesium carbonate, or sodium hydride, in an appropriate solvent such as for example N,N-dimethylformamide, N,N-dimethylacetamide or acetonitrile, to generate a compound of formula XXI, wherein R_8 , R_4 and R_{2a} are as described under formula I above and finally
 iv. a reaction of reduction of compound XXI in classical conditions, for example, see for example, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Fourth Edition by Jerry March,
 15 1992 (Publisher Wiley New York, N. Y.) p 1216-1217. See scheme 11.

Scheme 11



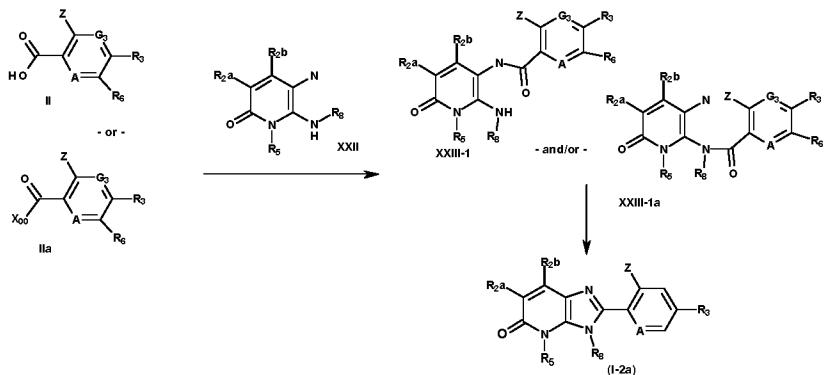
Compounds of formula XVIII are commercially available or may be made by methods known to a person skilled in the art.

20 Compounds of formula I-2a, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R_{2a}, R_{2b}, R₃, R₆, G₃, R₈ and A are as described under formula I above, may be prepared by reaction between compounds of formula II respectively IIa, wherein Z is X-R₁ or a leaving group, for example halogen, and wherein X, R₁, R_{2a}, R_{2b}, R₃, R₆, G₃ and A are as described under formula I above, and in which X₀₀ is as described above, and compounds of formula XXII, wherein R₅, R₈ and

-25-

R_{2a} are as described under formula I above, under similar conditions as for the preparation of compounds of formula Ia from compounds of formula II/Ila and III described above (see scheme 1 and 2). This is illustrated for compounds of formula XXII in scheme 12:

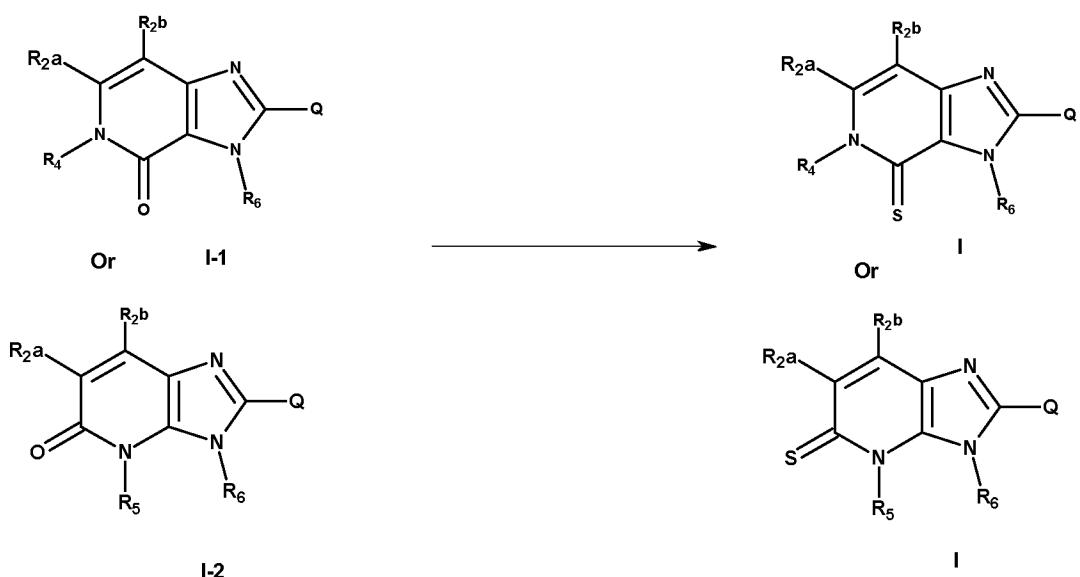
Scheme 12



5

Compounds of formula I, wherein Y is S, can be prepared (scheme 13) by reacting compounds of formula I-1 or I-2, wherein Y is O with a reagent that could transfer a sulphur atom such as, for example, the Lawesson's reagent in a solvent such as, for example dimethylformamide or toluene, usually at temperature between 50 to 150°C. This type of transformation is known to a person skilled in the art and are, for example, described in Tetrahedron (2007), 63(48), 11862-11877 or 10 US20120309796.

Scheme 13



Compounds of formula Ic, wherein A, R₁, R_{2a}, R_{2b}, R₃, R₆, G₁, G₂ and X Q as defined in formula I above, can be prepared (as shown in scheme 14) by a Suzuki reaction, which involves for example,

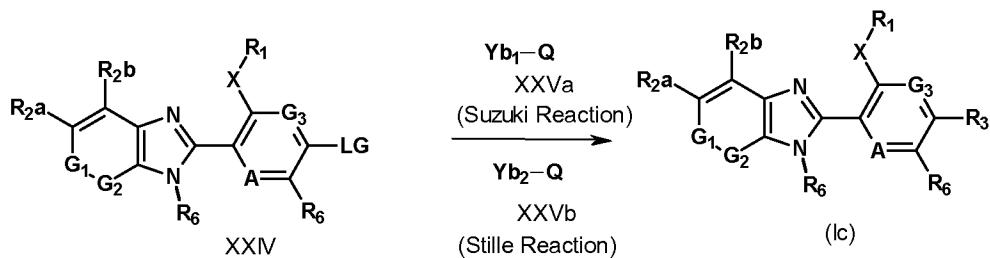
-26-

reacting compounds of formula XXIV, wherein LG is a leaving group, for example, chlorine, bromine or iodine, or an aryl- or alkylsulfonate such as trifluoromethanesulfonate with compounds of formula XXVa, wherein Y_{b1} can be a boron-derived functional group, as for example $B(OH)_2$ or $B(OR_{b1})_2$ wherein R_{b1} can be a C_1 - C_4 alkyl group or the two groups OR_{b1} can form together with the boron atom

5 a five membered ring, as for example a pinacol boronic ester. The reaction can be catalyzed by a palladium based catalyst, for example *tetrakis(triphenylphosphine)-palladium* or $(1,1'\text{bis(diphenylphosphino)-ferrocene})\text{dichloropalladium-dichloromethane}$ (1:1 complex), in presence of a base, like sodium carbonate or cesium fluoride, in a solvent or a solvent mixture, like, for example a mixture of 1,2-dimethoxyethane and water, or of dioxane and water, preferably under an inert

10 atmosphere. The reaction temperature can preferentially range from room temperature to the boiling point of the reaction mixture. Such Suzuki reactions are well known to those skilled in the art and have been reviewed, for example *J.Orgmet. Chem.* 576, **1999**, 147–168.

Scheme 14:



15 Alternatively, compounds of formula I can be prepared by a Stille reaction of compounds of formula XXVb wherein Y_{b2} is a trialkyl tin derivative, preferably tri-n-butyl tin, with compounds of formula XXIV. Such Stille reactions are usually carried out in the presence of a palladium catalyst, for example *tetrakis(triphenylphosphine)palladium(0)*, or $(1,1'\text{bis(diphenylphosphino)-ferrocene})\text{dichloropalladium-dichloromethane}$ (1:1 complex), in an inert solvent such as DMF, acetonitrile, or dioxane, optionally in

20 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.

25 In the particular case where compounds of formula I have the group R_3 attached through a nitrogen atom (i.e. those situations where R_3 is a nitrogen containing heteroaromatic system), these compounds can be advantageously accessed by reacting a compound of the formula XXIV, wherein LG is a leaving group like, for example, chlorine, bromine or iodine with a compound of the formula XXVI ($H-R_3$), wherein R_3 is as described in compounds of formula I, with the condition that the

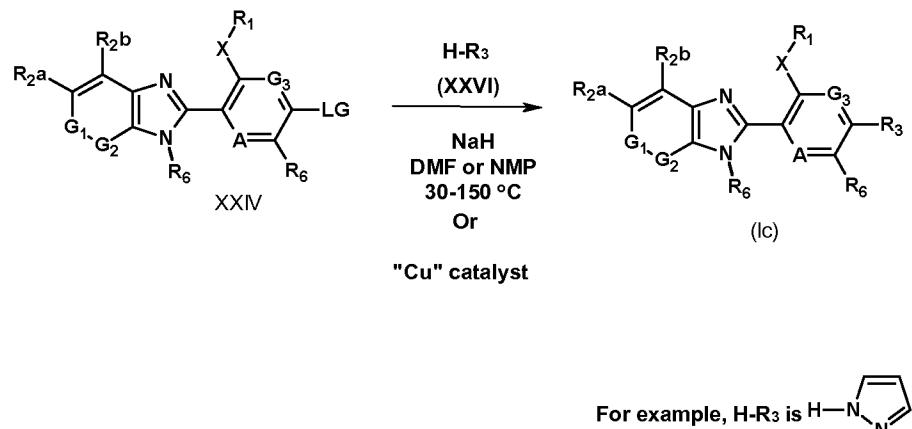
30 attachment point is a nitrogen atom. This reaction is well known in the literature (call Ullmann reaction or variation around this type of reaction), see for example *Coord. Chem. Rev.* 2004, 248, 2337-2364, *Tetrahedron*, 67(29), 5282-5288; 2011, *Angew. Chem., Int. Ed.* 2003, 42, 5400-5449; *Synlett* 2003,

-27-

2428-2439; (d) Manifar, T.; Ind. Eng. Chem. Res. 2005, 44, 789-798. The reaction is commonly performed with one to two equivalents of a base, like potassium phosphate, in presence of a copper catalyst, like for example copper (I) iodine and under an oxygen-containing atmosphere. The reaction can be run in an inert solvent, like dioxane or toluene, usually at temperature between 50 to 150°C and in presence or not of a additional ligand such as for example diamine ligands (e.g. *trans*-cyclohexyldiamine.) or, for example, dibenzylideneacetone (dba) and 1,10-phenanthroline. Alternatively compounds of formula I can be prepared from compounds of formula Iaa wherein A, G₁, G₂, R₁, R₂, R₃, R₇, X, X₁, and Q are as previously defined and wherein LG is a leaving group like, for example, fluorine or chlorine, by reaction of the heterocycle H-Q (which contains a an appropriate NH functionality), in the presence of a base, for example an alkaline metal hydride such as sodium hydride, or an alkali metal carbonate, for example cesium or potassium carbonate, in an appropriate solvent such as N-methyl pyrrolidone or DMF at temperatures between 30-150°C. The reaction is illustrated, for example, when H-Q is the heterocycle J-19 in scheme 15, which gives compounds of formula Iaa.

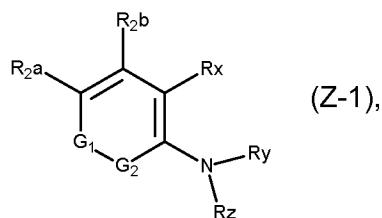
15

Scheme 15



Alternatively, the O of the C(O) can be transformed on S on previous intermediates such as for example, compounds of formula XVIII or XIX.

20 Compounds of the formula Z-1



-28-

wherein G₁, G₂, R_{2a}, and R_{2b} are as defined under formula I above;

Rx is NO₂ or NH₂; Ry is hydrogen and Rz is C₁-C₄alkyl; are novel and especially prepared for the preparation of the compounds of formula I and therefore constitute a further object of this invention.

5 The preferred embodiments of the substituents G₁, G₂, R_{2a}, and R_{2b} as described under formula I above are also valid for the compounds of formula Z-1.

For preparing all further compounds of the formula (I) functionalized according to the definitions of III and Q, there are a large number of suitable known standard methods, for example alkylation,

10 halogenation, acylation, amidation, oximation, oxidation and reduction, the choice of the preparation methods which are suitable depending on the properties (reactivity) of the substituents in the intermediates.

The reactants can be reacted in the presence of a base. Examples of suitable bases are alkali metal

15 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

20 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-

25 (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

30 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 reaction is 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

35 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.

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

5 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

10 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.

15

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.

20

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.

25

The compounds of formula I and, where appropriate, the tautomer's 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.

30

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

35

-30-

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

5 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
10 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.

15

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.

20

N-oxides can be prepared by reacting a compound of the formula I with a suitable oxidizing agent, for example the H₂O₂/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.* **1989**, 32, 2561 or WO 2000/15615.

25

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.

30

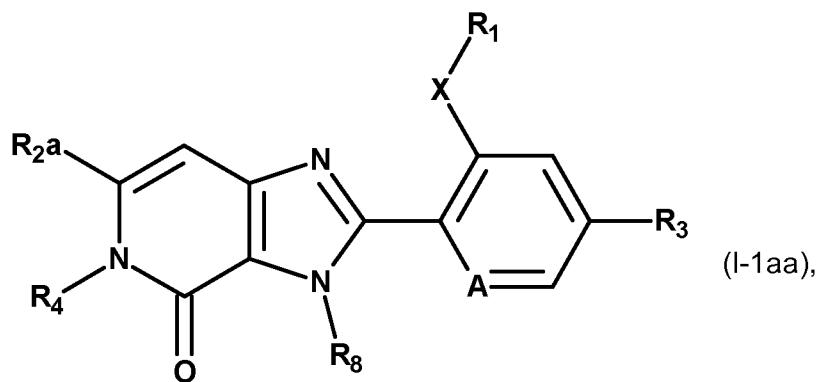
The compounds of formula I and, where appropriate, the tautomers thereof, in each case in free form or in salt form, can, if appropriate, also be obtained in the form of hydrates and/or include other solvents, for example those which may have been used for the crystallization of compounds which are present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

35

The compounds according to the following Tables 1 to 2 below 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. "Ph" represents the phenyl group.

Table 1: This table discloses the 10 compounds of the formula I-1aa:

-31-

Table 1:

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₄	R ₈
1.001	S	-CH ₂ CH ₃	H	CH	CF ₃	CH ₃	CH ₃
1.002	SO ₂	-CH ₂ CH ₃	H	CH	CF ₃	CH ₃	CH ₃
1.003	S	-CH ₂ CH ₃	H	N	CF ₃	CH ₃	CH ₃
1.004	SO ₂	-CH ₂ CH ₃	H	N	CF ₃	CH ₃	CH ₃
1.005	S	-CH ₂ CH ₃	CF ₃	CH	CF ₃	CH ₃	CH ₃
1.006	SO ₂	-CH ₂ CH ₃	CF ₃	CH	CF ₃	CH ₃	CH ₃
1.007	S	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
1.008	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
1.009	S	-CH ₂ CH ₃	4-Cl-Ph-	N	CF ₃	CH ₃	CH ₃
1.010	SO ₂	-CH ₂ CH ₃	4-Cl-Ph-	N	CF ₃	CH ₃	CH ₃

and the N-oxides of the compounds of Table 1.

5

Table 2: This table discloses the 10 compounds of the formula I-1b:

-32-

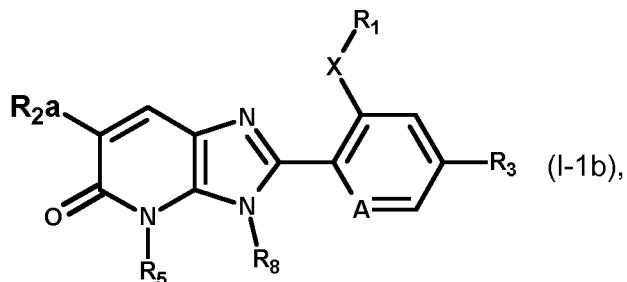


Table 2:

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₅	R ₈
2.001	S	-CH ₂ CH ₃	H	CH	CF ₃	CH ₃	CH ₃
2.002	SO ₂	-CH ₂ CH ₃	H	CH	CF ₃	CH ₃	CH ₃
2.003	S	-CH ₂ CH ₃	H	N	CF ₃	CH ₃	CH ₃
2.004	SO ₂	-CH ₂ CH ₃	H	N	CF ₃	CH ₃	CH ₃
2.005	S	-CH ₂ CH ₃	CF ₃	CH	CF ₃	CH ₃	CH ₃
2.006	SO ₂	-CH ₂ CH ₃	CF ₃	CH	CF ₃	CH ₃	CH ₃
2.007	S	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
2.008	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
2.009	S	-CH ₂ CH ₃	4-Cl-Ph-	N	CF ₃	CH ₃	CH ₃
2.010	SO ₂	-CH ₂ CH ₃	4-Cl-Ph-	N	CF ₃	CH ₃	CH ₃

and the N-oxides of the compounds of Table 2.

5

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

10 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 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.

Examples of the abovementioned 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, Calipitrimerus spp., Chorioptes spp., Dermanyssus gallinae, Dermatophagoides spp, Eotetranychus spp, Eriophyes spp., Hemitarsonemus spp, Hyalomma spp., Ixodes spp., Olygonychus spp, Ornithodoros spp., Polyphagotarsone latus, Panonychus spp., Phyllocoptuta oleivora, Phytonemus 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,

Agriotes spp., Amphimallon majale, Anomala orientalis, Anthonomus spp., Aphodius spp, Astylus

15 atramaculatus, 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, Melighetes aeneus, Melolontha spp., Myochrous armatus,

20 Orycaophilus spp., Otiorhynchus spp., Phyllophaga spp, Phlyctinus spp., Popillia spp., Psylliodes spp., Rhysomatus 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,

Aedes spp., Anopheles spp, Antherigona soccata, Bactrocea oleae, Bibio hortulanus, Bradysia spp,

25 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., Stomoxyx spp., Tabanus spp., Tannia spp. and

30 Tipula spp.;

from the order *Hemiptera*, for example,

Acanthocoris scabrator, Acrosternum spp, Adelphocoris lineolatus, Amblypelta nitida, Bathycelia thalassina, Blissus spp, Cimex spp., Clavigralla tomentosicollis, Creontiades spp, Distantiella theobroma, Dichelops furcatus, Dysdercus spp., Edessa spp, Euchistus spp., Eurydema pulchrum,

35 Eurygaster spp., Halyomorpha halys, Horcias nobilellus, Leptocorisa spp., Lygus spp, Margarodes spp, Murgantia histrionic, 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., Vatiga illudens;

-34-

Acyrthosium pisum, Adalges spp, Agalliana ensigera, Agonoscena targionii, Aleurodicus spp,
Aleurocanthus spp, Aleurolobus barodensis, Aleurothrixus 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, Diaurodes 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, Nephrotettix spp., Nilaparvata spp., Nippolachnus piri Mats, Odonaspis
ruthae, Oregma lanigera Zehnter, Parabemisia myricae, Paratriozza 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
erytreae, Unaspis citri, Zygina flammigera, Zygina scutellaris, ;
20 from the order *Hymenoptera*, for example,
Acromyrmex, Arge spp, Atta spp., Cephus spp., Diprion spp., Diprionidae, Gilpinia polytoma, Hoplo-
campa spp., Lasius spp., Monomorium pharaonis, Neodiprion spp., Pogonomyrmex 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 gemmatalis, Archips spp., Argyresthia spp, Argyrotaenia spp., Autographa spp., Bucculatrix
30 thurberiella, Busseola fusca, Cadra cautella, Carposina nipponensis, Chilo spp., Choristoneura spp.,
Chrysoteuchia topiaria, Clysia ambigua, 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, Etiella
35 zinckinella, Eucosma spp., Eupoecilia ambiguella, Euproctis spp., Euxoa spp., Feltia jaculifera, Gra-
pholita spp., Heda 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

-35-

nubilalis, Pammene spp., Pandemis spp., Panolis flammea, Papaipema nebris, Pectinophora gossypiella, 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 derogata, Synanthonedon 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., Gryllotalpa 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, latex plants and ornamentals.

The active ingredients according to the invention are especially suitable for controlling *Aphis craccivora*, *Diabrotica balteata*, *Heliothis virescens*, *Myzus persicae*, *Plutella xylostella* and

-36-

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), *Cydia pomonella* (preferably in apples), *Empoasca* (preferably in vegetables, vineyards), *Leptinotarsa* (preferably in potatos) and *Chilo suppressalis* (preferably in rice).

5

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* species, *Criconemoides* species, *Mesocriconema* species; Stem and bulb nematodes, *Ditylenchus destructor*, *Ditylenchus dipsaci* and other *Ditylenchus* species; Awl nematodes, *Dolichodorus* species;

15 Spiral nematodes, *Helicotylenchus multicinctus* and other *Helicotylenchus* species; Sheath and sheathoid nematodes, *Hemicyclophora* 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 curvitatus*, *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..

30

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. trunculata*); *Helicelia* (*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. canaliculata*); *Vallonia* and *Zanitoides*.

-37-

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*.

5

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

10 insecticidal proteins of bacteria colonising nematodes, for example *Photorhabdus* spp. or *Xenorhabdus* spp., such as *Photorhabdus luminescens*, *Xenorhabdus nematophilus*; toxins produced by animals, such as scorpion toxins, arachnid toxins, wasp toxins and other insect-specific neurotoxins; toxins produced by fungi, such as *Streptomyces* toxins, plant lectins, such as pea lectins, barley lectins or snowdrop lectins; agglutinins; proteinase inhibitors, such as trypsin inhibitors, 15 serine protease inhibitors, patatin, cystatin, papain inhibitors; ribosome-inactivating proteins (RIP), such as ricin, maize-RIP, abrin, luffin, saporin or bryodin; steroid metabolism enzymes, such as 3-hydroxysteroidoxidase, ecdysteroid-UDP-glycosyl-transferase, cholesterol oxidases, ecdysone inhibitors, HMG-COA-reductase, ion channel blockers, such as blockers of sodium or calcium channels, juvenile hormone esterase, diuretic hormone receptors, stilbene synthase, bibenzyl 20 synthase, chitinases and glucanases.

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

25 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).

30 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.

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. Cry1-type

35 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.

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).

-38-

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

5 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 10 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'Habit 27, F-31 790 St. Sauveur, France,

15 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'Habit 27, F-31 790 St. Sauveur, France,

20 registration number C/FR/96/05/10. Genetically modified *Zea mays* which has been rendered resistant to attack by the European corn borer (*Ostrinia nubilalis* and *Sesamia nonagrioides*) by transgenic expression of a 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'Habit 27, F-31 790 St. Sauveur, France,

25 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,

30 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.

35 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.

-39-

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,

10 (<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 15 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.

20 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.

25 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.

30 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. 35 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 ambients and the protection of raw materials, such as wood, textiles, floor coverings or

-40-

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

5 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
10 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. A further object of the invention is therefore a substrate selected from nonwoven and fabric material comprising a composition which contains a compound of formula I.

15

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

20 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.

25

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,
30 WO 2006/128870, 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

35 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.

-41-

Family	Species	Host or Crop Infested
Buprestidae	<i>Agrilus planipennis</i>	Ash
Cerambycidae	<i>Anoplura glabripennis</i>	Hardwoods
	<i>Xylosandrus crassiusculus</i>	Hardwoods
Scolytidae	<i>X. multilatus</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

-42-

Family	Species	Host or Crop Infested
	<i>Neoclytus acuminatus</i>	Ash, Hickory, Oak, Walnut, Birch, Beech, Maple, Eastern hophornbeam, Dogwood, Persimmon, Redbud, Holly, 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

-43-

Family	Species	Host or Crop Infested
	<i>Monarthrum fasciatum</i>	Oak, Maple, Birch, Chestnut, Sweetgum, Blackgum, Poplar, Hickory, Mimosa, Apple, Peach, Pine
	<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

5 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*),

10 *Popillia* spp. (e.g. Japanese beetle, *P. japonica*), *Phyllophaga* spp. (e.g. May/June beetle), *Ataenius*

-44-

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.*).

5 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*).

10 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 (*Propsapia bicincta*), leafhoppers, cutworms (*Noctuidae* family), and greenbugs.

15 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:

20 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.*

25 Of the order Diptera and the suborders Nematocerina and Brachycerina, 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.*, *Stomoxyx 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.*

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

-45-

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

Of the order Blattaria, for example *Blatta orientalis*, *Periplaneta americana*, *Blattelagermanica* and

5 *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., *Ornithochyletia* spp., *Myobia* spp., *Psorergatess* 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 *Laminoziopites* 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*

25 *rufovillosum*, *Ptilinuspecticornis*, *Dendrobium pertinex*, *Ernobius mollis*, *Priobium carpini*, *Lyctus*

brunneus, *Lyctus africanus*, *Lyctus planicollis*, *Lyctus linearis*, *Lyctus pubescens*, *Trogoxylon aequale*,

Minthesrusicollis, *Xyleborus* spec., *Tryptodendron* spec., *Apate monachus*, *Bostrychus capucins*,

Heterobostrychus brunneus, *Sinoxylon* spec. and *Dinoderus minutus*, and also hymenopterans such

as *Sirex juvencus*, *Urocerus gigas*, *Urocerus gigas tagnus* and *Urocerus augur*, and termites such as

30 *Kalotermes flavicollis*, *Cryptotermes brevis*, *Heterotermes indicola*, *Reticulitermes flavipes*,

Reticulitermes santonensis, *Reticulitermes lucifugus*, *Mastotermes darwiniensis*, *Zootermopsis*

nevadensis and *Coptotermes 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-

-46-

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

5 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,

10 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

15 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

25 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, isoctane, 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,

-47-

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, Kieselguhr, limestone, calcium carbonate, bentonite, calcium montmorillonite, cottonseed husks, wheat 10 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 emulsifiers, wetting agents or suspending agents or for other purposes. Typical surface-active

15 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 alkylnaphthalenesulfonates, such as sodium dibutylnaphthalenesulfonate; dialkyl esters of sulfosuccinate salts, such as sodium di(2-ethylhexyl)sulfosuccinate; sorbitol esters, such as sorbitol oleate; quaternary amines, such as 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 Emulsifiers Annual, MC Publishing Corp., Ridgewood New Jersey (1981).

25 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 inhibitors, fragrances, wetting agents, take-up enhancers, micronutrients, plasticisers, glidants, lubricants, dispersants, thickeners, antifreezes, microbicides, and liquid and solid fertilisers.

30 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 %, 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 35 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

-48-

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 1000 l/ha.

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

Emulsifiable concentrates:

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

20

Dusts:

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

25

Suspension concentrates:

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

30

Wettable powders:

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

35

Granules:

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

-49-

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 diisobutylnaphthalenesulfonate	-	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

5 suitable mill, affording wettable powders that can be diluted with water to give suspensions of the desired concentration.

<u>Powders for dry seed treatment</u>	a)	b)	c)
active 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.

<u>Emulsifiable concentrate</u>	
active ingredients	10 %

-50-

octylphenol polyethylene glycol ether (4-5 mol of ethylene oxide)	3 %
calcium dodecylbenzenesulfonate	3 %
castor oil polyglycol ether (35 mol of ethylene oxide)	4 %
Cyclohexanone	30 %
xylene mixture	50 %

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

<u>Dusts</u>	a)	b)	c)
Active 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 %

5 The combination is mixed and ground with the adjuvants, and the mixture is moistened with water. The mixture is extruded and then dried in a stream of air.

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

-51-

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.

<u>Suspension concentrate</u>	
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

5 dilutions, living plants as well as plant propagation material can be treated and protected against infestation by microorganisms, by spraying, pouring or immersion.

<u>Flowable concentrate for seed treatment</u>	
active ingredients	40 %
propylene glycol	5 %
copolymer butanol PO/EO	2 %
Tristyrenepheno 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

-52-

dilutions, living plants as well as plant propagation material can be treated and protected against infestation by microorganisms, by spraying, pouring or immersion.

Slow Release Capsule Suspension

28 parts of the combination are mixed with 2 parts of an aromatic solvent and 7 parts of toluene

5 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.

10 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.

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

15 (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 and ¹⁹F NMR measurements were recorded on Brucker 400MHz or 300MHz spectrometers, chemical shifts are given in ppm relevant to a TMS standard. Spectra measured in deuterated solvents as indicated. RT is the retention time in minutes.

25

LCMS Methods:Method A (SQD13):

Spectra were recorded on a Mass Spectrometer from Waters (SQD Single quadrupole mass spectrometer) equipped with an electrospray source (Polarity: positive or negative ions, Capillary: 3.00

30 KV, Cone range: 30-60 V, Extractor: 2.00 V, Source Temperature: 150°C, Desolvation Temperature: 350°C, Cone Gas Flow: 0 L/Hr, Desolvation Gas Flow: 650 L/Hr, Mass range: 100 to 900 Da) and an Acquity UPLC from Waters: Binary pump, heated column compartment and diode-array detector.

Solvent degasser, binary pump, heated column compartment and diode-array detector. Column:

Waters UPLC HSS T3 , 1.8 µm, 30 x 2.1 mm, Temp: 60 °C, DAD Wavelength range (nm): 210 to 500, Solvent Gradient: A = water + 5% MeOH + 0.05 % HCOOH, B= Acetonitrile + 0.05 % HCOOH:

35 gradient: gradient: 0 min 0% B, 100% A; 1.2-1.5 min 100% B; Flow (ml/min) 0.85.

Method B (SQD13):

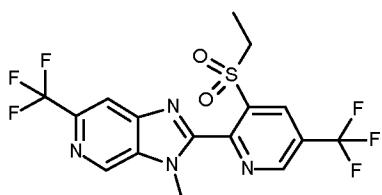
-53-

Mass Spectroscopy Method ESI-MS, LC-20AD Mass Spectrometer from Shimadzu (Single quadrupole mass spectrometer)

Instrument Parameters: Ionisation method: Electrospray. Polarity: positive and negative ions. Capillary (kV) 1.50. Cone (V) unknown. Extractor (V) 5.00. Source Temperature (°C) 200. Desolvation

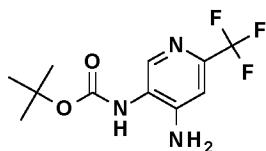
5 Temperature (°C) 250. Cone gas Flow (l/Hr) 90. Desolvation gas Flow (l/Hr) 90. Mass range: 50 to 1000 Da.

Example P1: Preparation of 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridine (starting material of formula VIIa):



10

Step A: tert-butyl N-[4-amino-6-(trifluoromethyl)-3-pyridyl]carbamate:

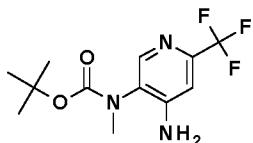


To a solution of 6-(trifluoromethyl)pyridine-3,4-diamine (3.14 g, 17.73 mmol, prepared as described in US 7,767,687) in tetrahydrofuran (50ml) was added tert-butoxycarbonyl tert-butyl carbonate (4.64 g,

15 21.27 mmol) and the mixture was stirred at 50°C. After 8 hours, a further 1.1g (5.0 mmol) of tert-butoxycarbonyl tert-butyl carbonate was added, and stirring at 50°C continued for a further 4 hours. The reaction mixture was then concentrated *in vacuo*, and the brown residue was suspended in dichloromethane, filtered and dried *in vacuo* to give the title compound as white crystals. LCMS (method A): retention time: 0.79min; 278 (M+H).

20

Step B: tert-butyl N-[4-amino-6-(trifluoromethyl)-3-pyridyl]-N-methyl-carbamate:



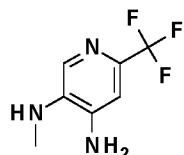
To a stirred suspension of sodium hydride (0.648 g, 14.85 mmol) in 30ml N,N-dimethylformamide, tert-butyl N-[4-amino-6-(trifluoromethyl)-3-pyridyl]carbamate (3.92 g, 14.14 mmol) dissolved in 20ml N,N-

25 dimethylformamide was added dropwise over a period of 20min at 20-25°C. After 15min stirring at RT, iodomethane (2.21 g, 15.55 mmol) was added. After 30min at ambient temperature the mixture was poured onto 200ml water, extracted twice with ethyl acetate, and the combined organic fractions washed successively with water and brine, dried over Na2SO4 and concentrated *in vacuo*. The crude

-54-

product was recrystallised from ethyl acetate/heptane to give the title compound (3.18g) as white crystals. LCMS (method A): retention time: 0.85min; 292 (M+H).

Step C: N3-methyl-6-(trifluoromethyl)pyridine-3,4-diamine:



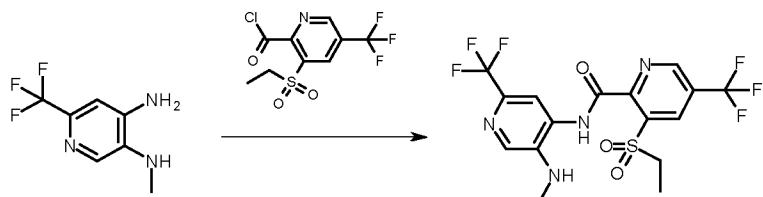
5

To a clear, colourless solution of tert-butyl N-[4-amino-6-(trifluoromethyl)-3-pyridyl]-N-methyl-carbamate (3.53 g, 12.119 mmol) in dioxan, hydrogen chloride (18ml of a 2M solution in water, 36.36 mmol) was added and the mixture was heated to reflux. After gas evolution had ceased, the reaction mixture was cooled to ambient temperature, and treated with solid sodium hydrogen carbonate (3.1 g, 16.9 mmol). The slurry was diluted with water and extracted twice with ethyl acetate. The combined organic layers were washed successively with water and brine, dried over Na₂SO₄ and concentrated *in vacuo* to give 2.25g of the title compound as colourless crystals, mp 138-140°C. LCMS (method A): retention time 0.24min, 192 (M+H).

10 15 Alternatively, N3-methyl-6-(trifluoromethyl)pyridine-3,4-diamine can be obtained by the following procedure:

To a solution of 6-(trifluoromethyl)pyridine-3,4-diamine (2.0 g, 12.2 mmol) and potassium carbonate (3.2 g, 23.1 mmol) in acetonitrile (10 mL) was added iodomethane (0.8 mL). The reaction mixture was stirred at 30°C for 18 hours. Potassium carbonate was filtered off, the filtrate was dried *in vacuo* and 20 purified with chromatography column on silica gel (petroleum:ethyl acetate = 4:3) to afford the title compound as a light yellow solid (0.32 g). ¹H NMR (400 MHz, DMSO-d₆): δ (ppm) 7.57 (s, 1H), 6.83 (s, 1H), 5.82 (s, 2 H), 5.23 (d, *J* = 4.8 Hz, 1H), 2.80 (d, *J* = 4.8 Hz, 3H). ¹⁹F NMR (300 MHz, DMSO-d₆): δ (ppm) -60.12 (s, 3 F).

25 Step D: 3-ethylsulfonyl-N-[5-(methylamino)-2-(trifluoromethyl)-4-pyridyl]-5-(trifluoromethyl)pyridine-2-carboxamide (in a mixture with the regioisomeric acylation product):

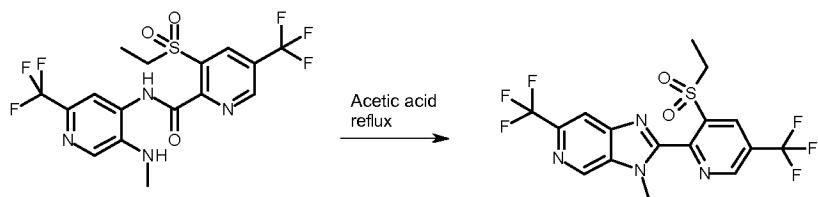


To a solution of N3-methyl-6-(trifluoromethyl)pyridine-3,4-diamine (11 g, step C) in tetrahydrofuran (500 mL) was added N,N-diethylethanamine (14.56 g, 20.1 mL). The reaction mixture was cooled down at 0-5°C and a solution of 3-ethylsulfonyl-5-(trifluoromethyl)pyridine-2-carbonyl chloride (19.095 g, prepared as proposed in WO 2013018928 via the reaction of the 3-ethylsulfonyl-5-(trifluoro-

-55-

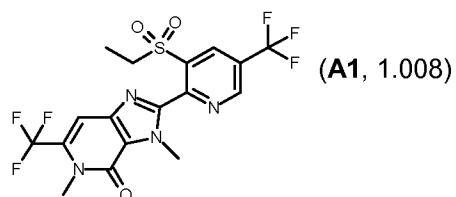
methyl)pyridine-2-carboxylic acid, prepared as in WO 2013180194, and oxalyl chloride) in 250 ml of tetrahydrofuran was added slowly, while keeping the temperature below 5°C. The reaction mixture was stirred 2 hours at 0°C. The reaction mixture was poured into aqueous ammonium chloride and extracted 3 times with 150 ml of ethyl acetate. The combined organic fractions were washed with 5 water, then brine, dried over sodium sulfate, and concentrated under vacuum. The crude product was purified by chromatography (cyclohexane/ethyl acetate) to give the title compound in a mixture with the regioisomeric acylation product (23.7g) as a white solid. This material (two position isomer acylation products, whereby acylation occurs either on NH₂ or on NHMe of the diamino substrate) is used without extra purification into the next step.

10 Step E: 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridine:



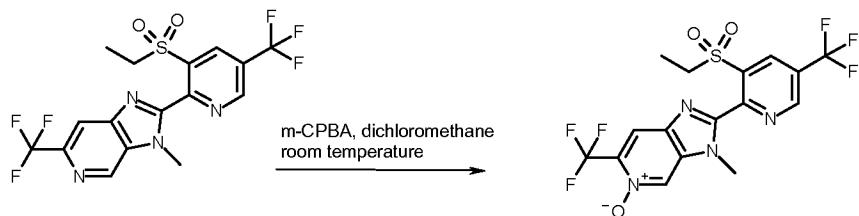
A mixture of 3-ethylsulfonyl-N-[5-(methylamino)-2-(trifluoromethyl)-4-pyridyl]-5-(trifluoromethyl)pyridine-2-carboxamide and its acylated isomer (8.6 g, 19 mmol, the product of step D) in 100ml of 15 acetic acid AcOH was refluxed for 4 hours. The reaction mixture was poured into water (100 mL) and the formed precipitate was filtered and washed with water. The precipitate was dried under vacuum to give 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridine (7.2g). ¹H NMR (400Mz, CDCl₃): δ 9.28(s, 1H), 9.04 (s, 1H), 8.78(s, 1H), 8.12 (s, 1H), 3.95 (s, 3H), 3.90(q, 2H), 1.38 (t, 3H).

20 Example P2: Preparation of 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one A1 (compound 1.008):



Step A: 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-5-oxido-6-(trifluoromethyl)imidazo[4,5-c]pyridin-5-ium:

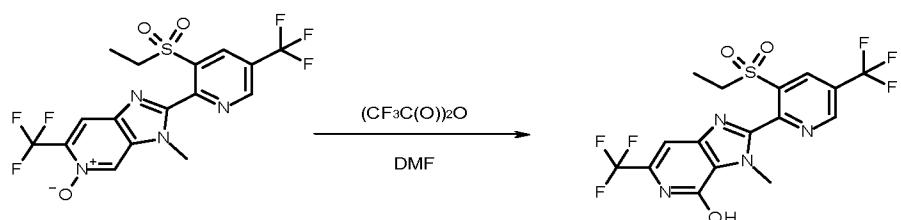
-56-



2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridine (example P1, 0.9g) was dissolved in dichloromethane (41 mL). Meta-chloroperbenzoic acid m-CPBA (2.2 g) was added, and the mixture was stirred 28 hours at reflux. The reaction mixture was poured

5 into aqueous sodium thiosulfate and extracted twice with dichloromethane. The combined organic fractions were washed with a saturated solution of potassium carbonate, dried over magnesium sulfate, and concentrated under vacuum. The crude product was purified by chromatography (cyclohexane/ethyl acetate) to give the title compound (63mg) as a white solid. ¹H NMR (400MHz, CDCl₃): δ (ppm) 9.24 (s, 1H), 8.78 (s, 1H), 8.68 (s, 1H), 8.10 (s, 1H), 3.88(q, 2H), 3.80 (s, 3H), 1.40 (t, 3H) ppm.

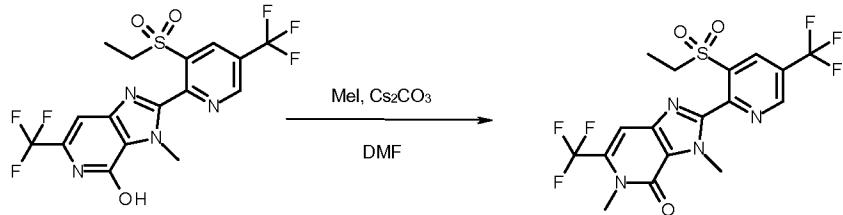
10 Step B: 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-ol:



15 To a solution of 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-5-oxido-6-(trifluoromethyl)imidazo[4,5-c]pyridin-5-ium (Step A, 0.150 g) in N,N-dimethylformamide DMF (4 mL) at 0°C was added trifluoroacetic anhydride (CF₃C(O))₂O (2.974 g, 2 mL). The mixture was stirred for 2 hours at 0°C. The reaction mixture was poured into water (200mL) and the resulting white precipitate was filtered, washed with water and dried under vacuum to give 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-ol (0.139 g) as a white solid. This 20 compound was used into the next step without extra purification. ¹H NMR (400MHz, CDCl₃): δ (ppm) 9.22 (s, 1H), 8.75 (s, 1H), 7.10 (s, 1H), 4.12 (s, 3H), 3.88(q, 2H) 1.38 (t, 3H) ppm.

Step C: 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A1** (compound 1.008):

-57-

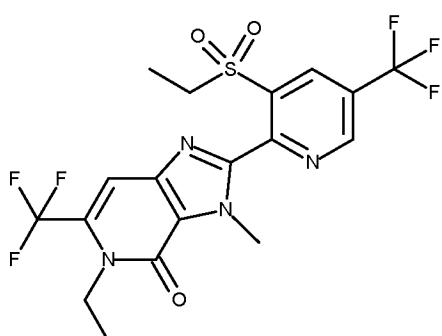


To a solution of 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-ol (Step B, 0.113 g) in N,N-dimethylformamide DMF (10 mL) was added cesium carbonate Cs₂CO₃ (0.243 g). After stirring the solution for 10 minutes, 0.0311 mL of methyl iodide was added.

5 The mixture was stirred overnight at ambient temperature. The yellow solution was poured into water and extracted 3 times with ethyl acetate. The combined organic fractions were washed with a saturated solution of potassium carbonate, dried over magnesium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography to give 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (title compound

10 **A1**, No. 1.008, 0.026 g) as a white solid. ¹H NMR (400MHz, CDCl₃): δ (ppm) 9.22 (s, 1H), 8.74 (s, 1H), 7.20 (s, 1H), 4.12 (s, 3H), 3.88 (q, 2H), 3.74 (s, 3H), 1.38 (t, 3H) ppm. ¹³C NMR (400MHz, CDCl₃): 31.12 ppm (N(CH₃)-CO). In general, with this method, the O-alkylation was obtained as by product (and in some case as the major product as function of the electrophile used).

Example P3: Preparation of 5-ethyl-2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one :

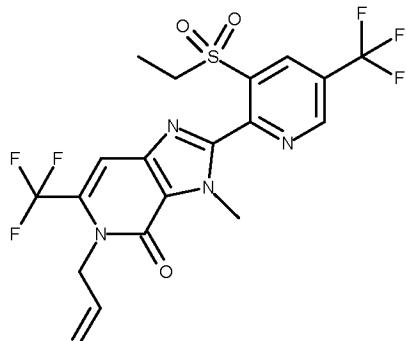


Compound **A2** (5-ethyl-2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo [4,5-c]pyridin-4-one) from table A was prepared by the same method (Example P2, Step C) using ethyl iodine as reagent. ¹H NMR (400 MHz, CDCl₃): 9.22(s, 1H), 8.74 (s, 1H), 7.27 (s, 1H), 4.25

20 (q, 2H), 4.12 (s, 3H), 1.35-1.42 (m, 6H) ppm.

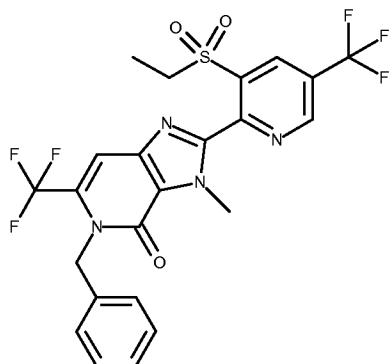
Example P4: Preparation of 5-allyl-2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A3:**

-58-



Compound **A3** (5-ethyl-2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one) from table A was prepared by the same method (Example P2, Step C) using allyl bromide as reagent. ¹H NMR (400 MHz, CDCl₃): 9.22(s, 1H), 8.74 (s, 1H), 7.22 (s, 1H), 5.96 (m, 1H), 5.74 (m, 2H), 4.82 (m, 2H), 4.12 (s, 3H), 3.87 (q, 2H), 1.40 (t, 3H) ppm.

Example P5: Preparation of 5-benzyl-2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A4:**



Compound **A4** (5-ethyl-2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one) from table A was prepared by the same method (Example P2, Step C) using benzyl bromide as reagent. ¹H NMR (400 MHz, CDCl₃): 9.22(s, 1H), 8.74 (s, 1H), 7.35-7.24 (M, 4H), 7.14 (m, 2H), 5.46 (s, 2H), 4.10 (s, 3H), 3.88 (q, 2H), 1.40 (t, 3H) ppm.

Example P6: Preparation of the compounds **A5 to A15:**

Compounds **A5** to **A15** were prepared by the following general protocol: To a solution of 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (Step B, 0.04mmol) in N,N-dimethylformamide DMF was added cesium carbonate Cs₂CO₃ (3 eq.). After stirring the solution for 10 minutes at ambient temperature, 2.5eq of methyl iodide was added. The mixture was stirred for 18 hours at ambient temperature. The desired compounds were isolated by HPLC and identified by LC-MS. The O-alkylated compounds are identified as by-product in this experiment.

-59-

Analytic method used for identification:

SQ Detector 2 from Waters

Ionisation method: Electrospray

Polarity: positive ions

5 Capillary (kV) 3.5, Cone (V) 30.00, Extractor (V) 3.00, Source Temperature (°C) 150, Desolvation Temperature (°C) 400, Cone Gas Flow (L/Hr) 60, Desolvation Gas Flow (L/Hr) 700

Mass range: 140 to 800 Da

DAD Wavelength range (nm): 210 to 400

Method Waters ACQUITY UPLC with the following HPLC gradient conditions

10 (Solvent A: Water/Methanol 9:1,0.1% formic acid and Solvent B: Acetonitrile,0.1% formic acid)

	Time (minutes)	A (%)	B (%)	Flow rate (ml/min)
	0	100	0	0.75
	2.5	0	100	0.75
	2.8	0	100	0.75
15	3.0	100	0	0.75

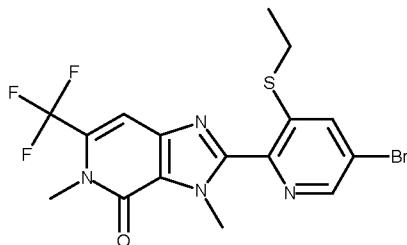
Type of column: Waters ACQUITY UPLC HSS T3; Column length: 30 mm; Internal diameter of column: 2.1 mm; Particle Size: 1.8 micron; Temperature: 60°C.

	RT	M (calculated)	(M+H) ⁺ (measured)
A5	1.95	510.12	511.09
A6	1.84	496.10	497.06
A7	1.76	506.08	507.07
A8	1.62	542.11	543.11
A9	2.15	550.15	551.13
A10	1.62	492.07	493.04
A11	1.61	498.08	499.03
A12	2.3	514.06	515.22
A13	1.85	574.11	575.09
A14	1.51	521.10	522.08
A15	1.99	570.12	571.11

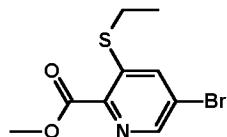
Example P7: Preparation of 2-(5-bromo-3-ethylsulfanyl-2-pyridyl)-3,5-dimethyl-6-

20 **(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (A20):**

-60-

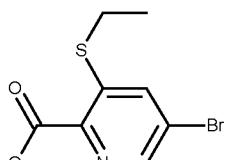


Step A : Preparation of methyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate:



To a solution of methyl 5-bromo-3-chloro-pyridine-2-carboxylate (0.100 g, 0.399 mmol) (commercial product) in tetrahydrofuran, stirred at 0°C, was added ethylsulfanylsodium (0.034 g, 1 equiv.). After 1 hour at that temperature, the ice bath was removed and stirring was continued for 20 hours. The reaction mixture was then poured onto water (15 ml) and extracted twice with ethyl acetate. The organic phases were dried over sodium sulfate and the solvent was removed. The residue was submitted to flash chromatography over silica gel and the selected fractions evaporated to yield methyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate as a colorless solid. LCMS (method 1): 276, 278 (M+H); retention time: 0.92 min. ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.46 (s, 1 H); 7.79 (s, 1 H); 4.00 (s, 3 H); 2.94 (q, J = 7.4 Hz, 2H); 1.42 (t, J= 7.4 Hz, 3H).

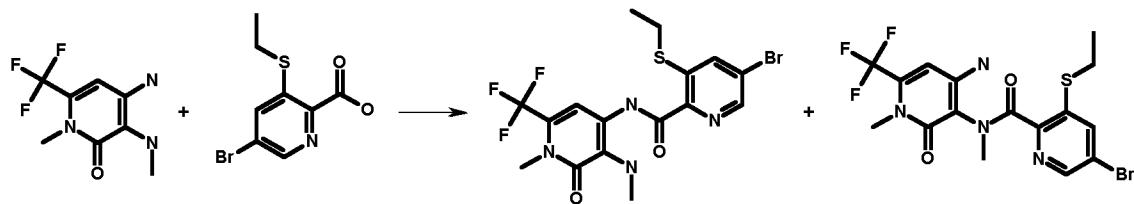
Step B: Preparation of 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylic acid:



A solution of methyl 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylate (3.900 g, 14.12 mmol) (preparation described here above) in a mixture of methyl alcohol (75 ml) and water (20 ml) stirred at 20°C was treated with 2N aqueous sodium hydroxide solution (7.04 ml, 1.05 equiv.). The mixture was stirred for two hours, then most of the alcohol was eliminated under reduced pressure. The residue was then treated with 2N aqueous HCl solution and the resulting precipitate was filtered off, washed with water and dried under vacuum. The title compound was obtained as a colorless solid. LCMS (method 1): 260, 262 (M-H); retention time: 0.77 min. ¹H NMR (400 MHz, d6-DMSO) δ ppm: 13.4 (br s, 1 H); 8.50 (s, 1 H); 8.07 (s, 1 H); 3.04 (q, J=7.53 Hz, 2 H); 1.27 (t, J=7.53 Hz, 3 H).

Step C: Preparation of 5-bromo-3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-6-(trifluoromethyl)-3-pyridyl]-5-bromo-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide:

-61-



To a suspension of 5-bromo-3-ethylsulfanyl-pyridine-2-carboxylic acid (2.61 g, 9.95 mmol) in dichloromethane (25 ml) was added one drop of N,N-dimethylformamide, followed by oxalyl chloride (2.93 g, 2.01 mL, 22.6 mmol). After the end of gas evolution, the reaction mixture was a pale red solution. The latter was evaporated under reduced pressure at a bath temperature of 60°C. The residue formed dark red crystals of 5-bromo-3-ethylsulfanyl-pyridine-2-carbonyl chloride and the residue was redissolved in a mixture AcOEt (20mL), DCM (15mL).

To a solution of 4-amino-1-methyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one (Prepared in Example I2, 2.00 g, 9.04 mmol) in ethyl acetate (100 ml) was added N,N-diethylethanamine (2.31 g, 3.18 mL, 22.6 mmol) then the resulting solution was cooled with an ice bath, before slow addition of the previous acid chloride solution. The resulting mixture was stirred 1hour at 0°C.. The solution was neutralized by addition of a saturated aqueous solution of sodium bicarbonate and the product was extracted twice with ethyl acetate. The organic solution was dried over sodium sulfate and evaporated under reduced pressure to yield the crude product. A mixture 70:30 of 5-bromo-3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-6-(trifluoromethyl)-3-pyridyl]-5-bromo-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide was obtained and used without extra purification for the next step. LC-MS(Method A) : RT 0.86, 467.1(M+H⁺), 465.1(M-H⁺).

Starting from the cited starting material, the following compounds were synthesised using the same

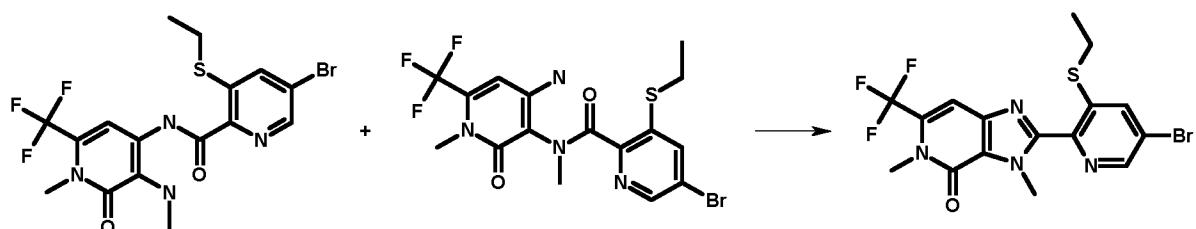
protocol:

Entry	Product	Starting material	NMR/LC-MS (method)
1	3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-6-(trifluoromethyl)-3-pyridyl]-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide	3-ethyl-sulfanylpyridine-2-carboxylic acid (commercially available)	LC-MS(Method A) : RT 0.76, 387.4 (M+H ⁺), 385.2 (M-H ⁺)
2	5-(4-chlorophenyl)-3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-	5-(4-chlorophenyl)-3-ethylsulfanyl-pyridine-2-carboxylic acid (See Example I1)	LC-MS(Method A) : RT 1.08, 497.3 (M+H ⁺), 495.2 (M-H ⁺)

-62-

	<p>6-(trifluoromethyl)-3-pyridyl]-5-(4-chlorophenyl)-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide</p> <p>The compounds were used without extra purification</p>		
--	--	--	--

Step D: 2-(5-bromo-3-ethylsulfanyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (**A20**):



5 A mixture of 5-bromo-3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-6-(trifluoromethyl)-3-pyridyl]-5-bromo-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide (4.21 g, 9.05 mmol, the product of step C) in 30 ml of acetic acid AcOH was heated at 150°C for 1 hour under MW. The dark brown solutions were poured into 500mL of water. The precipitate was filtered and washed several time with water, dried under 10 vacuum to give the pure compound **A20** (3.85 g, 8.61 mmol). ¹H NMR (400 MHz, CDCl₃) δ ppm: 8.52 (s, 1 H); 7.82 (s, 1 H); 7.32 (s, 1 H); 4.20 (s, 3 H); 3.72 (s, 3 H); 2.94 (q, 2 H); 1.34 (t, 3H).

Starting from the cited starting material, the following compounds were synthesised using the similar protocol:

Product	Starting material	NMR/LC-MS (method)
A16	Step C: mixture of 3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-6-(trifluoromethyl)-3-pyridyl]-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide (Entry 1)	¹ H NMR (400 MHz, CDCl ₃) δ ppm: 8.52 (d, 1 H); 7.78 (d, 1 H); 7.38 (q, 1 H); 7.82 (s, 1H), 4.18 (s, 3 H); 3.74(s, 3 H); 2.94 (q, 2 H); 1.34 (t, 3H).
A18	Step C: mixture of 5-(4-chlorophenyl)-3-ethylsulfanyl-N-[1-methyl-3-(methylamino)-2-oxo-6-(trifluoromethyl)-4-pyridyl]pyridine-2-carboxamide and N-[4-amino-1-methyl-2-oxo-6-	¹ H NMR (400 MHz, CDCl ₃): 8.68(s, 1H), 7.85(s, 1H), 7.58 (d, 2H), 7.52 (d, 2H), 7.32 (s, 1H), 4.22 (s, 3H), 3.72 (s,

-63-

(trifluoromethyl)-3-pyridyl]-5-(4-chlorophenyl)-3-ethylsulfanyl-N-methyl-pyridine-2-carboxamide(Entry 2)	3H), 2.98 (q, 2H), 1.38 (t, 3H) ppm
--	-------------------------------------

The similar serial of protocol (step C and D) was used to synthesize: **A30** using as starting material Example I4, **A37** using as starting material Example I2 and Example I5 and **A38** using as starting material Example I4 and Example I5.

5 **A30:** ^1H NMR (400 MHz, CDCl_3) δ ppm 1.32 - 1.42 (m, 6 H), 2.98 (q, 2 H), 4.20 - 4.30 (m, 5 H), 7.38 (s, 1 H), 7.86 (ds, 1 H), 8.56 (s, 1 H).

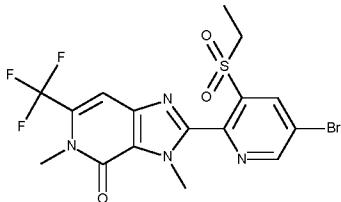
10 **A37:** ^1H NMR (400 MHz, CDCl_3) δ ppm 0.82 (m, 2 H), 1.10 (m, 2 H), 1.23 (t, 3 H), 1.97 (m, 1 H), 2.84 (q, 2 H), 3.74 (s, 3 H), 3.95 (s, 3 H), 6.99 (dd, 1 H), 7.19 (d, 1 H), 7.27 (m, 1 H), 7.29 (s, 1 H).

15 **A38:** ^1H NMR (400 MHz, CDCl_3) δ ppm 0.78 (m, 2 H), 1.08 (m, 2 H), 1.23 (t, 3 H), 1.40 (t, 3 H), 1.98 (m, 1 H), 2.85 (q, 2 H), 3.96 (s, 3 H), 4.26 (q, 2 H), 6.99 (dd, 1 H), 7.20 (d, 1 H), 7.25 (s, 1 H), 7.29 (s, 1 H).

20 **A29:** LC-MS(Method A) : RT 1.11, 437 ($\text{M}+\text{H}^+$).

15

Example P8: Preparation of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (A21):



20 A solution of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A20** (1g, 2.24 mmol) in dichloromethane (45 ml) was stirred in an ice bath and *meta*-chloroperbenzoic acid (1.3 g, 5.365742 mmol, 70% purity) was added in portions, in such a way that the temperature of the reaction mixture was kept below 10°C. The bath was then removed and the mixture was stirred 2 further hours at 20°C. After completion of the reaction, the mixture was stirred with saturated aqueous sodium bicarbonate solution. The phases were separated and the aqueous phase was extracted with dichloromethane. The organic layers were combined, dried over sodium sulfate and evaporated. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound as colorless solid. ^1H NMR (400 MHz, CDCl_3) δ ppm 9.02 (s, 1 H); 8.64 (s, 1 H); 7.21 (s, 1 H); 4.07 (s, 3 H); 3.79 (q, 2 H); 3.73 (s, 3 H); 1.36 (t, 3H).

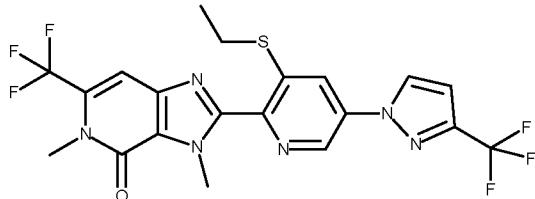
25

-64-

The same serial of protocol was used to synthesize: **A31** using as starting material **A30**

A31: ^1H NMR (400 MHz, CDCl_3) δ ppm 1.36 - 1.42 (m, 6 H), 3.82 (q, 2 H), 4.09 (s, 3 H), 4.25 (q, 2 H), 7.22 (s, 1 H), 8.66 (d, 1 H), 9.03 (d, 1 H).

5 **Example P9:** 2-[3-ethylsulfanyl-5-[3-(trifluoromethyl)pyrazol-1-yl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A26**



A solution of 2-(5-bromo-3-ethylsulfanyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A20** (preparation described before, 250 mg, 0.56 mmol) in N,N-dimethylformamide (0.5589 mL)

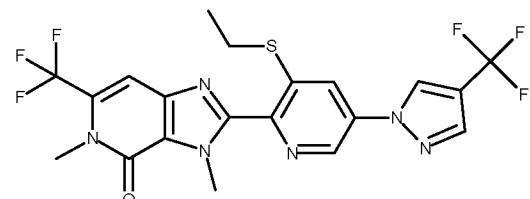
10 was added 3-trifluoromethyl-1H-pyrazole (83.7 mg, 0.61 mmol), N,N'-dimethylethylenediamine (4.97752 mg, 0.0559 mmol), potassium carbonate (15.5 mg, 0.11 mmol) and copper(I) iodide (5.31 mg, 0.028 mmol). The reaction mixture was stirred under reflux for 12 hours, then same quantity of N,N'-dimethylethylenediamine, potassium carbonate and copper(I) iodide was added. The reaction mixture was stirred under reflux overnight. The reaction mixture was filtered then the solvent was

15 evaporated under vacuum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound as colorless solid. ^1H NMR (400 MHz, CDCl_3) δ ppm 8.78 (s, 1 H); 8.16 (s, 1 H); 8.11 (s, 1 H); 7.35 (s, 1 H); 6.84 (s, 1 H); 4.24 (s, 3 H); 3.05 (q, 2 H); 1.39 (t, 3 H).

The same protocol was used to synthesize: **A32** using as starting material **A30**

20 **A32:** LC-MS(Method A) : RT 1.19, 517 ($\text{M}+\text{H}^+$).

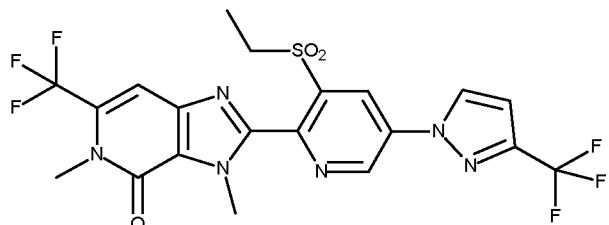
Example P10: 2-[3-ethylsulfanyl-5-[4-(trifluoromethyl)pyrazol-1-yl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound **A24**):



25 Compound **A24:** 2-[3-ethylsulfanyl-5-[4-(trifluoromethyl)pyrazol-1-yl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one from table A was prepared by the same method (Example P9) using 3-trifluoromethyl-1H-pyrazole as reagent. ^1H NMR (400 MHz, CDCl_3): 8.78 (s, 1 H), 8.33 (s, 1 H), 8.14 (s, 1 H), 8.01 (s, 1 H), 7.34 (s, 2 H), 4.25 (s, 3 H), 3.74 (s, 3 H), 3.05 (q, 2 H), 1.40 (t, 3 H) ppm.

-65-

Example P11: 2-[3-ethylsulfanyl-5-[3-(trifluoromethyl)pyrazol-1-yl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound A27):



A solution of 2-[3-ethylsulfanyl-5-[3-(trifluoromethyl)pyrazol-1-yl]-2-pyridyl]-3,5-dimethyl-6-

5 (trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A26** (preparation described before) in dichloromethane (4 ml) was added mCPBA (70 wt% in water) (117.8 mg, 0.48 mmol) in one portion and mixture was stirred at ambient temperature for 2 hours. The reaction mixture was diluted with dichloromethane and water, then after separation, the organic phase was washed with solution of NaOH 1M. The organic phase is dried over sodium sulfate and concentrated under vacuum. The residue was purified over 10 silica by flash column chromatography (ethyl acetate in heptane). The fractions containing product were combined and concentrated to afford the title compound (25 mg) as a solid. $^1\text{H-NMR}$ (CDCl_3 , ppm) 9.44 (s, 1H), 8.80 (s, 1H), 8.20 (sb, 1H), 7.23 (s, 1H), 6.90 (s, 1H), 4.11 (s, 3H), 3.87 (q, 2H), 3.74 (s, 3H), 1.40 (t, 3H).

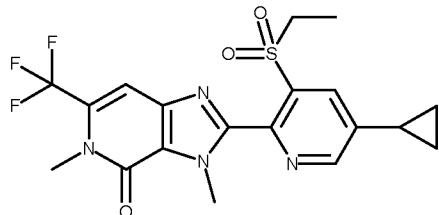
Starting from the cited starting material, the following compounds were synthesised using the same

15 protocol:

Product	Starting material	NMR / LC-MS (method) - product
A25	A24	$^1\text{H NMR}$ (400 MHz, CDCl_3): 9.42(s, 1H), 8.78 (s, 1H), 8.44 (s, 1H), 8.07 (s, 1H), 7.23 (s, 2H), 4.11 (s, 3H), 3.86 (q, 2H), 3.74 (s, 3H), 1.40 (t, 3H) ppm
A17	A16	$^1\text{H NMR}$ (400 MHz, CDCl_3): 9.0(d, 1H), 8.57 (d, 1H), 7.72 (q, 1H), 7.22 (s, 1H), 4.05 (s, 3H), 3.74 (m, 5H), 1.34 (t, 3H) ppm
A19	A18	$^1\text{H NMR}$ (400 MHz, CDCl_3): 9.18(s, 1H), 8.64(s, 1H), 7.68 (d, 2H), 7.55 (d, 2H), 7.22 (s, 1H), 4.12 (s, 3H), 3.8 (q, 2H), 3.72 (s, 3H), 1.38 (t, 3H) ppm
A33	A32	LC-MS(Method A) : RT 1.12, 549 ($\text{M}+\text{H}^+$).
A39	A37	LC-MS(Method A) : RT 1.01, 441 ($\text{M}+\text{H}^+$).
A40	A38	LC-MS(Method A) : RT 1.06, 454 ($\text{M}+\text{H}^+$).

-66-

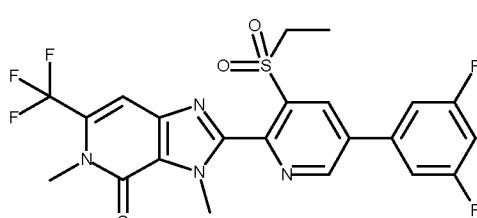
Example P12: 2-[3-ethylsulfanyl-5-[3-(trifluoromethyl)pyrazol-1-yl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (A23):



A solution of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-

5 4-one **A21** (preparation described before, 0.16 g, 0.3338 mmol) in DME (3.338 mL) was added sodium carbonate (0.8346 mL, 0.8346 mmol), cyclopropylboronic acid (0.034 g, 0.40 mmol), and tetrakis(triphenylphosphine)palladium (0.01968 g, 0.01669 mmol) in a vial. The reaction mixture was stirred at 100°C. The reaction mixture was diluted with water and extracted two time with ethyl acetate. The combined organic phases were washed with water, brine and dried over sodium sulfate and concentrated under vaccum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (50 mg). ¹H NMR (400 MHz, CDCl₃) δ ppm 8.73 (s, 1 H); 8.03 (s, 1 H); 7.21 (s, 1 H), 4.03 (s, 3 H), 3.70 (m, 5 H); 2.11 (m, 1H), 1.30 (m, 5H).

Example P13: 2-[5-(3,5-difluorophenyl)-3-ethylsulfonyl-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound A28):

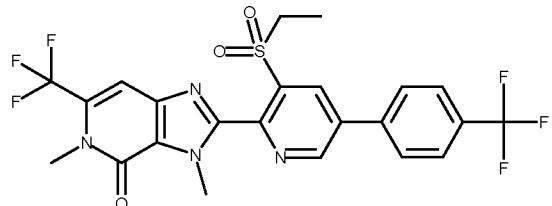


A solution of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-

4-one **A21** (preparation described before, 0.3 g, 0.6259 mmol) in isopropanol (6.2mL) was added sodium hydrogenocarbonate (3.378 g, 1.565 mmol), (3,5-difluorophenyl)boronic acid (0.12 g, 0.75 mmol) and tetrakis(triphenylphosphine)palladium (0.03690 g, 0.03130 mmol) in a vial. The reaction mixture was stirred at 100°C. The reaction mixture was diluted with water and extracted two time with ethyl acetate. The combined organic phases were washed with water, brine and dried over sodium sulfate and concentrated under vaccum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (98 mg). ¹H NMR (400 MHz, CDCl₃) δ ppm 9.14 (s, 1 H); 8.62 (s, 1 H); 7.23-7.28 (m, 3 H), 7.00 (m, 1 H), 4.13(s, 3H); 3.82 (q, 2H), 3.74 (s, 3H), 1.39 (t, 3H).

Example P13B: 2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound A22):

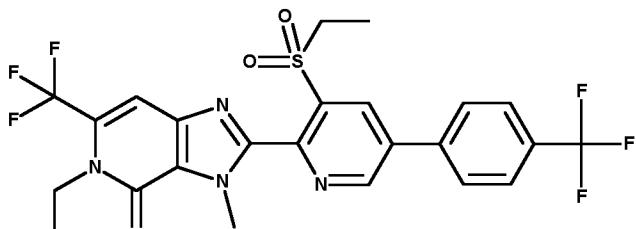
-67-



A solution of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A21** (preparation described before, 0.08 g) in acetonitrile (4.6 mL) was added disodium carbonate (0.0536 g, 3.000), 4-trifluoromethyl phenyl boronic acid (0.065 g) in a vial. The vial was

5 flushed with argon and bis(triphenylphosphine)palladium (ii) chloride (0.01183 g). The reaction mixture was stirred at 120°C in MW for 45 minutes. The reaction mixture was diluted with water and extracted two time with ethyl acetate. The combined organic phases were washed with brine (2 times) and dried over sodium sulfate and concentrated under vacuum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were 10 evaporated and the final purification was realized by HPLC to yield the title compound (40 mg). ¹H NMR (400 MHz, CDCl₃) δ ppm 9.20 (s, 1 H); 8.70 (s, 1 H), 7.84 (s, 3 H), 7.22 (s, 1 H), 4.12 (s, 3 H), 3.82 (q, 2 H), 3.74 (s, 3 H), 1.39 (t, 3 H).

Example P13C: 5-ethyl-2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound **A35**):



15

A solution of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-5-ethyl-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one **A31** (preparation in same method that described before for **A21** via Example P8 with **A30**, 0.3 g) in a mixture of water (3 mL) and toluene (3 mL) was added potassium phosphate tribasic (0.798 g, 0.311 mL, 3.65 mmol), 4-trifluoromethyl phenyl boronic acid (0.424 g, 2.19 mmol) in a vial.

20 The vial was flushed with argon and tetrakis(triphenylphosphine)palladium(0) (0.0704 g, 0.0608 mmol) was added. The reaction mixture was stirred at reflux for 4 hours. The reaction mixture was diluted with water and extracted two time with ethyl acetate. The combined organic phases were washed with brine (2 times) and dried over sodium sulfate and concentrated under vacuum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane to yield the title compound (0.26 g). ¹H NMR (400 MHz, CDCl₃) δ ppm 1.40 - 1.46 (m, 6 H), 3.88 (q, 2 H), 4.17 (s, 3 H), 4.29 (q, 2 H), 7.26 (s, 1 H), 7.88 (s, 4 H), 8.72 (s, 1 H), 9.23 (s, 1 H).

25

-68-

The same protocol was used to synthesize: **A36** starting from **A31**; **A34** starting from **A31** and the cyclopropylboronic acid; **A49** starting from **A31** and the (2-fluoro-4-pyridyl)boronic acid; **A48** starting from **A21** and the (2-fluoro-4-pyridyl)boronic acid.

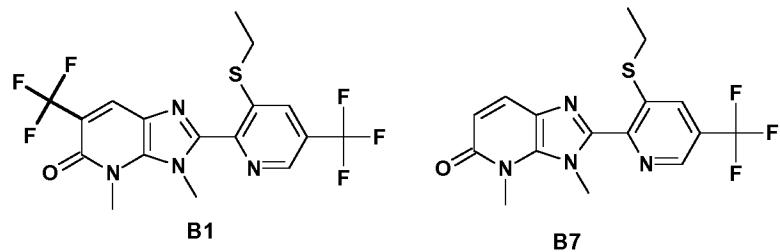
A36: ^1H NMR (400 MHz, CDCl_3) δ ppm 1.37 - 1.44 (m, 6 H), 3.86 (q, 2 H), 4.14 (s, 3 H), 4.27 (q, 2 H),

A34: ^1H NMR (400 MHz, CDCl_3) δ ppm 1.10 (m, 2 H), 1.40-1.58 (m, 8 H), 2.25 (m, 1 H), 3.88 (q, 2 H), 4.20 (s, 3 H), 4.40 (q, 2 H), 7.35 (s, 1 H), 8.20 (d, 1 H), 8.88 (d, 1 H).

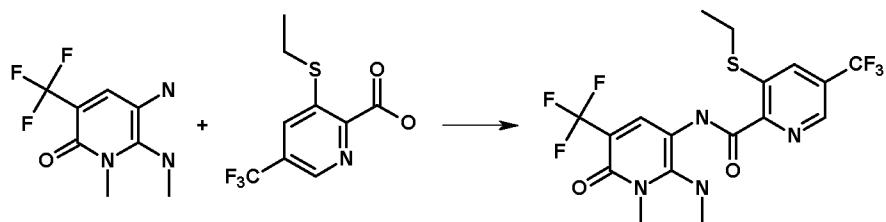
A48: ^1H NMR (400 MHz, CDCl_3) δ ppm 1.39 (t, 3 H), 3.74 (s, 3 H), 3.85 (q, 2 H), 4.13 (s, 3 H), 7.22 (s, 1 H), 7.27 - 7.30 (m, 1 H), 7.54 (m, 1 H), 8.46 (d, 1 H), 8.71 (d, 1 H), 9.21 (d, 1 H)

A49: ^1H NMR (400 MHz, CDCl_3) δ ppm 1.37 - 1.43 (m, 6 H), 3.87 (q, 2 H), 4.14 (s, 3 H), 4.26 (q, 2 H), 7.22 (s, 1 H), 7.29 (s, 1 H), 7.54 (m, 1 H), 8.46 (d, 1 H), 8.71 (d, 1 H), 9.21 (d, 1 H).

Example P14: 2-[3-ethylsulfanyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-6-(trifluoromethyl)imidazo[4,5-b]pyridin-5-one (**B1**) and 2-[3-ethylsulfanyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-imidazo[4,5-b]pyridin-5-one (compound **B7**):



Step A: 5- trifluoromethyl -3-ethylsulfanyl-N-[1-methyl-2-(methylamino)-6-oxo-5-(trifluoromethyl)-3-pyridyl]pyridine-2-carboxamide:



20 To a suspension of 3-ethylsulfanyl-5-(trifluoromethyl)pyridine-2-carboxylic acid (1.12 g, 4.48 mmol) in dichloromethane (20 ml) was added one drop of N,N-dimethylformamide, followed by oxalyl chloride (1.32 g, 0.906 mL, 10.2 mmol). After the end of gas evolution, the reaction mixture was a pale red solution. The latter was evaporated under reduced pressure at a bath temperature of 60°C. The residue formed dark red crystals of 5-bromo-3-ethylsulfanyl-pyridine-2-carbonyl chloride and the
 25 residue was redissolved in a mixture AcOEt (5mL), DCM (5mL).

To a solution of 5-amino-1-methyl-6-(methylamino)-3-(trifluoromethyl)pyridin-2-one (Prepared in Example I3, 0.9g, 4.07mmol) in ethyl acetate (30 ml) was added N,N-diethylethanamine (1.04 g, 1.43

-69-

mL, 10.2 mmol) then The resulting solution was cooled with an ice bath, before slow addition of the previous acyl chloride solution. The resulting mixture was stirred 1hour at 0°C. The solution was neutralized by addition of a saturated aqueous solution of sodium bicarbonate and the product was extracted twice with ethyl acetate. The organic solution was dried over sodium sulfate and evaporated under reduced pressure to yield the crude product. 5-bromo-3-ethylsulfanyl-N-[1-methyl-2-(methylamino)-6-oxo-5-(trifluoromethyl)-3-pyridyl]pyridine-2-carboxamide (1.17g) was obtained after column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. ¹H NMR (400 MHz, CDCl₃) δ ppm 9.29 (s, 1 H), 8.54 (s, 1 H), 7.90 (s, 1 H), 7.60 (s, 1 H), 4.60(bs, 1H), 3.58 (s, 3H), 3.02 (d, 3H), 2.98 (q, 2H), 1.44 (t, 3H).

10 The use of a similar protocol between 5-amino-1-methyl-6-(methylamino)-3-(trifluoromethyl)pyridin-2-one (Prepared in Example I3) and the 3-ethylsulfanyl-5-[4-(trifluoromethyl)phenyl]pyridine-2-carboxylic acid (See Example I3) gave the 3-ethylsulfanyl-N-[1-methyl-2-(methylamino)-6-oxo-5-(trifluoromethyl)-3-pyridyl]-5-[4-(trifluoromethyl)phenyl]pyridine-2-carboxamide. LC-MS (Method A) RT 1.08 531 (MH⁺), 529 (M-H⁺).

15 Step B: 2-[3-ethylsulfanyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-6-(trifluoromethyl)imidazo[4,5-b]pyridin-5-one (**B1**) and 2-[3-ethylsulfanyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-imidazo[4,5-b]pyridin-5-one (**B7**):

20 A 20mL microwave vial was charged with 5-bromo-3-ethylsulfanyl-N-[1-methyl-2-(methylamino)-6-oxo-5-(trifluoromethyl)-3-pyridyl]pyridine-2-carboxamide (0.250 g, 0.550 mmol) , 1,2-dichloroethane (18.84 g, 15 mL, 190 mmol) and p-toluenesulfonic acid monohydrate (0.0488 g, 0.275 mmol) .Then, the mixture was stirred for 60 min at 170°C under microwaves. The reaction mixture was diluted with water and extracted two time with ethyl acetate. The combined organic phases were washed with water and dried over sodium sulfate and concentrated under vaccum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated and the final purification was realized by HPLC to yield the title compound **B1** (47 mg). ¹H NMR (400 MHz, CDCl₃) δ ppm 8.68 (s, 1 H); 8.28 (s, 1 H), 7.88 (s, 1 H), 4.10 (s, 3H), 3.98(s, 3H), 3.0 (q, 2H), 1.40 (t, 3H) and **B7** (40 mg) ¹H NMR (400 MHz, CDCl₃) δ ppm 8.68 (s, 1 H); 7.88 (s, 1 H), 7.82 (d, 1 H), 6.50 (d, 1 H), 4.08 (s, 3H), 3.96(s, 3H), 3.0 (q, 2H), 1.438 (t, 3H).

25 The same protocol was used to synthesize 2-[3-ethylsulfanyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3,4-dimethyl-6-(trifluoromethyl)imidazo[4,5-b]pyridin-5-one **B5** and 2-[3-ethylsulfanyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3,4-dimethyl-imidazo[4,5-b]pyridin-5-one **B9** from the 3-ethylsulfanyl-N-[1-methyl-2-(methylamino)-6-oxo-5-(trifluoromethyl)-3-pyridyl]-5-[4-(trifluoromethyl)phenyl]pyridine-2-carboxamide.

30 **B5:** LC-MS (Method A) RT 1.09 (513, MH⁺)
B9: LC-MS (Method A) RT 0.96 (445, MH⁺)

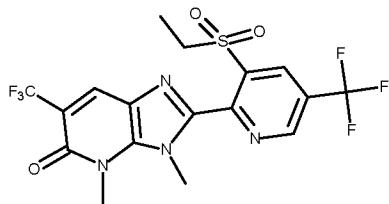
35 Step B2:

-70-

Alternatively, 2-[3-ethylsulfanyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-imidazo[4,5-b]pyridin-5-one **B7** could be obtained quantitatively by reaction of 5-bromo-3-ethylsulfanyl-N-[1-methyl-2-(methylamino)-6-oxo-5-(trifluoromethyl)-3-pyridyl]pyridine-2-carboxamide in acetic acid for 60 min at 150°C under microwaves (analogue protocol as in Example P7, Step D).

5

Example P15: 2-[3-ethylsulfonyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-6-(trifluoromethyl)imidazo[4,5-b]pyridin-5-one (compound **B2):**



A solution of 2-[3-ethylsulfanyl-5-(trifluoromethyl)-2-pyridyl]-3,4-dimethyl-6-(trifluoromethyl)imidazo[4,5-b]pyridin-5-one **B1** (preparation described before, 0.047 g, 0.1077 mmol) in dichloromethane (5 ml) was added mCPBA (70 wt% in water) (0.05080 g, 0.2208 mmol) in one portion and mixture was stirred at ambient temperature for 2h. The reaction mixture was diluted with dichloromethane and water, then after separation, the organic phase was washed with solution of potassium carbonate, water and brine. The organic phase is dried over sodium sulfate and concentrated under vacuum to afford the title compound (34 mg) as a solid. ¹H-NMR (CDCl₃, ppm) 9.20 (s, 1H), 8.72 (s, 1H), 8.15 (s, 1H), 3.98 (s, 3H), 3.95 (s, 3H), 3.86 (q, 2H), 1.38 (t, 3H).

The same protocol was used to synthesize **B6** starting from **B7**

B6: ¹H NMR (400 MHz, CDCl₃) δ ppm 9.18 (s, 1H); 8.72 (s, 1H), 7.70 (d, 1H), 6.52 (d, 1H), 4.39-4.00 (m, 8H), 1.38 (t, 3H).

20 The same protocol was used to synthesize **B8** starting from **B9**

2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3,4-dimethyl-imidazo[4,5-b]pyridin-5-one **B8:** LC-MS (Method A) RT 0.91 (477, MH⁺)

The same protocol was used to synthesize **B4** starting from **B5**

B4: LC-MS (Method A) RT 1.03 (545, MH⁺)

25

Example P16: Preparation of (A50 to A69):

Compound A50 to A69 were prepared by the following general protocol: To a microwave vial containing a boronic acid (2eq., 0.06 mmol) was added a solution of 2-(5-bromo-3-ethylsulfonyl-2-pyridyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (Example P8: A21, 0.03mmol, 1 eq.) in N,N-dimethylformamide DMF, a solution of sodium carbonate Na₂CO₃ (300 μL of 441 mg/18.0mLH₂O) and Xphos Pd (200 μL of a solution of 59 mg XPhos Pd in 5.2 ml DME). The vials were purged with Ar and submit 10 minutes to microwaves irradiation. 1 ml of water was added and extracted 3 times with ethyl acetate. The combined organic phase is dried over sodium sulfate and

-71-

concentrated under vacuum. The desired compounds were isolated by HPLC and identified by LC-MS, after dissolution in a solution of DMA and MeOH (250 μ L DMA and 500 μ L of methanol by vial).

Analytic method used for identification:

Waters SQD2 Mass Spectrometer (Single quadrupole mass spectrometer)

5 Ionisation method: Electrospray

Polarity: positive ions

Capillary (kV) 3.50, Cone (V) 30.00, Extractor (V) 3.00, Source Temperature (°C) 150, Desolvation

Temperature (°C) 400 Cone Gas Flow (L/Hr) 60, Desolvation Gas Flow (L/Hr) 700

Mass range: 140 to 800 Da

10 DAD Wavelength range (nm): 210 to 400

Method Waters ACQUITY UPLC with the following HPLC gradient conditions

(Solvent A: Water/Methanol 9:1,0.1% formic acid and Solvent B: Acetonitrile,0.1% formic acid)

	Time (minutes)	A (%)	B (%)	Flow rate (ml/min)
15	0	100	0	0.75
	2.5	0	100	0.75
	2.8	0	100	0.75
	3.0	100	0	0.75

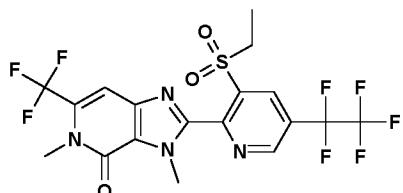
20 Type of column: Waters ACQUITY UPLC HSS T3; Column length: 30 mm; Internal diameter of column: 2.1 mm; Particle Size: 1.8 micron; Temperature: 60°C.

	RT	M (calculated)	(M+H) ⁺ (measured)
A50	1.54	501.1	502.0
A51	1.85	562.1	563.2
A52	1.87	504.1	505.2
A53	1.21	491.1	492.3
A54	1.66	494.1	495.2
A55	1.35	508.1	509.0
A56	1.67	494.1	495.0
A57	1.21	478.1	479.0
A58	1.17	477.1	478.2
A59	1.75	508.1	509.2

-72-

A60	1.80	544.1	545.2
A61	1.79	544.1	545.2
A62	1.88	544.0	544.9
A63	1.90	544.0	544.9
A64	1.66	524.1	525.0
A65	1.61	545.1	546.1
A66	1.85	560.1	561.1
A67	1.54	440.1	441.2
A68	1.69	512.1	513.2
A69	1.76	510.1	511.0

Example P17: Preparation of 2-[3-ethylsulfonyl-5-(1,1,2,2,2-pentafluoroethyl)-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (**A46**):



5 A 5mL microwave vial under Argon was charged with **A21** (0.2 g, 0.4173 mmol) , NMP (3 mL) and (1, 1,2,2,2-Pentafluoroethyl)(1,10-phenanthroline- κ N1, κ N10)-copper (commercially available, 0.191 g, 0.50 mmol) . The mixture was stirred at 90°C for 2 hours under microwave. The reaction mixture was diluted with water and ethyl acetate then, after separation of the phases, the aqueous phase was extracted two time with ethyl acetate. The combined organic phases were dried over sodium sulfate and concentrated under vaccum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (150 mg). LC-MS(Method A) : RT 1.14, 519 (M+H⁺).

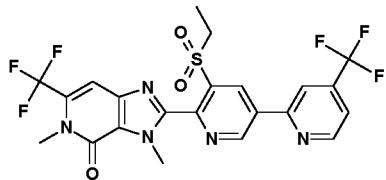
10 Using the same protocol, **A47** was prepared from **A31**.

A47: LC-MS(Method A) : RT 1.19, 533 (M+H⁺).

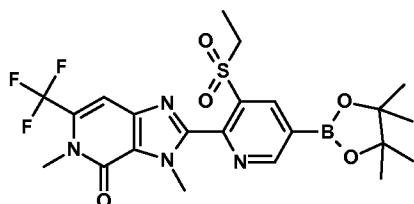
15

Example P18: Preparation of 2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)-2-pyridyl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (**A42**):

-73-



Step A: 2-[3-ethylsulfonyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one:

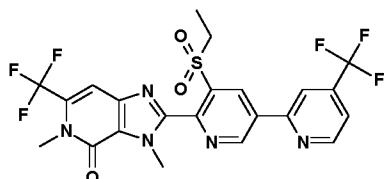


5 A mixture of **A21** (preparation described above) (2.00 g, 4.17 mmol), potassium acetate (2.13 g, 20.9 mmol) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (3.24 g, 12.5 mmol) in dioxane (15 mL) was gently flushed with argon, then 1,1'-bis(diphenylphosphino)-ferrocene dichloropalladium-dichloromethane (1:1) complex (0.0688 g, 0.0835 mmol) was added and the pale yellow mixture was heated at 100°C for 30 min. under microwave. After consumption of the starting bromide, the dark reaction mixture was diluted with water (30 ml) and extracted twice with ethyl acetate (3x30 mL). The combined organic phases were dried over sodium sulfate and concentrated under reduced pressure. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (1.8g) as a slightly yellow solid. ^1H NMR (400 MHz, CDCl_3) δ ppm 1.35 (t, 3 H), 1.41 (s, 12 H), 3.73 (m, 5 H), 4.05 (s, 3 H), 7.22 (s, 1 H), 8.83 (s, 1 H), 9.25 (s, 1 H).

10

15

Step B: 2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)-2-pyridyl]-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound **A42**):



20 A 5mL microwave vial flushed with Argon was charged with 2-bromo-4-(trifluoromethyl)pyridine (0.2656 g, 1.140 mmol), 2-[3-ethylsulfonyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (Step A, 0.3 g, 0.57 mmol), tetrakis (triphenylphosphine) palladium(0) (0.066 g, 0.057 mmol), potassium phosphate tribasic (0.7484 g, 3.420 mmol), toluene (2 mL) and water (2 mL). The mixture was then heated 15' at 110°C under

-74-

microwave. The reaction mixture was diluted with water and ethyl acetate then, after separation of the phases, the aqueous phase was extracted two time with ethyl acetate. The combined organic phases were dried over sodium sulfate and concentrated under vacuum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound as a white solid (90 mg). ^1H NMR (400 MHz, CDCl_3) δ ppm 1.41 (t, 3 H), 3.75 (s, 3 H), 3.85 (q, 2 H), 4.13 (s, 3 H), 7.25 (s, 1 H), 7.67 (d, 1 H), 8.12 (s, 1 H), 9.02 (d, 1 H), 9.12 (s, 1 H), 9.65 (s, 1 H).

Using the same starting material and the corresponding pyridine derivatives, the following compounds were synthesised using the same protocol:

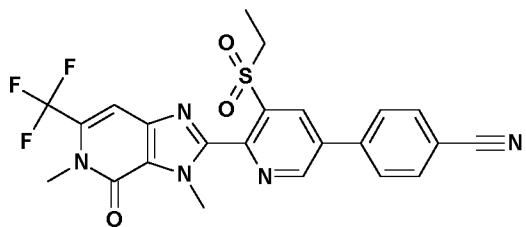
10 **A43**: LC-MS(Method A) : RT 1.11, 546 ($\text{M}+\text{H}^+$).

A44: LC-MS(Method A) : RT 1.05, 514 ($\text{M}+\text{H}^+$).

A45: LC-MS(Method A) : RT 1.02, 496 ($\text{M}+\text{H}^+$).

Example P19: Preparation of 4-[6-[3,5-dimethyl-4-oxo-6-(trifluoromethyl)imidazo[4,5-c]pyridin-2-yl]-5-

15 **ethylsulfonyl-3-pyridyl]benzonitrile (compound A41):**



Solution A: A solution of sulfuric acid 50mM was prepared with sulfuric acid (0.0268 mL, 0.490 mmol) and DMA (10mL, degassed with Argon for 30min). This solution was degassed with Argon for 10min.

Preparation of the ligand-metal complex: A 5mL sealed vial was charged with palladium diacetate

20 (0.0224 g, 0.1 mmol) , XPHOS (0.098 g, 0.20 mmol) . The vial was evacuated and re-filled with Argon 3 times. 2mL of the solution A was added and the mixture was heated at 80°C for an hour. The solution becoming a dark brown solution.

A 5mL sealed vial was charged with **A19** (0.255 g, 0.499 mmol) , zinc (0.00131 g, 0.020 mmol,) , zinc cyanide (0.036 g, 0.3 mmol) . It was purged 3 times with Argon. DMA (2mL degassed with Argon for

25 30min) was added followed by 100 μ L of the ligand-metal complex solution prepared before.

The resulting mixture was stirred for an hour at 120°C (20% conversion) and 100 μ L more of ligand-

metal complex solution were added, and it was stirred 1 hour more and finally 500 μ L more of ligand-metal complex solution were added. After 1 hour reaction was cool down. The reaction mixture was diluted with water and ethyl acetate then, after separation of the phases, the aqueous phase was

30 extracted two times with ethyl acetate. The combined organic phases were washed with water and brine, dried over sodium sulfate and concentrated under vacuum. The residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions

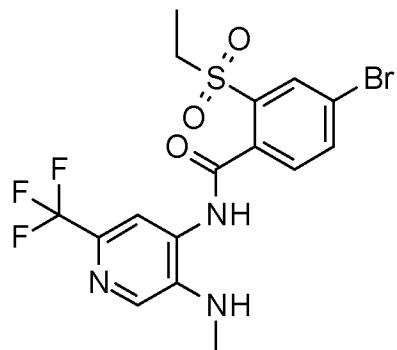
were evaporated to yield the title compound (0.062g) as a white solid.

-75-

A41: LC-MS(Method A) : RT 1.01, 502 (M+H⁺).

Example P20: Preparation of 2-(4-bromo-2-ethylsulfonyl-phenyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo [4,5-c] pyridin-4-one (**A74**), 2-(2-ethylsulfonyl-4-pyrimidin-2-yl-phenyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (**A71**), 2-[4-(4-chlorophenyl)-2-ethylsulfonyl-phenyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo [4,5-c] pyridin-4-one (**A72**) and 2-[2-ethylsulfonyl-4-[4-(trifluoromethyl)phenyl]phenyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound **A70**):

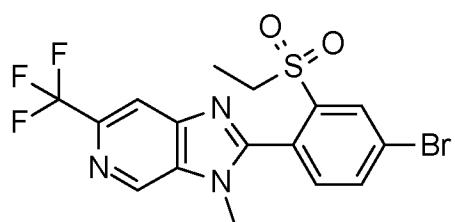
Step A: 4-bromo-2-ethylsulfonyl-N-[5-(methylamino)-2-(trifluoromethyl)-4-pyridyl]benzamide:



10 To a stirred solution of 4-bromo-2-ethylsulfonyl-benzoic acid (Example I6, 300 mg, 1.0 mmol), N3-methyl-6-(trifluoromethyl)pyridine-3,4-diamine (190 mg, 1.0 mmol, prepared as described in WO 2015/000715) and 1-[Bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate (HATU, 580 mg, 1.5 mmol) in DMF (2.0 mL) was added di-isopropyl ethyl amine (0.4 ml, 2.0 mmol). The system was stirred at room temperature overnight and then diluted with EtOAc and water. The organic layer was separated, washed with brine and water, dried over anhydrous sodium sulfate. After filtration and concentration in *vacuo*, the residue was purified by chromatography on silica gel eluting with PE: EtOAc=2:1, to give the title compound as white solid. ¹H NMR (400 MHz, d⁶-DMSO): δ (ppm) 10.26(d, 1H), 8.05-8.14(m, 3H), 7.89-7.92 (m, 2H), 5.88(q, 1H), 3.54 (q, 2H), 2.88 (d, 3H), 1.21 (t, 3H). ESI-MS(method B): 468 (M+H)⁺.

15 Step B: 2-(4-bromo-2-ethylsulfonyl-phenyl)-3-methyl-6-(trifluoromethyl)imidazo[4,5-c]pyridine:

20



A solution 4-bromo-2-ethylsulfonyl-N-[5-(methylamino)-2-(trifluoromethyl)-4-pyridyl]benzamide (100 mg, 0.22 mmol) in acetic acid (2 mL) was stirred at 120 °C overnight. The mixture was evaporated to

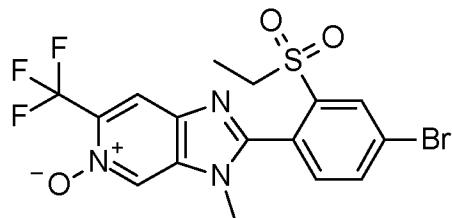
-76-

dryness, and the residue was purified by chromatography on silica gel (eluting with petroleum: EtOAc = 3:1) to afford the title compound as white solid, mp: 180-181°C.

¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.93 (s, 1H), 8.35 (s, 1H), 8.07 (s, 1H), 7.97 (d, 1H), 7.42 (d, 1H), 3.73 (s, 3H), 3.36 (q, 2H), 1.26 (t, 3H). ESI-MS(method B): 450 (M+H)⁺, 472 (M+Na)⁺. LC/MS

5 (Standard method): Rt=0.95 min. M+H[448]⁺

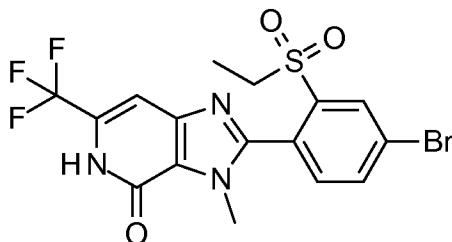
Step C: 2-(4-bromo-2-ethylsulfonyl-phenyl)-3-methyl-5-oxido-6-(trifluoromethyl)imidazo[4,5-c]pyridin-5-ium:



To a solution of 2-(4-bromo-2-ethylsulfonyl-phenyl)-3-methyl-6-(trifluoromethyl)

10 imidazo[4,5-c]pyridine (46 mg, 0.1mmol) in dichloromethane (1 mL) was added urea hydrogen peroxide (37 mg, 0.37 mmol), and the mixture was cooled to 0 °C. To this solution was added Trifluoroacetic anhydride (0.05ml, 0.76 mmol) and the resulting mixture was then stirred at rt overnight. The mixture was then diluted with dichloromethane and water. The aqueous phase was back extracted with dichloromethane (x2) and the combined organic phases washed with brine, dried with 15 Na₂SO₄, and concentrated in *vacuo*. The residue was further purified by flash chromatography on silica gel eluting with petroleum ether: EtOAc =1:3, to give the title compound as a solid. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 9.24 (s, 1H), 8.35 (s, 1H), 8.21 (m, 2H), 7.80 (d, 1H), 3.55 (s, 3H), 3.53 (q, 2H), 1.09 (t, 3H). ¹⁹FNMR (400 MHz, CDCl₃): δ -63.83 (s, 3F).

20 Step D: 2-(4-bromo-2-ethylsulfonyl-phenyl)-3-methyl-6-(trifluoromethyl)-5H-imidazo[4,5-c]pyridin-4-one:



To a solution of 2-(4-bromo-2-ethylsulfonyl-phenyl)-3-methyl-5-oxido-6-(trifluoromethyl) imidazo [4,5-c]

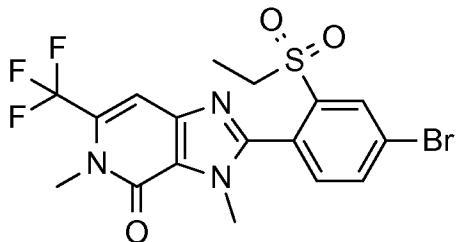
25 pyridin-5-ium (100 mg, 0.22mmol) in DMF (2mL) was added trifluoroacetic anhydride (0.1 ml, 1.5 mmol). The mixture was stirred at rt overnight and then diluted with dichloromethane and water. The aqueous phase was back-extracted with dichloromethane (X2) and the combined organic phases

-77-

washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by chromatography on silica gel, eluting with PE: $\text{EtOAc}=1:1$, to give the title compound as white solid.

^1H NMR (400 MHz, CDCl_3): δ (ppm) 12.53 (br, 1H), 8.17 (m, 2H), 7.75 (d, 1H), 7.18 (m, 1H), 3.73 (s, 3H), 3.50 (q, 2H), 1.08 (t, 3H). ^{19}F NMR (400 MHz, CDCl_3): δ -62.19 (s, 3F).

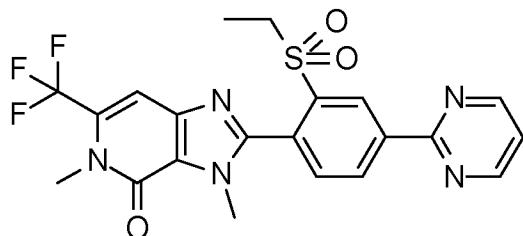
5 **Example P20:2-(4-bromo-2-ethylsulfonyl-phenyl)-3,5-dimethyl-6-(trifluoromethyl) imidazo [4,5-c] pyridin-4-one (compound A74):**



Sodium hydride (100 mg, 0.21 mmol) was added to a solution of 2-(4-bromo-2-ethylsulfonyl-phenyl)-3-methyl-6-(trifluoromethyl)-5H-imidazo[4,5-c] pyridin-4-one (100 mg, 0.21 mmol) in DMF (2 mL) at 0 °C and stirred for 10 min. and then treated with iodomethane (18 mg, 0.42 mmol). The reaction mixture was stirred at rt for 2 h. After this time, the reaction mixture was diluted with EtOAc and H_2O , the organic layer was washed with brine and water, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (eluting with PE: $\text{EtOAc}=3:1$) to give the title compound as white solid.

15 ^1H NMR (400 MHz, CDCl_3): δ (ppm) 8.32 (s, 1H), 7.93 (d, 1H), 7.36 (d, 1H), 7.19 (s, 1H), 3.88 (s, 3H), 3.70 (s, 3H), 3.40 (q, 2H), 1.25 (t, 3H). ^{19}F NMR (400 MHz, CDCl_3): δ -58.80 (s, 3F). ESI-MS(method B): 478 ($\text{M}+\text{H}$)⁺.

Example P20a: 2-(2-ethylsulfonyl-4-pyrimidin-2-yl-phenyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo [4,5-c] pyridin-4-one (compound A71):



20

A mixture of 2-(4-bromo-2-ethylsulfonyl-phenyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c] pyridin-4-one (24 mg, 0.05 mmol), $\text{Pd}(\text{PPh}_3)_4$ (5 mg, 0.005 mmol), tributyl(1,2-dihydropyrimidin-2-yl)stannane (20 mg, 1.0 mmol), and toluene(2 mL) was refluxed overnight under a N_2 atmosphere. The reaction mixture was then quenched with water, extracted with EtOAc , and the combined organic layers

-78-

washed with brine, and dried over anhydrous sodium sulfate. After filtration and concentration in *vacuo*, the crude product was purified with column chromatography on silica gel (eluting with petroleum ether: EtOAc = 1:1) to afford the title compound as a white solid, mp > 250 °C.

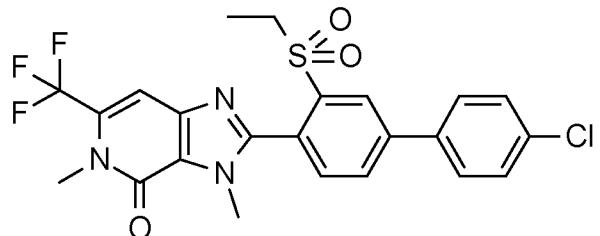
¹H NMR (400 MHz, CDCl₃): δ (ppm) 9.28 (s, 1H), 8.88-8.95 (m, 3H), 7.63-7.64 (m, 1H), 7.44-7.45(m,

5 1H), 7.31-7.32 (m, 1H) 3.93 (s, 3H), 3.72 (s, 3H), 3.44 (q, 2H), 1.29 (t, 3H). ¹⁹FNMR (400 MHz, CDCl₃):

δ -63.02 (s, 3F). ESI-MS(method B): 478 (M+H)⁺. LC/MS (Standard method A): Rt=0.96 min.

M+H[478]⁺

Example 20b: 2-[4-(4-chlorophenyl)-2-ethylsulfonyl-phenyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c] pyridin-4-one (compound A72):



10

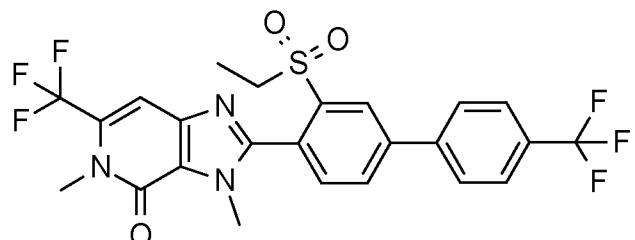
A mixture of 2-(4-bromo-2-ethylsulfonyl-phenyl)-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c] pyridin-4-one (24 mg, 0.05 mmol), (4-chlorophenyl)boronic acid (8.0 mg, 0.05 mmol), Pd(PPh₃)₄ (5 mg, 0.005 mmol), K₂CO₃ (20 mg, 1.0 mmol), in dioxane (2 mL) was refluxed overnight under N₂ atmosphere. After aqueous work-up, drying over anhydrous sodium sulfate, and concentration in *vacuo*, the crude

15 product was obtained which was purified by column chromatography on silica gel (eluting with petroleum ether: EtOAc = 2:1) to afford the title compound as a white solid, mp > 250 °C.

¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.35 (s, 1H), 7.97 (d, 1H), 7.61 (d, 2H), 7.57(d, 1H), 7.49 (d, 2H) , 7.19 (s, 1H), 3.93 (s, 3H), 3.72 (s, 3H), 3.40 (q, 2H), 1.28 (t, 3H). ¹⁹FNMR (400 MHz, CDCl₃): δ -58.76 (s, 3F). ESI-MS(method B): 510 (M+H)⁺, 532(M+Na)⁺. LC/MS (Standard method A): Rt=1.14 min.

20 M+H[510/512]⁺

Example 20c: 2-[2-ethylsulfonyl-4-[4-(trifluoromethyl)phenyl]phenyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound A70):



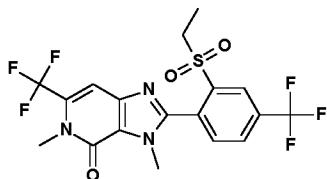
-79-

The reaction was carried out analogously to the example above and the title compound was obtained as a white solid, mp 160-162 °C

¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.40 (d, 1H), 8.02 (d, 1H), 7.78 (s, 4H), 7.60 (d, 1H), 7.22 (s, 1H), 3.94 (s, 3H), 3.72 (s, 3H), 3.45 (q, 2H), 1.26 (t, 3H). ¹⁹FNMR (400 MHz, CDCl₃): δ -62.75 (s, 3F). ESI-

5 MS: 544(M+H)⁺. LC/MS (Standard method A): Rt=1.12 min. M+H[544]⁺

Example P21: 2-[2-ethylsulfonyl-4-(trifluoromethyl)phenyl]-3,5-dimethyl-6-(trifluoromethyl)imidazo[4,5-c]pyridin-4-one (compound A73):



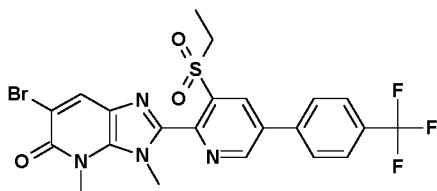
Prepared from 2-[2-ethylsulfonyl-4-(trifluoromethyl)phenyl]-3-methyl-6-(trifluoromethyl)imidazo[4,5-

10 c]pyridine (prepared as described in WO 2015/000715) in analogous manner to example P20. The title product was obtained as a white solid, MP. 134-136 °C, ¹H NMR (400 MHz, d₆-DMSO): δ (ppm) 8.38 (d, 1H), 8.30 (s, 1H), 8.10 (d, 1H), 7.40 (s, 1H), 3.78 (s, 3H), 3.60 (s, 3H), 3.56 (q, 2H), 1.09 (t, 3H).

¹⁹FNMR (400 MHz, CDCl₃): δ -59.94 (s, 3F), -59.91 (s, 3F). ESI-MS (Method B): 468 (M+H)⁺, 490(M+Na)⁺. LC/MS (Standard method A): Rt=1.01 min. M+H[468]⁺

15

Example P22: Preparation of 6-bromo-2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3,4-dimethyl-imidazo[4,5-b]pyridin-5-one (B3):



To a solution of 2-[3-ethylsulfonyl-5-[4-(trifluoromethyl)phenyl]-2-pyridyl]-3,4-dimethyl-imidazo[4,5-

20 b]pyridin-5-one (B8, 0.0610 g, 0.128 mmol) in DMF (3mL) was added N-bromosuccinimide (0.023 g, 0.128 mmol. The mixture was stirred at ambient temperature for 45 minutes and then diluted with ethyl acetate and water. The aqueous phase was back-extracted with ethyl acetate (X2) and the combined organic phases washed with water (x2, 30 mL), brine (30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified two time by chromatography on silica gel, eluting with cyclohexane: EtOAc, to give the title compound as white solid (0.011 g, 15.5% Yield).

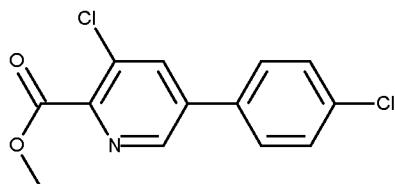
¹H NMR (400 MHz, CDCl₃): δ (ppm) 9.20(s, 1H), 8.70(s, 1H), 8.20(s, 1H), 8.88(s, 4H), 4.06 (s, 3H), 3.98 (s, 3H), 3.84 (q, 2H), 1.42 (t, 3H).

-80-

Synthesis of intermediates:

Example I1: 5-(4-chlorophenyl)-3-ethylsulfanyl-pyridine-2-carboxylic acid:

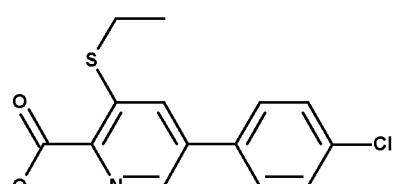
5 **Step A:** methyl 3-chloro-5-(4-chlorophenyl)pyridine-2-carboxylate:



A solution of 2-Pyridinecarboxylic acid, 5-bromo-3-chloro-, methyl ester (commercially available, 17.33 g.) in a solution of DME (500 mL) and water (50 mL) was added sodium carbonate (14.7g) and 4-chlorophenylboronic acid (11.36g) and flushed with argon. Tetrakis(triphenylphosphine)palladium (4.0

10 g) was added and the mixture was stirred at 90°C bath-temp for 7h. The reaction was not finish and two time 0.5g of Tetrakis(triphenylphosphine)palladium was added. the mixture was stirred at 90°C bath-temp for 2h extra hours. The reaction mixture was diluted with water and extracted two time with ethyl acetate. The combined organic phases were washed with water, brine and dried over sodium sulfate and concentrated under vacuum. The residue was subjected to column chromatography over 15 silica gel, eluting with ethyl acetate / heptane. The selected fractions were evaporated to yield the title compound (10.5 g). ¹H NMR (400 MHz, CDCl₃) δ ppm 8.77 (s, 1 H); 7.78 (s, 1 H); 7.52 (m, 4 H), 4.03 (s, 3 H).

Step B: 5-(4-chlorophenyl)-3-ethylsulfanyl-pyridine-2-carboxylic acid:

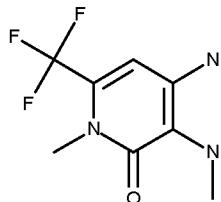


20 A solution of methyl 3-chloropyridine-2-carboxylate (preparation described before, 10g) in DMF (250 mL) was added sodium ethanethiol (16.3g). The reaction mixture was stirred at ambient temperature for 1h. The reaction mixture was diluted with ice then water and TBME were added. The organic phase was remove and the aqueous phase was acidified with acetic acid and extracted with TBME 25 and EtOAc (5 times). The combined organic phases dried over sodium sulfate and concentrated under vacuum to yield the title compound (17.67g). This compound was used without extra purification. LC-MS(Method A) : RT 1.41, 294 (M+H⁺), 292 (M-H⁺).

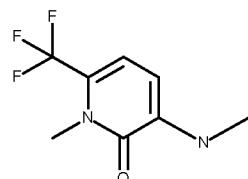
Using the same protocol from methyl 3-chloro-5-[4-(trifluoromethyl)phenyl]pyridine-2-carboxylate (CAS 1261768-92-6, commercially available) to synthesize the 3-ethylsulfanyl-5-[4-(trifluoromethyl)phenyl]pyridine-2-carboxylic acid. LC-MS (Method A) RT 1.54 328 (MH⁺)

-81-

Example I2: 4-amino-1-methyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one:



Step A: 1-methyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one:

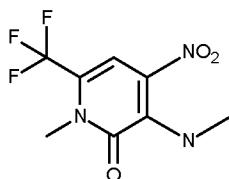


5 To a solution of 3-amino-1-methyl-6-(trifluoromethyl)pyridin-2-one (1.00 g, 5.20 mmol, Commercially available or synthesised as described for example in Synthesis 2005, No. 8, pp 1269–1278, Synthesis 2011, No. 7, pp 1149–1156) in 1,4-dioxane (62.5 mL, 726 mmol) and pyridine (1.49 mL, 18.2 mmol) under argon was added diacetoxycopper (2.39 g, 13.0 mmol). The mixture was stirred for 15 min before addition of methylboronic acid (0.803 g, 13.0 mmol). The resulting green/blue suspension was

10 refluxed for 5 hours. After cooling, the solution was filtered through a Celite pad. The dark green solution was concentrated under vacuum and was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (0.71 g). ^1H NMR (400 MHz, CDCl_3) δ ppm 7.27 (s, 1 H); 6.72 (d, 1 H); 6.04 (d, 2 H), 5.46 (bs, 1 H), 3.68 (s, 3H), 2.88 (d, 3H).

15

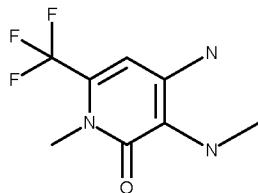
Step B: 1-methyl-3-(methylamino)-4-nitro-6-(trifluoromethyl)pyridin-2-one:



A solution of 1-methyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one (4.00 g, 19.4 mmol) sulfuric acid (58.2 mL) was cooled with an ice bath at 0°C. Then, Ice (20.0 g) and nitric acid (1.88 g, 1.35 mL, 19.4 mmol) were added. After 15 min at 0–10°C, the brown thick solution was poured into iced water. The orange precipitate formed was filtrated off, rinsing with water and drying under vacuum to give an orange solid. The water phase was extracted 3 times with AcOEt and the orange solid, obtained before, was added to the combined organic phase. The combined organic phase was washed with a saturated solution of sodium hydrogenocarbonate, water and brine, dried over magnesium sulfate and concentrated under vacuum to give yield the title compound (4.0 g). The compound was used without extra purification for the next step. LC-MS(Method A) : RT 0.91, 252 ($\text{M}+\text{H}^+$), 250 ($\text{M}-\text{H}^+$).

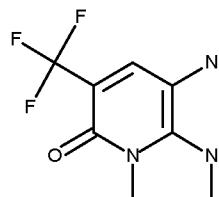
Step C: 4-amino-1-methyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one:

-82-



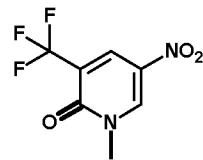
To a solution of 1-methyl-3-(methylamino)-4-nitro-6-(trifluoromethyl)pyridin-2-one (3.0 g, 11.9 mmol) in propan-2-ol (98.1 g, 125 mL, 1620 mmol) was added tin(II) chloride dihydrate (8.24 g, 43.0 mmol) 5 followed by hydrogen chloride (10 mL, 120 mmol, 37%). The resulting solution was stirred at 70°C for one hour, and, then allowed to cool down to ambient temperature. The reaction mixture was poured into water, and pH was adjusted to 10-12 with a concentrated solution of sodium hydroxide (30%). The aqueous phase was extracted three times with ethyl acetate, the organic phases were combined, dried over magnesium sulfate and concentrated under vacuum. subjected to column 10 chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (2.15 g). ^1H NMR (400 MHz, CDCl_3) δ ppm 6.30 (s, 1 H); 4.15 (bs, 2 H), 3.8 (bs, 1 H), 3.60 (s, 3H), 2.64 (s, 3H).

Example I3: 5-amino-1-methyl-6-(methylamino)-3-(trifluoromethyl)pyridin-2-one:



15

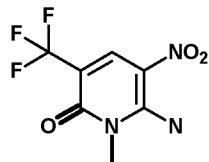
Step A: 1-methyl-5-nitro-3-(trifluoromethyl)pyridin-2-one:



To a stirred suspension of 5-nitro-3-(trifluoromethyl)-1H-pyridin-2-one (Commercially available, 13.95 g, 63.68 mmol) in 250ml N,N-dimethylformamide, cesium carbonate (62.7 g, 191.0 mmol) was added 20-25°C. After 15min stirring at ambient temperature, iodomethane (13.6 g, 5.98 mL, 95.52 mmol) was added. After 18 hours at ambient temperature the mixture was poured onto 200ml water, extracted twice with ethyl acetate, and the combined organic fractions washed successively with water and brine, dried over sodium sulfate and concentrated *in vacuo*. The crude product (**12.8 g**) was 25 pure enough to be used for the next step. LCMS (method A): retention time: 0.65min; 223 ($\text{M}+\text{H}^+$).

Step B: 6-amino-1-methyl-5-nitro-3-(trifluoromethyl)pyridin-2-one:

-83-



To a solution of potassium tert-butoxide (0.523 g, 4.57 mmol) and copper (II) acetate monohydrate (0.0125 g, 0.0675 mmol, 0.100) in DMF (5 mL) was added, slowly to a solution of methoxylamine hydrochloride (0.111 g, 1.30 mmol) and 1-methyl-5-nitro-3-(trifluoromethyl)pyridin-2-one (0.150 g, 0.675 mmol) in DMF (5mL) at 0°C. After 60 minutes, the reaction mixture was poured into water, and pH was adjusted to 6-7 with a concentrated solution of hydrogen chloride (37%). The aqueous phase was extracted three times with ethyl acetate, the organic phases were combined, dried over magnesium sulfate and concentrated under vacuum. the residue was subjected to column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (0.08 g). LCMS (method A): retention time: 0.72 min; 238 (M+H⁺), 236 (M-H⁺).

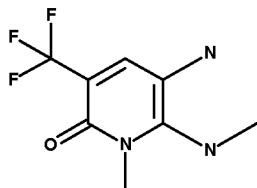
Step C: 1-methyl-6-(methylamino)-5-nitro-3-(trifluoromethyl)pyridin-2-one:



Sodium hydride (0.233 g, 5.82 mmol, 60% in oil) was added to a stirred solution of 6-amino-1-methyl-5-nitro-3-(trifluoromethyl)pyridin-2-one (0.920 g, 3.88 mmol,) in 30ml N,N-dimethylformamide. After 60min stirring at ambient temperature, iodomethane (0.609 g, 0.267 mL, 4.27 mmol) was added. After 4h at ambient temperature, iodomethane (0.609 g, 0.267 mL, 4.27 mmol, 1.10) was added again and it was stirred over night at ambient temperature. The mixture was poured onto 200ml water, extracted twice with ethyl acetate, and the combined organic fractions washed successively with water and brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by column chromatography over silica gel, eluting with ethyl acetate / cyclohexane. The selected fractions were evaporated to yield the title compound (0.44 g) and the starting material. LCMS (method A): retention time: 0.74 min; 252 (M+H⁺), 250 (M-H⁺).

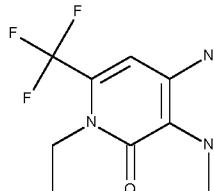
Step D: 5-amino-1-methyl-6-(methylamino)-3-(trifluoromethyl)pyridin-2-one:

-84-

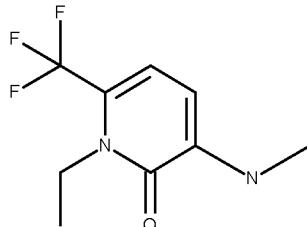


To a solution of 1-methyl-6-(methylamino)-5-nitro-3-(trifluoromethyl)pyridin-2-one (0.200 g, 0.796 mmol) in ethanol (6 mL) under argon was added palladium on carbon (0.02 g, 0.1878 mmol). An hydrogen atmosphere was applied and the solution was stirred for 1h and half. The black suspension
 5 was filtered through an Hyflo pad, and the resulting yellow solution was concentrated under vacuum to give 4-amino-1-methyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one (0.176 g). The compound was used without extra purification for the next step. ^1H NMR (400 MHz, CDCl_3) δ ppm 7.48 (s, 1 H); 5.45 (bs, 1 H), 3.8 (bs, 1 H), 3.60 (s, 3H), 2.95 (d, 3H), 2.75-2.60 (bs, 2H).

10 **Example I4:** 4-amino-1-ethyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one:



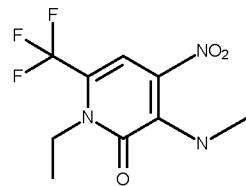
Step A: 1-ethyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one:



To a solution of 3-amino-1-ethyl-6-(trifluoromethyl)pyridin-2-one (5.00 g, 24.3 mmol, Commercially
 15 available or synthesised by analogy with literature, for example, Synthesis 2005, No. 8, pp 1269-1278 and Synthesis 2011, No. 7, pp 1149-1156) in acetonitrile (150 mL) was added formaldehyde (37 mass%) in aqueous solution (14.5 ml, 194 mmol) and acetic acid (6.96 ml, 121 mmol). The resulting suspension stirred for 1 hour, then sodium cyanoborohydride (6.42 g, 97.0 mmol) was added in 5 portions over 3 hours and the mixture was stirred for 18 hours. The solution was diluted with water and
 20 extracted with ethyl acetate (3x). The combined organic layer was dried over Na_2SO_4 , filtered, concentrated and purified by column chromatography using cyclohexane-ethyl acetate (100-200 silica gel) to give the desired compound as a white solid. ^1H NMR (400 MHz, CDCl_3) δ ppm 6.70 (d, 1 H), 6.04 (d, 1 H), 5.44 (sb, 1 H), 4.15 (q, 2H), 2.85 (s, 3H), 1.32 (t, 3H).

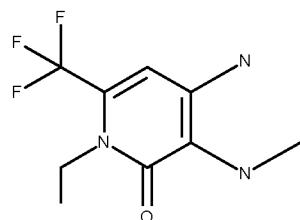
Step B: 1-ethyl-3-(methylamino)-4-nitro-6-(trifluoromethyl)pyridin-2-one:

-85-



The 1-ethyl-3-(methylamino)-4-nitro-6-(trifluoromethyl)pyridin-2-one was prepared as for Example I2, step C. LC-MS(Method A) : RT 0.98, 266 ($M+H^+$), 264 ($M-H^+$).

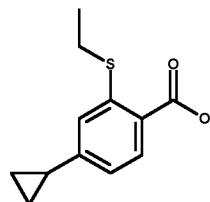
Step C: 4-amino-1-ethyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one:



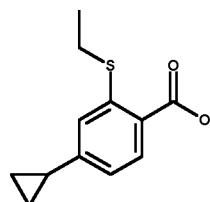
5

The 4-amino-1-ethyl-3-(methylamino)-6-(trifluoromethyl)pyridin-2-one was prepared as for Example I2, step D. LC-MS(Method A) : RT 0.47, 236 ($M+H^+$).

Example I5: 4-cyclopropyl-2-ethylsulfanyl-benzoic acid:



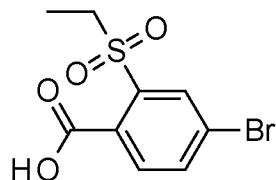
10 Step A: 4-cyclopropyl-2-ethylsulfanyl-benzoic acid:



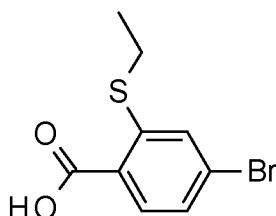
The title compound was synthesised by a similar protocol described in Example I1 (step B), starting from the methyl 4-cyclopropyl-2-fluoro-benzoate (commercially available or synthesised as in WO 2014089364). LC-MS(Method A) : RT 0.92, 221 ($M-H^+$). 1H NMR (400 MHz, $CDCl_3$) δ ppm 8.08 (d, 1 H), 7.12 (s, 1H), 6.88 (d, 1H), 2.97(q, 2H), 1.95 (m, 1H), 1.44(t, 3H), 1.12 (m, 2H), 0.84 (m, 2H).

Example I6: 4-Bromo-2-ethylsulfonyl-benzoic acid:

-86-



Step A: 4-bromo-2-ethylsulfanyl-benzoic acid:

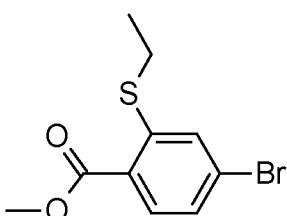


To a solution of 4-bromo-2-fluoro-benzoic acid (25.0 g, 0.11 mol) in NMP (200 mL) was slowly added

5 sodium ethanethiol (28.8 g, 0.33 mol), and the mixture was stirred at 120°C for 24 h. It was then cooled to room temperature, and quenched with water. The aqueous phase was adjusted to pH< 3 with 3N HCl and extracted with EtOAc (X3). The combined organic phases were washed with brine, dried over Na₂SO₄, and concentrated *in vacuo*. This gave the title compound as light yellow solid, which was used in the next step without further purification. ¹H NMR (400 MHz, d⁶-DMSO): δ (ppm) 12.13 (brs, 1H), 7.76 (d, 1H), 7.44 (s, 1H), 7.37 (d, 1H) 2.94 (q, 2H), 1.25 (t, 3H). ESI-MS: 261 (M+H)⁺.

10

Step B: Methyl 4-bromo-2-ethylsulfanyl-benzoate:



To a solution of 4-bromo-2-ethylsulfanyl-benzoic acid (25.0 g, 0.09 mol) in methanol (150 mL) was

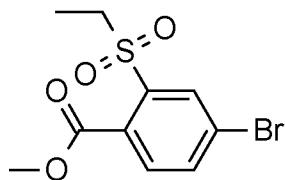
added drop wise thionyl chloride (14.0 mL, 0.18 mol) and the reaction mixture refluxed overnight. After 15 concentration *in vacuo*, the residue was taken up in EtOAc and diluted with water. The aqueous was adjusted to pH>8 with saturated sodium bicarbonate, the organic phase removed, and the aqueous phase back extracted with EtOAc(X3). The combined organic phases were washed with brine, dried over Na₂SO₄, and concentrated *in vacuo* to the pure title compound.

¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.81 (d, 1H), 7.38 (s, 1H), 7.25(d, 1H), 3.88 (s, 3H), 2.93 (q, 2H),

20 1.39 (t, 3H).

-87-

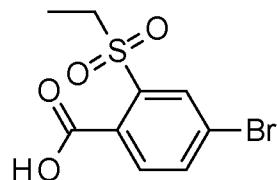
Step C: Methyl 4-bromo-2-ethylsulfonyl-benzoate:



To a solution of methyl-4-bromo-2-ethylsulfanyl-benzoate (9.6 g, 35.0 mmol) in dichloromethane (150 mL) was added 3-chloroperbenzoic acid (15.6 g, 70.0 mmol). The mixture was stirred at rt overnight.

5 Then it was diluted with dichloromethane and washed with saturated sodium bicarbonate. The organic phase was washed with saturated sodium thiosulfate solution, dried over Na_2SO_4 , and evaporated to dryness. The residue was purified by chromatography on silica gel, eluting with PE: EtOAc =3:1) to get the pure title compound as white solid, that was used in the next step without further purification. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 8.06 (m, 2H), 7.70 (d, 1H), 3.50 (s, 3H), 2.93 (q, 2), 1.17 (t, 3H).

10 Step D: 4-Bromo-2-ethylsulfonyl-benzoic acid:



A solution of Methyl 4-bromo-2-ethylsulfanyl-benzoate (2.0 g, 6.5 mmol) in THF (30 ml) and H_2O (10 ml) was treated with NaOH (520 mg, 13.0 mmol), and the reaction mixture was stirred overnight at room temperature. The reaction mixture was then acidified with 3M HCl to pH 4, and extracted with 15 EtOAc (X3). The combined organic phases were washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo* to give the title compound.

^1H NMR (400 MHz, $d^6\text{-DMSO}$): δ (ppm) 12.95 (brs, 1H), 8.01 (s, 1H), 7.99 (d, 1H), 7.68 (d, 1H) 3.54 (q, 2H), 1.15 (t, 3H).

Table A: This table discloses compounds of the formula I-1a. "Ph" represents the phenyl group, "Et" is

20 the ethyl group:

-88-

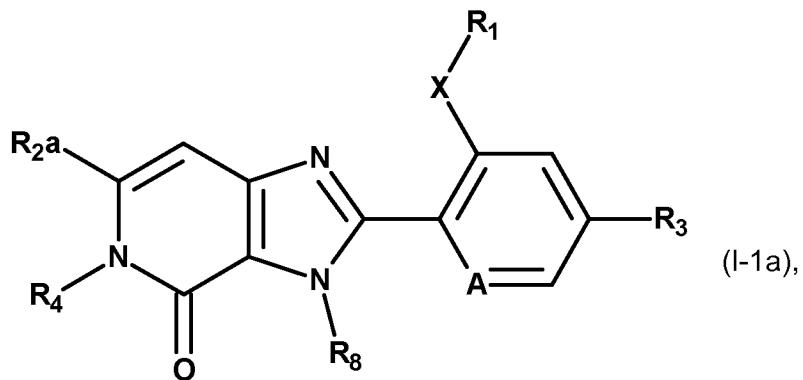


Table A:

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₄	R ₈
A1 (1.008)	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
A2	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ CH ₃	CH ₃
A3	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ CHCH ₂	CH ₃
A4	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ Ph	CH ₃
A5	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	n-butyl	CH ₃
A6	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	n-propyl	CH ₃
A7	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ C≡CCH ₃	CH ₃
A8	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	-CH ₂ O-CH ₂ CH ₂ OCH ₃	CH ₃
A9	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ C ₆ H ₁₁	CH ₃
A10	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ CCH	CH ₃
A11	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ OCH ₃	CH ₃
A12	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ SCH ₃	CH ₃
A13	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ (3-OMePh)	CH ₃
A14	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	-(CH ₂) ₃ CN	CH ₃
A15	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₂ CHCHPh	CH ₃

-89-

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₄	R ₈
A16 (1.003)	S	-CH ₂ CH ₃	H	N	CF ₃	CH ₃	CH ₃
A17 (1.004)	SO ₂	-CH ₂ CH ₃	H	N	CF ₃	CH ₃	CH ₃
A18 (1.009)	S	-CH ₂ CH ₃	4-ClPh	N	CF ₃	CH ₃	CH ₃
A19 (1.010)	SO ₂	-CH ₂ CH ₃	4-ClPh	N	CF ₃	CH ₃	CH ₃
A20	S	-CH ₂ CH ₃	Br	N	CF ₃	CH ₃	CH ₃
A21	SO ₂	-CH ₂ CH ₃	Br	N	CF ₃	CH ₃	CH ₃
A22	SO ₂	-CH ₂ CH ₃	4CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
A23	SO ₂	-CH ₂ CH ₃	cyclopropyl	N	CF ₃	CH ₃	CH ₃
A24	S	-CH ₂ CH ₃	1-(4-(trifluoromethyl)pyrazolyl)	N	CF ₃	CH ₃	CH ₃
A25	SO ₂	-CH ₂ CH ₃	1-(4-(trifluoromethyl)pyrazolyl)	N	CF ₃	CH ₃	CH ₃
A26	S	-CH ₂ CH ₃	1-(3-(trifluoromethyl)pyrazolyl)	N	CF ₃	CH ₃	CH ₃
A27	SO ₂	-CH ₂ CH ₃	1-(3-(trifluoromethyl)pyrazolyl)	N	CF ₃	CH ₃	CH ₃
A28	SO ₂	-CH ₂ CH ₃	3,5-F-Ph	N	CF ₃	CH ₃	CH ₃
A29	S	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
A30	S	-CH ₂ CH ₃	Br	N	CF ₃	-CH ₂ CH ₃	CH ₃
A31	SO ₂	-CH ₂ CH ₃	Br	N	CF ₃	-CH ₂ CH ₃	CH ₃
A32	S	-CH ₂ CH ₃	1-(3-(trifluoromethyl)pyrazolyl)	N	CF ₃	-CH ₂ CH ₃	CH ₃
A33	SO ₂	-CH ₂ CH ₃	1-(3-(trifluoromethyl)pyrazolyl)	N	CF ₃	-CH ₂ CH ₃	CH ₃

-90-

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₄	R ₈
A34	SO ₂	-CH ₂ CH ₃	cyclopropyl	N	CF ₃	-CH ₂ CH ₃	CH ₃
A35	SO ₂	-CH ₂ CH ₃	p-CF ₃ Ph	N	CF ₃	-CH ₂ CH ₃	CH ₃
A36	SO ₂	-CH ₂ CH ₃	m-CF ₃ Ph	N	CF ₃	-CH ₂ CH ₃	CH ₃
A37	S	-CH ₂ CH ₃	cyclopropyl	CH	CF ₃	CH ₃	CH ₃
A38	S	-CH ₂ CH ₃	cyclopropyl	CH	CF ₃	-CH ₂ CH ₃	CH ₃
A39	SO ₂	-CH ₂ CH ₃	cyclopropyl	CH	CF ₃	CH ₃	CH ₃
A40	SO ₂	-CH ₂ CH ₃	cyclopropyl	CH	CF ₃	-CH ₂ CH ₃	CH ₃
A41	SO ₂	-CH ₂ CH ₃	p-CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
A42	SO ₂	-CH ₂ CH ₃	2-(4-CF ₃)pyridinyl	N	CF ₃	CH ₃	CH ₃
A43	SO ₂	-CH ₂ CH ₃	2-(5-CF ₃)pyridinyl	N	CF ₃	CH ₃	CH ₃
A44	SO ₂	-CH ₂ CH ₃	2-(3,5-di-F)pyridinyl	N	CF ₃	CH ₃	CH ₃
A45	SO ₂	-CH ₂ CH ₃	2-(5-F)pyridinyl	N	CF ₃	CH ₃	CH ₃
A46	SO ₂	-CH ₂ CH ₃	CF ₂ CF ₃	N	CF ₃	CH ₃	CH ₃
A47	SO ₂	-CH ₂ CH ₃	CF ₂ CF ₃	N	CF ₃	CH ₃	CH ₃
A48	SO ₂	-CH ₂ CH ₃	4-(6-F)pyridinyl	N	CF ₃	CH ₃	CH ₃
A49	SO ₂	-CH ₂ CH ₃	4-(6-F)pyridinyl	N	CF ₃	-CH ₂ CH ₃	CH ₃
A50	SO ₂	-CH ₂ CH ₃	2-CNPh	N	CF ₃	CH ₃	CH ₃
A51	SO ₂	-CH ₂ CH ₃	2-F,4-CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
A52	SO ₂	-CH ₂ CH ₃	3-EtPh	N	CF ₃	CH ₃	CH ₃
A53	SO ₂	-CH ₂ CH ₃	3-(5-methyl)pyridinyl	N	CF ₃	CH ₃	CH ₃
A54	SO ₂	-CH ₂ CH ₃	4-FPh	N	CF ₃	CH ₃	CH ₃
A55	SO ₂	-CH ₂ CH ₃	2-methoxy-pyrimidine-5-yl	N	CF ₃	CH ₃	CH ₃

-91-

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₄	R ₈
A56	SO ₂	-CH ₂ CH ₃	2-FPh	N	CF ₃	CH ₃	CH ₃
A57	SO ₂	-CH ₂ CH ₃	pyrimidine-5-yl	N	CF ₃	CH ₃	CH ₃
A58	SO ₂	-CH ₂ CH ₃	4-pyridinyl	N	CF ₃	CH ₃	CH ₃
A59	SO ₂	-CH ₂ CH ₃	(4-F,6-Me)Ph	N	CF ₃	CH ₃	CH ₃
A60	SO ₂	-CH ₂ CH ₃	3-CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
A61	SO ₂	-CH ₂ CH ₃	2-CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
A62	SO ₂	-CH ₂ CH ₃	4,5-diClPh	N	CF ₃	CH ₃	CH ₃
A63	SO ₂	-CH ₂ CH ₃	4,6-diClPh	N	CF ₃	CH ₃	CH ₃
A64	SO ₂	-CH ₂ CH ₃	(3-F,4-OMe)Ph	N	CF ₃	CH ₃	CH ₃
A65	SO ₂	-CH ₂ CH ₃	3-(6-CF ₃)pyridinyl	N	CF ₃	CH ₃	CH ₃
A66	SO ₂	-CH ₂ CH ₃	4-OCF ₃ Ph	N	CF ₃	CH ₃	CH ₃
A67	SO ₂	-CH ₂ CH ₃	CHCHCH ₃	N	CF ₃	CH ₃	CH ₃
A68	SO ₂	-CH ₂ CH ₃	2, 5-diFPh	N	CF ₃	CH ₃	CH ₃
A69	SO ₂	-CH ₂ CH ₃	6-ClPh	N	CF ₃	CH ₃	CH ₃
A70	SO ₂	-CH ₂ CH ₃	4-CF ₃ Ph	CH	CF ₃	CH ₃	CH ₃
A71	SO ₂	-CH ₂ CH ₃	1-pyrimidinyl	CH	CF ₃	CH ₃	CH ₃
A72	SO ₂	-CH ₂ CH ₃	4-ClPh	CH	CF ₃	CH ₃	CH ₃
A73 (1.006)	SO ₂	-CH ₂ CH ₃	CF ₃	CH	CF ₃	CH ₃	CH ₃
A74	SO ₂	-CH ₂ CH ₃	Br	CH	CF ₃	CH ₃	CH ₃

-92-

Table B: This table discloses compounds of the formula I-2a:

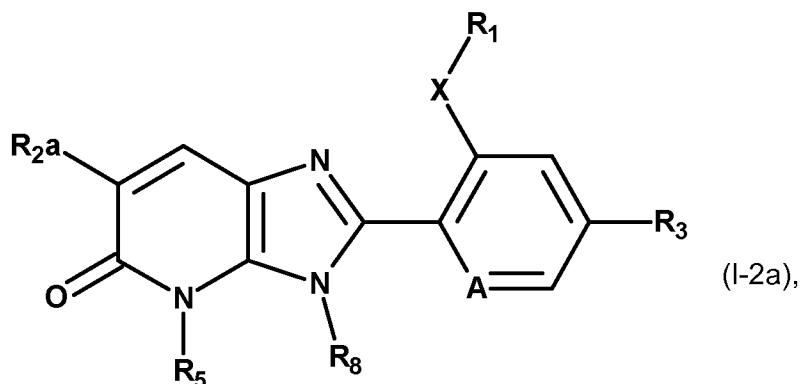


Table B:

Comp. No.	X	R ₁	R ₃	A	R _{2a}	R ₅	R ₈
B1 (2.003)	S	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
B2 (2.004)	SO ₂	-CH ₂ CH ₃	CF ₃	N	CF ₃	CH ₃	CH ₃
B3	SO ₂	-CH ₂ CH ₃	p-CF ₃ Ph	N	Br	CH ₃	CH ₃
B4	SO ₂	-CH ₂ CH ₃	p-CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
B5	S	-CH ₂ CH ₃	p-CF ₃ Ph	N	CF ₃	CH ₃	CH ₃
B6 (2.002)	SO ₂	-CH ₂ CH ₃	CF ₃	N	H	CH ₃	CH ₃
B7 (2.001)	S	-CH ₂ CH ₃	CF ₃	N	H	CH ₃	CH ₃

5 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.

10 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,

-93-

pyrethroids, chlorinated hydrocarbons, acylureas, pyridylmethylenamino derivatives, macrolides, neonicotinoids and *Bacillus thuringiensis* preparations.

The following mixtures of the compounds of formula I with active ingredients are preferred (the

5 abbreviation "TX" means "one compound selected from the group consisting of the compounds described in Table 1, 2, A and B of the present invention"):

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

10 an acaricide selected from the group of substances consisting of 1,1-bis(4-chlorophenyl)-2-ethoxyethanol (IUPAC name) (910) + TX, 2,4-dichlorophenyl benzenesulfonate (IUPAC/Chemical Abstracts name) (1059) + TX, 2-fluoro-N-methyl-N-1-naphthylacetamide (IUPAC name) (1295) + TX, 4-chlorophenyl phenyl sulfone (IUPAC name) (981) + TX, abamectin (1) + TX, acequinocyl (3) + TX, acetoprole [CCN] + TX, acrinathrin (9) + TX, aldicarb (16) + TX, aldoxycarb (863) + TX, alpha-15 cypermethrin (202) + TX, amidithion (870) + TX, amidoflumet [CCN] + TX, amidothioate (872) + TX, amiton (875) + TX, amiton hydrogen oxalate (875) + TX, amitraz (24) + TX, aramite (881) + TX, arsenous oxide (882) + TX, AVI 382 (compound code) + TX, AZ 60541 (compound code) + TX, azinphos-ethyl (44) + TX, azinphos-methyl (45) + TX, azobenzene (IUPAC name) (888) + TX, azocyclotin (46) + TX, azothoate (889) + TX, benomyl (62) + TX, benoxafos (alternative name) 20 [CCN] + TX, benzoximate (71) + TX, benzyl benzoate (IUPAC name) [CCN] + TX, bifenazate (74) + TX, bifenthrin (76) + TX, binapacryl (907) + TX, brofenvalerate (alternative name) + TX, bromocyclen (918) + TX, bromophos (920) + TX, bromophos-ethyl (921) + TX, bromopropylate (94) + TX, buprofezin (99) + TX, butocarboxim (103) + TX, butoxycarboxim (104) + TX, butylpyridaben (alternative name) + TX, calcium polysulfide (IUPAC name) (111) + TX, camphechlor (941) + TX, 25 carbanolate (943) + TX, carbaryl (115) + TX, carbofuran (118) + TX, carbophenothion (947) + TX, CGA 50'439 (development code) (125) + TX, chinomethionat (126) + TX, chlorbenside (959) + TX, chlordimeform (964) + TX, chlordimeform hydrochloride (964) + TX, chlorfenapyr (130) + TX, chlorfenethol (968) + TX, chlorfenson (970) + TX, chlorfensulfide (971) + TX, chlorfenvinphos (131) + TX, chlorobenzilate (975) + TX, chloromebuform (977) + TX, chloromethiuron (978) + TX, 30 chloropropylate (983) + TX, chlorpyrifos (145) + TX, chlorpyrifos-methyl (146) + TX, chlorthiophos (994) + TX, cinerin I (696) + TX, cinerin II (696) + TX, cinerins (696) + TX, clofentezine (158) + TX, closantel (alternative name) [CCN] + TX, coumaphos (174) + TX, crotamiton (alternative name) [CCN] + TX, crotoxyphos (1010) + TX, cufraneb (1013) + TX, cyanthoate (1020) + TX, cyflumetofen (CAS Reg. No.: 400882-07-7) + TX, cyhalothrin (196) + TX, cyhexatin (199) + TX, 35 cypermethrin (201) + TX, DCPM (1032) + TX, DDT (219) + TX, demephion (1037) + TX, demephion-O (1037) + TX, demephion-S (1037) + TX, demeton (1038) + TX, demeton-methyl (224) + TX, demeton-O (1038) + TX, demeton-O-methyl (224) + TX, demeton-S (1038) + TX, demeton-S-methyl (224) + TX, demeton-S-methylsulfon (1039) + TX, diafenthiuron (226) + TX, dialifos (1042) + TX, diazinon (227) + TX, dichlofluanid (230) + TX, dichlorvos (236) + TX,

dicliphos (alternative name) + TX, dicofol (242) + TX, dicrotophos (243) + TX, dienochlor (1071) + TX, dimefox (1081) + TX, dimethoate (262) + TX, dinactin (alternative name) (653) + TX, dinex (1089) + TX, dinex-diclexine (1089) + TX, dinobuton (269) + TX, dinocap (270) + TX, dinocap-4 [CCN] + TX, dinocap-6 [CCN] + TX, dinocton (1090) + TX, dinopenton (1092) + TX, dinosulfon 5 (1097) + TX, dinoterbon (1098) + TX, dioxathion (1102) + TX, diphenyl sulfone (IUPAC name) (1103) + TX, disulfiram (alternative name) [CCN] + TX, disulfoton (278) + TX, DNOC (282) + TX, dofenapyn (1113) + TX, doramectin (alternative name) [CCN] + TX, endosulfan (294) + TX, endothion (1121) + TX, EPN (297) + TX, eprinomectin (alternative name) [CCN] + TX, ethion (309) + TX, ethoate-methyl (1134) + TX, etoxazole (320) + TX, etrimfos (1142) + TX, fenazaflor (1147) 10 + TX, fenazaquin (328) + TX, fenbutatin oxide (330) + TX, fenothiocarb (337) + TX, fenpropothrin (342) + TX, fenpyrad (alternative name) + TX, fenpyroximate (345) + TX, fenson (1157) + TX, fentrifanil (1161) + TX, fenvalerate (349) + TX, fipronil (354) + TX, fluacrypyrim (360) + TX, fluazuron (1166) + TX, flubenzimine (1167) + TX, flucycloxuron (366) + TX, flucythrinate (367) + TX, fluenetil (1169) + TX, flufenoxuron (370) + TX, flumethrin (372) + TX, fluorbenside (1174) + TX, 15 fluvalinate (1184) + TX, FMC 1137 (development code) (1185) + TX, formetanate (405) + TX, formetanate hydrochloride (405) + TX, formothion (1192) + TX, formparanate (1193) + TX, gamma-HCH (430) + TX, glyodin (1205) + TX, halfenprox (424) + TX, heptenophos (432) + TX, hexadecyl cyclopropanecarboxylate (IUPAC/Chemical Abstracts name) (1216) + TX, hexythiazox (441) + TX, iodomethane (IUPAC name) (542) + TX, isocarbophos (alternative name) (473) + TX, 20 isopropyl O-(methoxyaminothiophosphoryl)salicylate (IUPAC name) (473) + TX, ivermectin (alternative name) [CCN] + TX, jasmolin I (696) + TX, jasmolin II (696) + TX, jodfenphos (1248) + TX, lindane (430) + TX, lufenuron (490) + TX, malathion (492) + TX, malonoben (1254) + TX, mecarbam (502) + TX, mephosfolan (1261) + TX, mesulfen (alternative name) [CCN] + TX, methacrifos (1266) + TX, methamidophos (527) + TX, methidathion (529) + TX, methiocarb (530) 25 + TX, methomyl (531) + TX, methyl bromide (537) + TX, metolcarb (550) + TX, mevinphos (556) + TX, mexacarbate (1290) + TX, milbemectin (557) + TX, milbemycin oxime (alternative name) [CCN] + TX, mipafox (1293) + TX, monocrotophos (561) + TX, morphothion (1300) + TX, moxidectin (alternative name) [CCN] + TX, naled (567) + TX, NC-184 (compound code) + TX, NC- 30 512 (compound code) + TX, nifluridide (1309) + TX, nikkomycins (alternative name) [CCN] + TX, nitrilacarb (1313) + TX, nitrilacarb 1:1 zinc chloride complex (1313) + TX, NNI-0101 (compound code) + TX, NNI-0250 (compound code) + TX, omethoate (594) + TX, oxamyl (602) + TX, oxydeprofos (1324) + TX, oxydisulfoton (1325) + TX, pp'-DDT (219) + TX, parathion (615) + TX, permethrin (626) + TX, petroleum oils (alternative name) (628) + TX, phenkapton (1330) + TX, phenthroate (631) + TX, phorate (636) + TX, phosalone (637) + TX, phosfolan (1338) + TX, 35 phosmet (638) + TX, phosphamidon (639) + TX, phoxim (642) + TX, pirimiphos-methyl (652) + TX, polychloroterpenes (traditional name) (1347) + TX, polynactins (alternative name) (653) + TX, proclonol (1350) + TX, profenofos (662) + TX, promacyl (1354) + TX, propargite (671) + TX, propetamphos (673) + TX, propoxur (678) + TX, prothidathion (1360) + TX, prothoate (1362) + TX, pyrethrin I (696) + TX, pyrethrin II (696) + TX, pyrethrins (696) + TX, pyridaben (699) + TX,

-95-

pyridaphenthion (701) + TX, pyrimidifen (706) + TX, pyrimitate (1370) + TX, quinalphos (711) + TX, quintiofos (1381) + TX, R-1492 (development code) (1382) + TX, RA-17 (development code) (1383) + TX, rotenone (722) + TX, schradan (1389) + TX, sebufos (alternative name) + TX, selamectin (alternative name) [CCN] + TX, SI-0009 (compound code) + TX, sophamide (1402) + TX, spirodiclofen (738) + TX, spiromesifen (739) + TX, SSI-121 (development code) (1404) + TX, sulfiram (alternative name) [CCN] + TX, sulfluramid (750) + TX, sulfotep (753) + TX, sulfur (754) + TX, SZI-121 (development code) (757) + TX, tau-fluvalinate (398) + TX, tebufenpyrad (763) + TX, TEPP (1417) + TX, terbam (alternative name) + TX, tetrachlorvinphos (777) + TX, tetradifon (786) + TX, tetranactin (alternative name) (653) + TX, tetrasul (1425) + TX, thiafenoxy (alternative name) + TX, thiocarboxime (1431) + TX, thiofanox (800) + TX, thiometon (801) + TX, thioquinox (1436) + TX, thuringiensin (alternative name) [CCN] + TX, triamiphos (1441) + TX, triarathene (1443) + TX, triazophos (820) + TX, triazuron (alternative name) + TX, trichlorfon (824) + TX, trifenofos (1455) + TX, trinactin (alternative name) (653) + TX, vamidothion (847) + TX, vaniliprole [CCN] and YI-5302 (compound code) + TX,

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, quinoclamine (714) + TX, quinonamid (1379) + TX, simazine (730) + TX, triphenyltin acetate (IUPAC name) (347) and triphenyltin hydroxide (IUPAC name) (347) + TX,

an anthelmintic selected from the group of substances consisting of abamectin (1) + TX, crufomate (1011) + 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, 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(dimethylthiocarbamate) (IUPAC name) (1308) + TX, nitrapyrin (580) + TX, octhilinone (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, *Anagrypha 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) + 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, *Eretmocerus eremicus* (alternative name) (300) + TX, *Helicoverpa zea* NPV (alternative name) (431) + TX, *Heterorhabdus 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. *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, *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 riobravis* (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 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, 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, tepea [CCN] + TX, thiohempa (alternative name) [CCN] + TX,

thiotepa (alternative name) [CCN] + TX, tretamine (alternative name) [CCN] and uredepa (alternative name) [CCN] + TX,
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) +
5 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*)-
hexadec-13-en-11-yn-1-yl acetate (IUPAC name) (438) + TX, (*Z*)-icos-13-en-10-one (IUPAC name)
10 (448) + TX, (*Z*)-tetradec-7-en-1-al (IUPAC name) (782) + TX, (*Z*)-tetradec-9-en-1-ol (IUPAC name)
(783) + TX, (*Z*)-tetradec-9-en-1-yl acetate (IUPAC name) (784) + TX, (*7E,9Z*)-dodeca-7,9-dien-1-yl
acetate (IUPAC name) (283) + TX, (*9Z,11E*)-tetradeca-9,11-dien-1-yl acetate (IUPAC name) (780) +
TX, (*9Z,12E*)-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,
15 codlelure (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, frontalin (alternative name)
20 [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
25 (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
30 (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
35 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,

an insecticide selected from the group of substances consisting of 1-dichloro-1-nitroethane (IUPAC/Chemical Abstracts name) (1058) + TX, 1,1-dichloro-2,2-bis(4-ethylphenyl)ethane (IUPAC name) (1056), + TX, 1,2-dichloropropane (IUPAC/Chemical Abstracts name) (1062) + TX, 1,2-dichloropropane with 1,3-dichloropropene (IUPAC name) (1063) + TX, 1-bromo-2-chloroethane (IUPAC/Chemical Abstracts name) (916) + TX, 2,2,2-trichloro-1-(3,4-dichlorophenyl)ethyl acetate (IUPAC name) (1451) + TX, 2,2-dichlorovinyl 2-ethylsulfinylethyl methyl phosphate (IUPAC name) (1066) + TX, 2-(1,3-dithiolan-2-yl)phenyl dimethylcarbamate (IUPAC/ Chemical Abstracts name) (1109) + TX, 2-(2-butoxyethoxy)ethyl thiocyanate (IUPAC/Chemical Abstracts name) (935) + TX, 2-(4,5-dimethyl-1,3-dioxolan-2-yl)phenyl methylcarbamate (IUPAC/ Chemical Abstracts name) (1084) + TX, 2-(4-chloro-3,5-xylyloxy)ethanol (IUPAC name) (986) + TX, 2-chlorovinyl diethyl phosphate (IUPAC name) (984) + TX, 2-imidazolidone (IUPAC name) (1225) + TX, 2-isovalerylindan-1,3-dione (IUPAC name) (1246) + TX, 2-methyl(prop-2-ynyl)aminophenyl methylcarbamate (IUPAC name) (1284) + TX, 2-thiocyanatoethyl laurate (IUPAC name) (1433) + TX, 3-bromo-1-chloroprop-1-ene (IUPAC name) (917) + TX, 3-methyl-1-phenylpyrazol-5-yl dimethylcarbamate (IUPAC name) (1283) + TX, 4-methyl(prop-2-ynyl)amino-3,5-xylyl methylcarbamate (IUPAC name) (1285) + TX, 5,5-dimethyl-3-oxocyclohex-1-enyl dimethylcarbamate (IUPAC name) (1085) + TX, abamectin (1) + TX, acephate (2) + TX, acetamiprid (4) + TX, acethion (alternative name) [CCN] + TX, acetoprole [CCN] + TX, acrinathrin (9) + TX, acrylonitrile (IUPAC name) (861) + TX, alanycarb (15) + TX, aldicarb (16) + TX, aldoxycarb (863) + TX, aldrin (864) + TX, allethrin (17) + TX, allosamidin (alternative name) [CCN] + TX, allyxycarb (866) + TX, alpha-cypermethrin (202) + TX, alpha-ecdysone (alternative name) [CCN] + TX, aluminium phosphide (640) + TX, amidithion (870) + TX, amidothioate (872) + TX, aminocarb (873) + TX, amiton (875) + TX, amiton hydrogen oxalate (875) + TX, amitraz (24) + TX, anabasine (877) + TX, athidathion (883) + TX, AVI 382 (compound code) + TX, AZ 60541 (compound code) + TX, azadirachtin (alternative name) (41) + TX, azamethiphos (42) + TX, azinphos-ethyl (44) + TX, azinphos-methyl (45) + TX, azothoate (889) + TX, *Bacillus thuringiensis* delta endotoxins (alternative name) (52) + TX, barium hexafluorosilicate (alternative name) [CCN] + TX, barium polysulfide (IUPAC/Chemical Abstracts name) (892) + TX, barthrin [CCN] + TX, Bayer 22/190 (development code) (893) + TX, Bayer 22408 (development code) (894) + TX, bendiocarb (58) + TX, benfuracarb (60) + TX, bensultap (66) + TX, beta-cyfluthrin (194) + TX, beta-cypermethrin (203) + TX, bifenthrin (76) + TX, bioallethrin (78) + TX, bioallethrin S-cyclopentenyl isomer (alternative name) (79) + TX, bioethanomethrin [CCN] + TX, biopermethrin (908) + TX, bioresmethrin (80) + TX, bis(2-chloroethyl) ether (IUPAC name) (909) + TX, bistrifluron (83) + TX, borax (86) + TX, brofenvalerate (alternative name) + TX, bromfenvinfos (914) + TX, bromocyclen (918) + TX, bromo-DDT (alternative name) [CCN] + TX, bromophos (920) + TX, bromophos-ethyl (921) + TX, bufencarb (924) + TX, buprofezin (99) + TX, butacarb (926) + TX, butathiofos (927) + TX, butocarboxim (103) + TX, butonate (932) + TX, butoxycarboxim (104) + TX, butylpyridaben (alternative name) + TX, cadusafos (109) + TX, calcium arsenate [CCN] + TX, calcium cyanide (444) + TX, calcium polysulfide (IUPAC name) (111) + TX, camphechlor (941) + TX, carbanolate (943) + TX, carbaryl (115) + TX, carbofuran (118) +

TX, carbon disulfide (IUPAC/Chemical Abstracts name) (945) + TX, carbon tetrachloride (IUPAC name) (946) + TX, carbophenothon (947) + TX, carbosulfan (119) + TX, cartap (123) + TX, cartap hydrochloride (123) + TX, cevadine (alternative name) (725) + TX, chlorbicyclen (960) + TX, chlordane (128) + TX, chlordecone (963) + TX, chlordimeform (964) + TX, chlordimeform hydrochloride (964) + TX, chlorethoxyfos (129) + TX, chlorfenapyr (130) + TX, chlorfenvinphos (131) + TX, chlorfluazuron (132) + TX, chlormephos (136) + TX, chloroform [CCN] + TX, chloropicrin (141) + TX, chlorphoxim (989) + TX, chlorprazophos (990) + TX, chlorpyrifos (145) + TX, chlorpyrifos-methyl (146) + TX, chlorthiophos (994) + TX, chromafenozide (150) + TX, cinerin I (696) + TX, cinerin II (696) + TX, cinerins (696) + TX, cis-resmethrin (alternative name) + TX, 10 cismethrin (80) + TX, clopythrin (alternative name) + TX, cloethocarb (999) + TX, closantel (alternative name) [CCN] + TX, clothianidin (165) + TX, copper acetoarsenite [CCN] + TX, copper arsenate [CCN] + TX, copper oleate [CCN] + TX, coumaphos (174) + TX, coumithoate (1006) + TX, crotamiton (alternative name) [CCN] + TX, crotoxyphos (1010) + TX, crufomate (1011) + TX, cryolite (alternative name) (177) + TX, CS 708 (development code) (1012) + TX, cyanofenphos 15 (1019) + TX, cyanophos (184) + TX, cyanthoate (1020) + TX, cyclethrin [CCN] + TX, cycloprothrin (188) + TX, cyfluthrin (193) + TX, cyhalothrin (196) + TX, cypermethrin (201) + TX, cyphenothon (206) + TX, cyromazine (209) + TX, cythioate (alternative name) [CCN] + TX, d-limonene (alternative name) [CCN] + TX, d-tetramethrin (alternative name) (788) + TX, DAEP (1031) + TX, dazomet (216) + TX, DDT (219) + TX, decarbofuran (1034) + TX, deltamethrin (223) 20 + TX, demephion (1037) + TX, demephion-O (1037) + TX, demephion-S (1037) + TX, demeton (1038) + TX, demeton-methyl (224) + TX, demeton-O (1038) + TX, demeton-O-methyl (224) + TX, demeton-S (1038) + TX, demeton-S-methyl (224) + TX, demeton-S-methylsulphon (1039) + TX, diafenthiuron (226) + TX, dialfos (1042) + TX, diamidafos (1044) + TX, diazinon (227) + TX, dicapthon (1050) + TX, dichlofenthion (1051) + TX, dichlorvos (236) + TX, dicliphos (alternative 25 name) + TX, dicresyl (alternative name) [CCN] + TX, dicrotophos (243) + TX, dicyclanil (244) + TX, dieldrin (1070) + TX, diethyl 5-methylpyrazol-3-yl phosphate (IUPAC name) (1076) + TX, diflubenzuron (250) + TX, dilor (alternative name) [CCN] + TX, dimefluthrin [CCN] + TX, dimefox (1081) + TX, dimetan (1085) + TX, dimethoate (262) + TX, dimethrin (1083) + TX, dimethylvinphos (265) + TX, dimetilan (1086) + TX, dinex (1089) + TX, dinex-diclexine (1089) + 30 TX, dinoprop (1093) + TX, dinosam (1094) + TX, dinoseb (1095) + TX, dinotefuran (271) + TX, diofenolan (1099) + TX, dioxabenzofos (1100) + TX, dioxacarb (1101) + TX, dioxathion (1102) + TX, disulfoton (278) + TX, dithicrofos (1108) + TX, DNOC (282) + TX, doramectin (alternative name) [CCN] + TX, DSP (1115) + TX, ecdysterone (alternative name) [CCN] + TX, EI 1642 (development code) (1118) + TX, emamectin (291) + TX, emamectin benzoate (291) + TX, EMPC 35 (1120) + TX, empenthrin (292) + TX, endosulfan (294) + TX, endothion (1121) + TX, endrin (1122) + TX, EPBP (1123) + TX, EPN (297) + TX, epofenonane (1124) + TX, eprinomectin (alternative name) [CCN] + TX, esfenvalerate (302) + TX, etaphos (alternative name) [CCN] + TX, ethiofencarb (308) + TX, ethion (309) + TX, ethiprole (310) + TX, ethoate-methyl (1134) + TX, ethoprophos (312) + TX, ethyl formate (IUPAC name) [CCN] + TX, ethyl-DDD (alternative name)

-100-

(1056) + TX, ethylene dibromide (316) + TX, ethylene dichloride (chemical name) (1136) + TX, ethylene oxide [CCN] + TX, etofenprox (319) + TX, etrimfos (1142) + TX, EXD (1143) + TX, famphur (323) + TX, fenamiphos (326) + TX, fenazaflor (1147) + TX, fenchlorphos (1148) + TX, fenethacarb (1149) + TX, fenfluthrin (1150) + TX, fenitrothion (335) + TX, fenobucarb (336) + TX, 5 fenoxacrim (1153) + TX, fenoxy carb (340) + TX, fenpirithrin (1155) + TX, fenpropothrin (342) + TX, fenpyrad (alternative name) + TX, fensulfothion (1158) + TX, fenthion (346) + TX, fenthion-ethyl [CCN] + TX, fenvalerate (349) + TX, fipronil (354) + TX, flonicamid (358) + TX, flubendiamide (CAS. Reg. No.: 272451-65-7) + TX, flucofurone (1168) + TX, flucycloxuron (366) + TX, flucythrinate (367) + TX, fluenetil (1169) + TX, flufennerim [CCN] + TX, flufenoxuron (370) + TX, 10 flufenprox (1171) + TX, flumethrin (372) + TX, fluvalinate (1184) + TX, FMC 1137 (development code) (1185) + TX, fonofos (1191) + TX, formetanate (405) + TX, formetanate hydrochloride (405) + TX, formothion (1192) + TX, formparanate (1193) + TX, fosmethilan (1194) + TX, fospirate (1195) + TX, fosthiazate (408) + TX, fosthietan (1196) + TX, furathiocarb (412) + TX, furethrin (1200) + TX, gamma-cyhalothrin (197) + TX, gamma-HCH (430) + TX, guazatine (422) + TX, 15 guazatine acetates (422) + TX, GY-81 (development code) (423) + TX, halfenprox (424) + TX, halofenozone (425) + TX, HCH (430) + TX, HEOD (1070) + TX, heptachlor (1211) + TX, heptenophos (432) + TX, heterophos [CCN] + TX, hexaflumuron (439) + TX, HHDN (864) + TX, hydramethylnon (443) + TX, hydrogen cyanide (444) + TX, hydroprene (445) + TX, hyquincarb (1223) + TX, imidacloprid (458) + TX, imiprothrin (460) + TX, indoxacarb (465) + TX, 20 iodomethane (IUPAC name) (542) + TX, IPSP (1229) + TX, isazofos (1231) + TX, isobenzan (1232) + TX, isocarbophos (alternative name) (473) + TX, isodrin (1235) + TX, isofenphos (1236) + TX, isolane (1237) + TX, isoprocarb (472) + TX, isopropyl O-(methoxy-aminothiophosphoryl)salicylate (IUPAC name) (473) + TX, isoprothiolane (474) + TX, isothioate (1244) + TX, isoxathion (480) + TX, ivermectin (alternative name) [CCN] + TX, jasmolin I (696) + TX, 25 jasmolin II (696) + TX, jodfenphos (1248) + TX, juvenile hormone I (alternative name) [CCN] + TX, juvenile hormone II (alternative name) [CCN] + TX, juvenile hormone III (alternative name) [CCN] + TX, kelevan (1249) + TX, kinoprene (484) + TX, lambda-cyhalothrin (198) + TX, lead arsenate [CCN] + TX, lepimectin (CCN) + TX, leptophos (1250) + TX, lindane (430) + TX, lirimfos (1251) + TX, lufenuron (490) + TX, lythidathion (1253) + TX, m-cumanyl methylcarbamate (IUPAC name) (1014) + TX, magnesium phosphide (IUPAC name) (640) + TX, malathion (492) + TX, 30 malonoben (1254) + TX, mazidox (1255) + TX, mecarbam (502) + TX, mecarphon (1258) + TX, menazon (1260) + TX, mephosfolan (1261) + TX, mercurous chloride (513) + TX, mesulfenfos (1263) + TX, metaflumizone (CCN) + TX, metam (519) + TX, metam-potassium (alternative name) (519) + TX, metam-sodium (519) + TX, methacrifos (1266) + TX, methamidophos (527) + TX, 35 methanesulfonyl fluoride (IUPAC/Chemical Abstracts name) (1268) + TX, methidathion (529) + TX, methiocarb (530) + TX, methocrotophos (1273) + TX, methomyl (531) + TX, methoprene (532) + TX, methoquin-butyl (1276) + TX, methothrin (alternative name) (533) + TX, methoxychlor (534) + TX, methoxyfenozide (535) + TX, methyl bromide (537) + TX, methyl isothiocyanate (543) + TX, methylchloroform (alternative name) [CCN] + TX, methylene chloride [CCN] + TX, metofluthrin

[CCN] + TX, metolcarb (550) + TX, metoxadiazone (1288) + TX, mevinphos (556) + TX, mexacarbate (1290) + TX, milbemectin (557) + TX, milbemycin oxime (alternative name) [CCN] + TX, mipafox (1293) + TX, mirex (1294) + TX, monocrotophos (561) + TX, morphothion (1300) + TX, moxidectin (alternative name) [CCN] + TX, naftalofos (alternative name) [CCN] + TX, naled 5 (567) + TX, naphthalene (IUPAC/Chemical Abstracts name) (1303) + TX, NC-170 (development code) (1306) + TX, NC-184 (compound code) + TX, nicotine (578) + TX, nicotine sulfate (578) + TX, nifluridide (1309) + TX, nitenpyram (579) + TX, nithiazine (1311) + TX, nitrilacarb (1313) + TX, nitrilacarb 1:1 zinc chloride complex (1313) + TX, NNI-0101 (compound code) + TX, NNI-0250 (compound code) + TX, nornicotine (traditional name) (1319) + TX, novaluron (585) + TX, noviflumuron (586) + TX, O-5-dichloro-4-iodophenyl O-ethyl ethylphosphonothioate (IUPAC name) (1057) + TX, O,O-diethyl O-4-methyl-2-oxo-2H-chromen-7-yl phosphorothioate (IUPAC name) (1074) + TX, O,O-diethyl O-6-methyl-2-propylpyrimidin-4-yl phosphorothioate (IUPAC name) (1075) + TX, O,O,O',O'-tetrapropyl dithiopyrophosphate (IUPAC name) (1424) + TX, oleic acid (IUPAC name) (593) + TX, omethoate (594) + TX, oxamyl (602) + TX, oxydemeton-methyl (609) + TX, oxydeprofos (1324) + TX, oxydisulfoton (1325) + TX, pp'-DDT (219) + TX, para-dichlorobenzene 15 [CCN] + TX, parathion (615) + TX, parathion-methyl (616) + TX, penfluron (alternative name) [CCN] + TX, pentachlorophenol (623) + TX, pentachlorophenyl laurate (IUPAC name) (623) + TX, permethrin (626) + TX, petroleum oils (alternative name) (628) + TX, PH 60-38 (development code) (1328) + TX, phenkapton (1330) + TX, phenothrin (630) + TX, phentoate (631) + TX, phorate 20 (636) + TX, phosalone (637) + TX, phosfolan (1338) + TX, phosmet (638) + TX, phosnichlor (1339) + TX, phosphamidon (639) + TX, phosphine (IUPAC name) (640) + TX, phoxim (642) + TX, phoxim-methyl (1340) + TX, pirimetaphos (1344) + TX, pirimicarb (651) + TX, pirimiphos-ethyl (1345) + TX, pirimiphos-methyl (652) + TX, polychlorodicyclopentadiene isomers (IUPAC name) (1346) + TX, polychloroterpenes (traditional name) (1347) + TX, potassium arsenite [CCN] + TX, 25 potassium thiocyanate [CCN] + TX, prallethrin (655) + TX, precocene I (alternative name) [CCN] + TX, precocene II (alternative name) [CCN] + TX, precocene III (alternative name) [CCN] + TX, primidophos (1349) + TX, profenofos (662) + TX, profluthrin [CCN] + TX, promacyl (1354) + TX, promecarb (1355) + TX, propaphos (1356) + TX, propetamphos (673) + TX, propoxur (678) + TX, prothidathion (1360) + TX, prothiofos (686) + TX, prothoate (1362) + TX, protrifenbute [CCN] + TX, 30 pymetrozine (688) + TX, pyraclofos (689) + TX, pyrazophos (693) + TX, pyresmethrin (1367) + TX, pyrethrin I (696) + TX, pyrethrin II (696) + TX, pyrethrins (696) + TX, pyridaben (699) + TX, pyridalyl (700) + TX, pyridaphenthion (701) + TX, pyrimidifen (706) + TX, pyrimitate (1370) + TX, pyriproxyfen (708) + TX, quassia (alternative name) [CCN] + TX, quinalphos (711) + TX, quinalphos-methyl (1376) + TX, quinothion (1380) + TX, quintofos (1381) + TX, R-1492 35 (development code) (1382) + TX, rafoxanide (alternative name) [CCN] + TX, resmethrin (719) + TX, rotenone (722) + TX, RU 15525 (development code) (723) + TX, RU 25475 (development code) (1386) + TX, ryania (alternative name) (1387) + TX, ryanodine (traditional name) (1387) + TX, sabadilla (alternative name) (725) + TX, schradan (1389) + TX, sebufos (alternative name) + TX, selamectin (alternative name) [CCN] + TX, SI-0009 (compound code) + TX, SI-0205 (compound

-102-

code) + TX, SI-0404 (compound code) + TX, SI-0405 (compound code) + TX, silafluofen (728) + TX, SN 72129 (development code) (1397) + TX, sodium arsenite [CCN] + TX, sodium cyanide (444) + TX, sodium fluoride (IUPAC/Chemical Abstracts name) (1399) + TX, sodium hexafluorosilicate (1400) + TX, sodium pentachlorophenoxide (623) + TX, sodium selenate (IUPAC name) (1401) + TX, sodium thiocyanate [CCN] + TX, sophamide (1402) + TX, spinosad (737) + TX, spiromesifen (739) + TX, spirotetramat (CCN) + TX, sulcofuron (746) + TX, sulcofuron-sodium (746) + TX, sulfuramid (750) + TX, sulfotep (753) + TX, sulfuryl fluoride (756) + TX, sulprofos (1408) + TX, tar oils (alternative name) (758) + TX, tau-fluvalinate (398) + TX, tazimcarb (1412) + TX, TDE (1414) + TX, tebufenozide (762) + TX, tebufenpyrad (763) + TX, tebupirimfos (764) + TX, teflubenzuron (768) + TX, tefluthrin (769) + TX, temephos (770) + TX, TEPP (1417) + TX, terallethrin (1418) + TX, terbam (alternative name) + TX, terbufos (773) + TX, tetrachloroethane [CCN] + TX, tetrachlorvinphos (777) + TX, tetramethrin (787) + TX, theta-cypermethrin (204) + TX, thiacloprid (791) + TX, thiafenox (alternative name) + TX, thiamethoxam (792) + TX, thicrofos (1428) + TX, thiocarboxime (1431) + TX, thiocyclam (798) + TX, thiocyclam hydrogen oxalate (798) + TX, thiodicarb (799) + TX, thiofanox (800) + TX, thiometon (801) + TX, thionazin (1434) + TX, thiosultap (803) + TX, thiosultap-sodium (803) + TX, thuringiensin (alternative name) [CCN] + TX, tolfenpyrad (809) + TX, tralomethrin (812) + TX, transfluthrin (813) + TX, transpermethrin (1440) + TX, triamiphos (1441) + TX, triazamate (818) + TX, triazophos (820) + TX, triazuron (alternative name) + TX, trichlorfon (824) + TX, trichlorometaphos-3 (alternative name) [CCN] + TX, trichloronat (1452) + TX, trifenofofos (1455) + TX, triflumuron (835) + TX, trimethacarb (840) + TX, triprene (1459) + TX, vamidothion (847) + TX, vaniliprole [CCN] + TX, veratridine (alternative name) (725) + TX, veratrine (alternative name) (725) + TX, XMC (853) + TX, xylylcarb (854) + TX, YI-5302 (compound code) + TX, zeta-cypermethrin (205) + TX, zetamethrin (alternative name) + TX, zinc phosphide (640) + TX, zolaprofos (1469) and ZXI 8901 (development code) (858) + TX, 25 cyantraniliprole [736994-63-19 + TX, chlorantraniliprole [500008-45-7] + TX, cyenopyrafen [560121-52-0] + TX, cyflumetofen [400882-07-7] + TX, pyrifluquinazon [337458-27-2] + TX, spinetoram [187166-40-1 + 187166-15-0] + TX, spirotetramat [203313-25-1] + TX, sulfoxaflor [946578-00-3] + TX, flufiprole [704886-18-0] + TX, meperfluthrin [915288-13-0] + TX, tetramethylfluthrin [84937-88-2] + TX, triflumezopyrim (disclosed in WO 2012/092115) + TX, 30 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, trifemorph (1454) + TX, trimethacarb (840) + TX, triphenyltin acetate (IUPAC name) (347) and triphenyltin hydroxide (IUPAC name) (347) + TX, pyriprole [394730-71-3] + TX, 35 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

-103-

(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-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)

5 + 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, benclothiaz [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, 10 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, 15 fensulfothion (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 20 (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 25 (773) + TX, tetrachlorothiophene (IUPAC/ Chemical Abstracts name) (1422) + TX, thiafenox (alternative name) + TX, thionazin (1434) + TX, triazophos (820) + TX, triazuron (alternative name) + TX, xyleneols [CCN] + TX, YI-5302 (compound code) and zeatin (alternative name) (210) + TX, fluensulfone [318290-98-1] + TX, a nitrification inhibitor selected from the group of substances consisting of potassium ethylxanthate 30 [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 35 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 (91) + TX, bromethalin (92) + TX, calcium cyanide (444) + TX, chloralose (127) + TX, chlorophacinone (140) + TX, cholecalciferol (alternative name) (850) + TX, coumachlor (1004)

-104-

+ TX, coumafuryl (1005) + TX, coumatetralyl (175) + TX, crimidine (1009) + TX, difenacoum (246) + TX, difethialone (249) + TX, diphacinone (273) + TX, ergocalciferol (301) + TX, flocoumafene (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, 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 (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,
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,
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,

and biologically active compounds selected from the group consisting of azaconazole (60207-31-0) + TX, bitertanol [70585-36-3] + TX, bromuconazole [116255-48-2] + TX, cyproconazole [94361-06-5] + TX, difenoconazole [119446-68-3] + TX, diniconazole [83657-24-3] + TX, epiconazole [106325-08-0] + TX, fenbuconazole [114369-43-6] + TX, fluquinconazole [136426-54-5] + TX, flusilazole [85509-19-9] + TX, flutriafol [76674-21-0] + TX, hexaconazole [79983-71-4] + TX, imazalil [35554-44-0] + TX, imibenconazole [86598-92-7] + TX, ipconazole [125225-28-7] + TX, metconazole [125116-23-6] + TX, myclobutanil [88671-89-0] + TX, pefurazoate [101903-30-4] + TX, penconazole [66246-88-6] + TX, prothioconazole [178928-70-6] + TX, pyrifenox [88283-41-4] + TX, prochloraz [67747-09-5] + TX, propiconazole [60207-90-1] + TX, simeconazole [149508-90-7] + TX, tebuconazole [107534-96-3] + TX, tetaconazole [112281-77-3] + TX, triadimefon [43121-43-3] + TX, triadimenol [55219-65-3] + TX, triflumizole [99387-89-0] + TX, triticonazole [131983-72-7] + TX, ancyimidol [12771-68-5] + TX, fenarimol [60168-88-9] + TX, nuarimol [63284-71-9] + TX, bupirimate [41483-43-6] + TX, dimethirimol [5221-53-4] + TX, ethirimol [23947-60-6] + TX,

dodemorph [1593-77-7] + TX, fenpropidine [67306-00-7] + TX, fenpropimorph [67564-91-4] + TX, spiroxamine [118134-30-8] + TX, tridemorph [81412-43-3] + TX, cyprodinil [121552-61-2] + TX, mepanipyrim [110235-47-7] + TX, pyrimethanil [53112-28-0] + TX, fenpiclonil [74738-17-3] + TX, fludioxonil [131341-86-1] + TX, benalaxyll [71626-11-4] + TX, furalaxyll [57646-30-7] + TX, meta-
5 laxyll [57837-19-1] + TX, R-metalaxyll [70630-17-0] + TX, ofurace [58810-48-3] + TX, oxadixyl [77732-09-3] + TX, benomyl [17804-35-2] + TX, carbendazim [10605-21-7] + TX, debacarb [62732-91-6] + TX, fuberidazole [3878-19-1] + TX, thiabendazole [148-79-8] + TX, chlozolinate [84332-86-5] + TX, dichlozoline [24201-58-9] + TX, iprodione [36734-19-7] + TX, myclozoline [54864-61-8] + TX, procymidone [32809-16-8] + TX, vinclozoline [50471-44-8] + TX, boscalid [188425-85-6] + TX, carboxin [5234-68-4] + TX, fenfuram [24691-80-3] + TX, flutolanil [66332-96-
10 5] + TX, mepronil [55814-41-0] + TX, oxycarboxin [5259-88-1] + TX, penthiopyrad [183675-82-3] + TX, thifluzamide [130000-40-7] + TX, guazatine [108173-90-6] + TX, dodine [2439-10-3] [112-65-
2] (free base) + TX, iminoctadine [13516-27-3] + TX, azoxystrobin [131860-33-8] + TX, dimoxystrobin [149961-52-4] + TX, enestroburin {Proc. BCPC, Int. Congr., Glasgow, 2003, 1, 93} +
15 TX, fluoxastrobin [361377-29-9] + TX, kresoxim-methyl [143390-89-0] + TX, metominostrobin [133408-50-1] + TX, trifloxystrobin [141517-21-7] + TX, orysastrobin [248593-16-0] + TX, picoxystrobin [117428-22-5] + TX, pyraclostrobin [175013-18-0] + TX, ferbam [14484-64-1] + TX, mancozeb [8018-01-7] + TX, maneb [12427-38-2] + TX, metiram [9006-42-2] + TX, propineb [12071-83-9] + TX, thiram [137-26-8] + TX, zineb [12122-67-7] + TX, ziram [137-30-4] + TX,
20 captafol [2425-06-1] + TX, captan [133-06-2] + TX, dichlofluanid [1085-98-9] + TX, fluoroimide [41205-21-4] + TX, folpet [133-07-3] + TX, tolylfluanid [731-27-1] + TX, bordeaux mixture [8011-
63-0] + TX, copperhydroxid [20427-59-2] + TX, copperoxychlorid [1332-40-7] + TX, coppersulfat [7758-98-7] + TX, copperoxid [1317-39-1] + TX, mancopper [53988-93-5] + TX, oxine-copper [10380-28-6] + TX, dinocap [131-72-6] + TX, nitrothal-isopropyl [10552-74-6] + TX, edifenphos
25 [17109-49-8] + TX, iprobenphos [26087-47-8] + TX, isoprothiolane [50512-35-1] + TX, phosdiphen [36519-00-3] + TX, pyrazophos [13457-18-6] + TX, tolclofos-methyl [57018-04-9] + TX, acibenzo-
lar-S-methyl [135158-54-2] + TX, anilazine [101-05-3] + TX, benthiavalicarb [413615-35-7] + TX, blasticidin-S [2079-00-7] + TX, chinomethionat [2439-01-2] + TX, chloroneb [2675-77-6] + TX, chlorothalonil [1897-45-6] + TX, cyflufenamid [180409-60-3] + TX, cymoxanil [57966-95-7] + TX,
30 dichlone [117-80-6] + TX, diclocymet [139920-32-4] + TX, diclomezine [62865-36-5] + TX, dicloran [99-30-9] + TX, diethofencarb [87130-20-9] + TX, dimethomorph [110488-70-5] + TX, SYP-LI90 (Flumorph) [211867-47-9] + TX, dithianon [3347-22-6] + TX, ethaboxam [162650-77-3] + TX, etridiazole [2593-15-9] + TX, famoxadone [131807-57-3] + TX, fenamidone [161326-34-7] + TX, fenoxanil [115852-48-7] + TX, fentin [668-34-8] + TX, ferimzone [89269-64-7] + TX, fluazinam
35 [79622-59-6] + TX, fluopicolide [239110-15-7] + TX, flusulfamide [106917-52-6] + TX, fenhexamid [126833-17-8] + TX, fosetyl-aluminium [39148-24-8] + TX, hymexazol [10004-44-1] + TX, iprovalicarb [140923-17-7] + TX, IKF-916 (Cyzafamid) [120116-88-3] + TX, kasugamycin [6980-18-
3] + TX, methasulfocarb [66952-49-6] + TX, metrafenone [220899-03-6] + TX, pencycuron [66063-
05-6] + TX, phthalide [27355-22-2] + TX, polyoxins [11113-80-7] + TX, probenazole [27605-76-1] +

-106-

TX, propamocarb [25606-41-1] + TX, proquinazid [189278-12-4] + TX, pyroquilon [57369-32-1] + TX, quinoxyfen [124495-18-7] + TX, quintozene [82-68-8] + TX, sulfur [7704-34-9] + TX, tiadinil [223580-51-6] + TX, triazoxide [72459-58-6] + TX, tricyclazole [41814-78-2] + TX, triforine [26644-46-2] + TX, validamycin [37248-47-8] + TX, zoxamide (RH7281) [156052-68-5] + TX,
5 mandipropamid [374726-62-2] + TX, isopyrazam [881685-58-1] + TX, sedaxane [874967-67-6] + TX, 3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid (9-dichloromethylene-1,2,3,4-tetrahydro-1,4-methano-naphthalen-5-yl)-amide (dislosed in WO 2007/048556) + TX, 3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid (3',4',5'-trifluoro-biphenyl-2-yl)-amide (dislosed in WO 2006/087343) + TX, [(3S,4R,4aR,6S,6aS,12R,12aS,12bS)-3-[(cyclopropylcarbonyl)oxy]-1,3,4,4a,5,6,6a,12,12a,12b-
10 decahydro-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(3-pyridinyl)-2H,11Hnaphtho[2,1-b]pyrano[3,4-e]pyran-4-yl]methyl-cyclopropanecarboxylate [915972-17-7] + TX and 1,3,5-trimethyl-N-(2-methyl-1-oxopropyl)-N-[3-(2-methylpropyl)-4-[2,2,2-trifluoro-1-methoxy-1-(trifluoromethyl)ethyl]phenyl]-1H-pyrazole-4-carboxamide [926914-55-8] + TX, and
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, *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, *Bacillus chitinoporosus* strain CM-1 + TX, *Bacillus chitinoporosus* strain AQ746 + TX, *Bacillus licheniformis* strain HB-2 (Biostart™ Rhizobost®) + TX, *Bacillus licheniformis* strain 3086 (EcoGuard® + TX, Green Releaf®) + TX, *Bacillus circulans* + TX, *Bacillus firmus* (BioSafe®, BioNem-
25 WP®, 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, *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 sphericus* (VectoLex®) + TX, *Bacillus* spp. + TX, *Bacillus* spp. strain AQ175 +
30 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, *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 tenius* + TX, *Cedecea dravisa* + TX, *Cellulomonas flavigena* + TX, *Chaetomium cochlioides* (Nova-Cide®) + TX, *Chaetomium globosum* (Nova-Cide®) + TX, *Chromobacterium subtsugae* strain PRAA4-1T (Grandevol®) + 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 infirmo-miniatus* + 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 hawaiensis* + 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 linacinus* 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 gigantean* (Rotstop®) + TX, phosphate solubilizing bacteria (Phosphomeal®) + TX, *Phytophthora cryptogea* + TX, *Phytophthora palmivora* (Devine®) + TX, *Pichia anomala* + TX, *Pichia guillermondii* + 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 corrugata* + 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 mucilaginosa* + 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*; and

10 Plant extracts including: pine oil (Retenol®) + TX, azadirachtin (Plasma Neem Oil® + TX, AzaGuard® + TX, MeemAzal® + TX, Molt-X® + TX, Botanical IGR (Neemazad®, 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,

15 20 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 glucam of brown algae (Laminarin®) + TX; and

25 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, Tetradecatrienyl acetate + TX, 13-Hexadecatrienol + 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; and

30 Macrobials 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, *Ageniaspis citricola* + TX, *Ageniaspis 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, *Anagyrus fusciventris* + TX, *Anagyrus kamali* + TX, *Anagyrus loecki* + TX, *Anagyrus 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 phylloconistoides* + 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, *Episyphus balteatus* (Syrphidend®) + TX, *Eretmoceris 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 ceratitivorus* + TX, Formononetin (Wireless 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

-111-

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* (Thripol-I® + TX, Oriline i®) + TX, *Orius laevigatus* (Thripol-L® + TX, Oriline I®) + TX, *Orius majusculus* (Oriline m®) + TX, *Orius strigicollis* (Thripol-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 tricuspis* + TX, *Pseudaphycus maculipennis* + TX, *Pseudoleptomastix mexicana* + TX, *Psyllaephagus pilosus* + TX, *Psyllalia 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, Nemasy F® + TX, BioNem F® + TX, Steinernema-System® + TX, NemAttack® + TX, Nemaplus® + TX, Exhibitline sf® + TX, Scia-rid® + TX, Entonem®) + TX, *Steinernema kraussei* (Nemasy L® + TX, BioNem L® + TX, Exhibitline srb®) + TX, *Steinernema riobrave* (BioVector® + TX, BioVektor®) + TX, *Steinernema scapterisci* (Nematac S®) + TX, *Steinernema* spp. + TX, *Steinernematid* spp. (Guardian Nematodes®) + TX, *Stethorus punctillum* (Stethorus®) + TX, *Tamarixia radiate* + 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 ostriniae* + TX, *Trichogramma platneri* + TX, *Trichogramma pretiosum* + TX, *Xanthopimpla stemmator*, and 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, *Mycoleptodiscus 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 + potassium thiocyanate (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.

35

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

-112-

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 10 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.

15 The active ingredient mixture of the compounds of formula I selected from Table 1, 2, A and B with active ingredients described above comprises a compound selected from Table 11, 2, A and B 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 20 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 25 ratios are by weight.

30 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 Table 1, 2, A and B 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 single active ingredient 35 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 Table 1, 2, A and B and the active ingredients as described above is not essential for working the present invention.

-113-

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 5 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

10 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

15 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 20 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 25 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.

30 The compounds of the invention and compositions thereof are also 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 compound can be applied to seed kernels (coating), either by soaking the kernels in a liquid 35 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

-114-

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

5 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

10 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

15 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

20 by dusting the seeds before sowing or during the sowing/planting of the seeds.

Biological Examples:

Example B1: Activity against *Bemisia tabaci* (Cotton white fly):

Cotton leaf discs were placed on agar in 24-well microtiter plates and sprayed with aqueous test

25 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.

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

B2, A1, A2, A3, A8, A10, A12, A14, A31, A33, A34, A35, A36 and A47.

A1, A2, A3, A8, A10, A14 and A12.

30

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

Maize sprouts, placed on 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 4 days after

35 infestation.

The following compounds resulted in at least 80% mortality at an application rate of 200 ppm: A1, A2, B2, B3, B4, B5, A1, A2, A3, A4 A5, A6, A7, A8, A10, A11, A12, A13, A14, A15, A16, A19, A21, A22, A23, A25, A28, A29, A30, A31, A32, A33, A34, A35, A36, A37, A38, A39, A40, A41, A42, A43, A44,

-115-

A45, A46, A47, A48, A49, A51, A54, A56, A57, A59, A60, A61, A62, A63, A65, A66, A67, A68, A69, A70, A72 and A73.

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

5 Soybean leaf on agar in 24-well microtiter plates were sprayed with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions. After drying the leaf were infested with N-2 nymphs. The samples were assessed for mortality 5days after infestation.

The following compounds resulted in at least 80% mortality at an application rate of 200 ppm A1, B2,

B3, B4, B5, A1, A2, A3, A6, A8, A10, A11, A12, A14, A16, A17, A19, A20, A21, A22, A23, A25, A28,

10 A29, A30, A31, A33, A34, A35, A36, A37, A38, A39, A40, A41, A42, A43, A44, A45, A46, A47, A48, A49, A51, A53, A54, A56, A57, A58, A60, A62, A63, A65, A66, A67, A68, A69, A70, A71, A72 and A73.

Example B4: Activity against *Frankliniella occidentalis* (Western flower thrips):

15 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.

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

A1, A10, A12, A19, A23, A34, A46, A47, A67 and A68.

20 Example B5: Activity against *Myzus persicae* (Green peach aphid):

Sunflower leaf discs were placed on 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.

25 The following compounds resulted in at least 80% mortality at an application rate of 200 ppm: B1, B2, B3, B4, A1, A2, A6, A8, A10, A11, A12, A14, A16, A17, A19, A20, A21, A22, A23, A30, A31, A34, A35, A36, A38, A39, A40, A41, A42, A44, A46, A47, A48, A49, A51, A53, A54, A56, A58, A59, A60, A66, A67, A68, A71 and A73.

30 Example B6: Activity against *Myzus persicae* (Green peach aphid):

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

The following compounds resulted in at least 80% mortality at a test rate of 24 ppm: B2, A1, A8, A11,

35 A12, A14, A17, A23, A34, A57 and A73.

Example B7: Activity against *Myzus persicae* (Green peach aphid):

-116-

Test compounds from 10'000 ppm DMSO stock solutions were applied by pipette into 24-well microtiter plates and mixed with sucrose solution. The plates were closed with a stretched Parafilm. A plastic stencil with 24 holes was placed onto the plate and infested pea seedlings were placed directly on the Parafilm. The infested plate was closed with a gel blotting paper and another plastic stencil and then turned upside down. The samples were assessed for mortality 5 days after infestation. The following compounds resulted in at least 80% mortality at a test rate of 12 ppm: B1, B2, A4, A7, A8, A10, A11, A12, A30 and A32.

Example B8: Activity against *Plutella xylostella* (Diamond back moth)

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 (10 to 15 per well). 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: B3, B4, A1, A2, A3, A4, A5, A6, A7, A8, A10, A11, A14, A15, A16, A17, A18, A19, A21, A22, A23, A25, A28, A29, A30, A31, A32, A33, A34, A35, A36, A37, A38, A39, A40, A41, A42, A43, A44, A45, A46, A47, A48, A49, A50, A51, A52, A53, A54, A56, A57, A58, A60, A61, A62, A63, A64, A65, A66, A67, A68, A69, A70, A71, A72 and A73.

20 Example B9: Activity against *Spodoptera littoralis* (Egyptian cotton leaf worm):

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 five L1 larvae. The samples were assessed for mortality, anti-feedant effect, and growth inhibition in comparison to untreated samples 3 days after infestation. Control of *Spodoptera littoralis* by a test sample is when at least one of 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:

B3, B4, B5, A1 A2, A3, A4, A5, A6, A7, A8, A10, A11, A12, A13, A14, A15, A16, A17, A18, A19, A21, A22, A23, A25, A26, A27, A28, A30, A31, A32, A33, A34, A35, A36, A38, A39, A40, A41, A42, A43, A44, A45, A46, A47, A48, A49, A50, A51, A52, A53, A54, A55, A56, A57, A59, A60, A61, A62, A63, A64, A65, A66, A67, A68, A69, A70, A71, A72 and A73.

Example B10: Activity against *Spodoptera littoralis* (Egyptian cotton leaf worm):

Test compounds were applied by pipette from 10'000 ppm DMSO stock solutions into 24-well plates and mixed with agar. Lettuce seeds were placed on the agar and the multi well plate was closed by another plate which contains also agar. After 7 days the roots have absorbed the compound and the lettuce has grown into the lid plate. The lettuce leafs were now cut off into the lid plate. *Spodoptera* eggs were pipetted through a plastic stencil on a humid gel blotting paper and the plate closed with it.

-117-

The samples were assessed for mortality, anti-feedant effect and growth inhibition in comparison to untreated samples 6 days after infestation.

The following compounds gave an effect of at least 80% in at least one of the three categories (mortality, anti-feedancy, or growth inhibition) at a test rate of 12.5 ppm:

5 A1, A6, A8, A11, A24, A21, A22, A30, A28, A31, A41, A42, A43, A39, A40, A41, A42, A43, A44, A46, A47, A49, A51, A57, A60, A66, A67 and A73.

Example B11: Activity against *Spodoptera littoralis* (Egyptian cotton leaf worm), systemic activity:

Test compounds were applied by pipette from 10'000 ppm DMSO stock solutions into 24-well plates and mixed with agar. Lettuce seeds were placed on the agar and the multi well plate was closed by another plate which contains also agar. After 7 days the roots have absorbed the compound and the lettuce has grown into the lid plate. The lettuce leafs were now cut off into the lid plate. *Spodoptera* eggs were pipetted through a plastic stencil on a humid gel blotting paper and the plate closed with it.

The samples were assessed for mortality 6 days after infestation.

15 The following compounds gave an effect of at least 80% mortality at a test rate of 12.5 ppm:

A1, A8, A14, A17, A21, A22, A23, A28, A31, A34, A35, A36, A39, A40, A41, A42, A43, A44, A46, A47, A49, A51, A57, A60, A66, A67 and A73.

Example B12: Activity against *Tetranychus urticae* (Two-spotted spider mite):Feeding/contact activity:

20 Bean leaf discs on agar in 24-well microtiter plates were sprayed with aqueous test solutions prepared from 10'000 ppm DMSO stock solutions. After drying the leaf discs were infested with a mite population of mixed ages. The samples were assessed for mortality on mixed population (mobile stages) 8 days after infestation.

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

25 A20 and A48.

Example B13: Activity against *Thrips tabaci* (Onion 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 ppm DMSO stock solutions. After drying the leaf discs were infested 30 with a thrips population of mixed ages. The samples were assessed for mortality 6 days after infestation.

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

A1, A12, A15, A46 and A54.

35 Example B14: Activity against *Aedes aegypti* (Yellow fever mosquito):

10 to 15 *Aedes* larvae (L2) together with a nutrition mixture were placed in 96-well microtiter plates.

Test compounds were pipetted into the wells. After an incubation period of 2 days insects were assessed for mortality and growth inhibition.

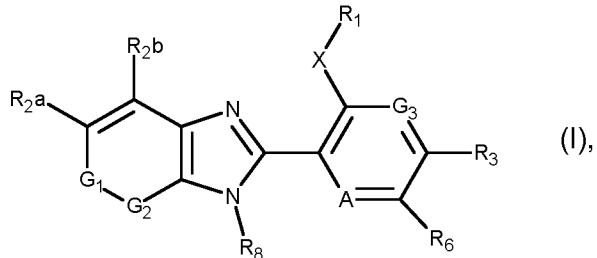
-118-

The following compounds gave an effect of at least 80% in at least one of the two categories (mortality or growth inhibition) at a test rate of 5 ppm:

A1, A2, A19, A22, A23, A28, A31, A34, A39, A41, A42, A43, A46, A47, A48, A49, A70 and A73.

Claims:

1. A compound of formula I



wherein

5 A represents CH, N or CR; wherein R is C₁-C₄alkyl, C₁-C₄haloalkyl, cyano, nitro or halogen;
 X is S, SO or SO₂;

R₁ is C₁-C₄alkyl, C₁-C₄haloalkyl, C₃-C₆cycloalkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl or C₃-C₆cycloalkyl mono - or polysubstituted by substituents selected from the group consisting of halogen, C₁-C₄haloalkyl, cyano and C₁-C₄alkyl; or R₁ is C₃-C₆cycloalkyl-C₁-C₄alkyl mono- or polysubstituted by substituents

10 selected from the group consisting of halogen, cyano, C₁-C₄haloalkyl and C₁-C₄alkyl;
 or R₁ is C₂-C₆alkenyl, C₂-C₆haloalkenyl or C₂-C₆alkynyl;
 R_{2a} and R_{2b} are, independently from each other, hydrogen, halogen, cyano, C₁-C₆haloalkoxy, C₁-C₆haloalkyl or C₁-C₆haloalkyl substituted by one or two substituents selected from the group consisting of hydroxyl, methoxy and cyano; or

15 R_{2a} and R_{2b} are, independently from each other, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl, O(C₁-C₄haloalkyl), or -C(O)C₁-C₄haloalkyl; or
 R_{2a} and R_{2b} are, independently from each other, C₃-C₆cycloalkyl which can be mono - or polysubstituted by substituents selected from the group consisting of halogen, cyano, C₁-C₄haloalkyl and C₁-C₄alkyl;

20 R₃ is hydrogen, halogen, cyano, nitro, C₁-C₆alkyl, C₁-C₆alkoxy, C₁-C₆alkoxyC₁-C₆alkyl, C₁-C₆haloalkyl, C₃-C₆cycloalkyl or C₃-C₆cycloalkyl-C₁-C₄alkyl; or
 R₃ is C₃-C₆cycloalkyl mono- or polysubstituted by substituents selected from the group consisting of halogen, C₁-C₄alkyl, C₁-C₄haloalkyl and cyano; or
 R₃ is phenyl which can be mono- or polysubstituted by substituents selected from the group consisting

25 of halogen, cyano, nitro, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, C₁-C₄alkylsulfonyl and -C(O)C₁-C₄haloalkyl; or
 R₃ is C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl or C₂-C₆haloalkynyl; or

30 R₃ is C₁-C₆haloalkylsulfanyl, C₁-C₆haloalkylsulfinyl, C₁-C₆haloalkylsulfonyl, C₁-C₆haloalkoxy, -C(O)C₁-C₄haloalkyl, C₁-C₆alkylsulfanyl, C₁-C₆alkylsulfinyl or C₁-C₆alkylsulfonyl; or
 R₃ is a five- to six-membered, aromatic, partially saturated or fully saturated ring system linked via a nitrogen atom to the ring which contains the substituent G₃, said ring system can be mono- or

-120-

polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, C₁-C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and

5 -C(O)C₁-C₄haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom; or

R₃ is a five-to six membered, aromatic, partially saturated or fully saturated ring system linked via a carbon atom to the ring which contains the substituent G₃, said ring system can be mono- or

10 polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, C₁-C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄haloalkylsulfonyl and

-C(O)C₁-C₄haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group

15 consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom;

R₈ is C₁-C₄alkyl which can be mono- or polysubstituted by substituents selected from the group consisting of halogen and C₁-C₂alkylsulfinyl;

G₁ is NR₄ and G₂ is C(Y); or

20 G₁ is C(Y) and G₂ is NR₅;

Y is O or S;

G₃ is N or CR₉;

R₄ is C₁-C₆alkyl, C₁-C₆haloalkyl; or

R₄ is C₃-C₆cycloalkyl which can be mono- or polysubstituted by R₇; or

25 R₄ is C₃-C₆cycloalkyl-C₁-C₄alkyl which can be mono- or polysubstituted by R₁₀; or

R₄ is C₁-C₄alkyl substituted by cyano, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfonyl, C₁-C₄alkylsulfinyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfonyl, C₁-C₄haloalkylsulfinyl, C₁-C₄alkoxy, C₁-C₄alkoxyC₁-C₄alkoxy, C₃-C₆ cycloalkyl or by phenyl, which itself can be mono - or polysubstituted by substituents selected from the group consisting of halogen, C₁-C₄alkyl, cyano, C₁-C₄haloalkyl and

30 C₁-C₄alkoxy;

R₄ is C₂-C₆alkenyl substituted by R₁₁ or C₂-C₆alkynyl substituted by R₁₁; or

R₄ is C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₆haloalkoxy, C₁-C₆alkoxy, C₁-C₆alkylsulfanyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfinyl, C₁-C₆haloalkylsulfanyl, C₁-C₆haloalkylsulfonyl, C₁-C₆haloalkylsulfinyl or hydroxyl; or

35 R₄ is a five- to six-membered, aromatic, partially saturated or fully saturated ring system, said ring system can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro, C₂-C₆alkenyl, C₂-C₆haloalkenyl, C₂-C₆alkynyl, C₂-C₆haloalkynyl, C₁-C₄alkoxy C₁-C₄alkyl, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, C₁-C₄alkoxy, C₁-C₄alkylsulfanyl, C₁-C₄alkylsulfinyl, C₁-C₄alkylsulfonyl and -C(O)C₁-C₄alkyl, C₁-C₄haloalkylsulfanyl, C₁-C₄haloalkylsulfinyl, C₁-C₄alkylsulfonyl and

-121-

C_4 haloalkylsulfonyl and $-C(O)C_1-C_4$ haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom;

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

5 R_5 is C_3-C_6 cycloalkyl which can be mono- or polysubstituted by R_7 ; or

R_5 is C_3-C_6 cycloalkyl- C_1-C_4 alkyl which can be mono- or polysubstituted by R_{10} ; or

R_5 is C_1-C_4 alkyl substituted by cyano, C_1-C_4 alkylsulfanyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylsulfinyl, C_1-C_4 haloalkylsulfanyl, C_1-C_4 haloalkylsulfonyl, C_1-C_4 haloalkylsulfinyl, C_1-C_4 alkoxy,

C_1-C_4 alkoxy C_1-C_4 alkoxy, C_3-C_6 cycloalkyl or by phenyl, which itself can be mono - or polysubstituted

10 by substituents selected from the group consisting of halogen, C_1-C_4 alkyl, cyano, C_1-C_4 haloalkyl and C_1-C_4 alkoxy; or

R_5 is C_2-C_6 alkenyl substituted by R_{11} or C_2-C_6 alkynyl substituted by R_{11} ; or

R_5 is C_2-C_6 alkenyl, C_2-C_6 haloalkenyl, C_2-C_6 alkynyl, C_2-C_6 haloalkynyl, C_1-C_6 haloalkoxy, C_1-C_6 alkoxy, C_1-C_6 alkylsulfanyl, C_1-C_6 alkylsulfonyl, C_1-C_6 alkylsulfinyl, C_1-C_6 haloalkylsulfanyl, C_1-C_6 haloalkylsulfonyl, C_1-C_6 haloalkylsulfinyl, C_1-C_6 haloalkylsulfonyl, C_1-C_6 haloalkylsulfinyl; or

15 C_6 haloalkylsulfonyl, C_1-C_6 haloalkylsulfinyl or hydroxyl; or

R_5 is a five- to six-membered, aromatic, partially saturated or fully saturated ring system, said ring system can be mono- or polysubstituted by substituents selected from the group consisting of halogen, cyano, nitro, C_2-C_6 alkenyl, C_2-C_6 haloalkenyl, C_2-C_6 alkynyl, C_2-C_6 haloalkynyl, C_1-C_4 alkoxy C_1-C_4 alkyl, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 alkoxy, C_1-C_4 alkylsulfanyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl and $-C(O)C_1-C_4$ alkyl, C_1-C_4 haloalkylsulfanyl, C_1-C_4 haloalkylsulfinyl, C_1-C_4 haloalkylsulfonyl and $-C(O)C_1-C_4$ haloalkyl; and said ring system contains 1, 2 or 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, where said ring system may not contain more than one oxygen atom and not more than one sulfur atom;

20 R_6 and R_9 , independently from each other, are hydrogen, halogen, nitro, cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_6 cycloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 alkoxy C_1-C_4 alkyl, or C_1-C_4 haloalkyl;

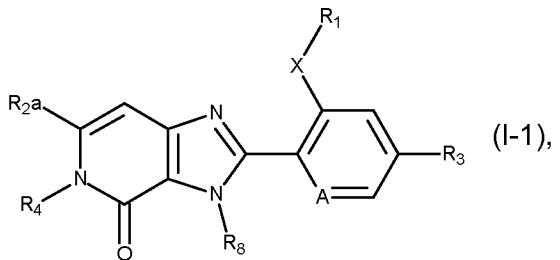
25 R_7 and R_{10} , independently from each other, are halogen, nitro, cyano, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, C_1-C_4 alkoxy C_1-C_4 alkyl, C_1-C_4 alkyl, C_1-C_4 haloalkyl;

R_{11} is nitro, cyano, C_1-C_4 alkoxy, C_1-C_4 alkoxy C_1-C_4 alkoxy, C_1-C_4 alkylsulfanyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkylsulfinyl, C_1-C_4 haloalkylsulfanyl, C_1-C_4 haloalkylsulfonyl, C_1-C_4 haloalkylsulfinyl or phenyl which

30 itself can be mono - or polysubstituted by substituents selected from the group consisting of halogen, C_1-C_4 alkyl, cyano, C_1-C_4 haloalkyl and C_1-C_4 alkoxy; and agrochemically acceptable salts, stereoisomers, enantiomers, tautomers and N-oxides of the compounds of formula I.

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

-122-



wherein the substituents X, A, R₁, R_{2a}, R₃, R₄ and R₈ are as defined under formula I in claim 1.

5 3. A compound of formula I-1 according to claim 2, wherein
 A is C-H or N;
 R₁ is C₁-C₄ alkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl or C₃-C₆cycloalkyl;
 R_{2a} is halogen, C₁-C₄haloalkyl, cyano or C₃-C₆cycloalkyl which can be mono - or polysubstituted by
 substituents selected from the group consisting of halogen, cyano and C₁-C₄alkyl;

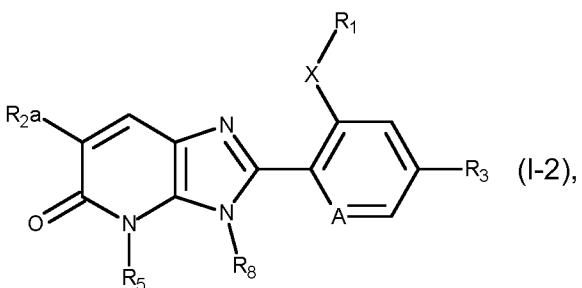
10 R₄ is C₁-C₄alkyl or C₁-C₄haloalkyl;
 R₃ is hydrogen, halogen or C₁-C₄haloalkyl;
 and X and R₈ are as defined under formula I in claim 1.

4. A compound of formula I-1 according to claim 2, wherein
 15 A is C-H or N;
 R₁ is methyl, ethyl, n-propyl, i-propyl or cyclopropylmethyl;
 R_{2a} is halogen, trifluoromethyl, cyano or cyclopropyl which can be monosubstituted by cyano;
 R₃ is hydrogen or trifluoromethyl;
 R₄ is methyl or ethyl;
 20 and X and R₈ are as defined under formula I in claim 1.

5. A compound of formula I-1 according to claim 2, wherein
 A is C-H or N;
 R₁ is ethyl;
 25 R_{2a} is trifluoromethyl;
 R₃ is hydrogen or trifluoromethyl;
 R₄ is methyl; and
 X and R₈ are as defined under formula I in claim 1.

30 6. A compound of formula I according to claim 1 represented by the compounds of formula (I-2)

-123-



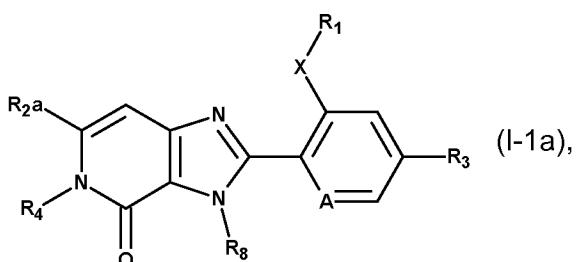
wherein the substituents X, A, R₁, R_{2a}, R₃, R₅ and R₈ are as defined under formula I in claim 1.

5 7. A compound of formula I-2 according to claim 6, wherein
 A is C-H or N;
 R₁ is C₁-C₄ alkyl, C₃-C₆cycloalkyl-C₁-C₄alkyl or C₃-C₆cycloalkyl;
 R_{2a} is halogen, C₁-C₄haloalkyl, cyano or C₃-C₆cycloalkyl which can be mono - or polysubstituted by substituents selected from the group consisting of halogen, cyano and C₁-C₄alkyl;

10 R₃ is hydrogen, halogen or C₁-C₄haloalkyl;
 R₅ is C₁-C₄alkyl or C₁-C₄haloalkyl; and X and R₈ are as defined under formula I in claim 1.

8. A compound of formula I-2 according to claim 6, wherein
 A is as C-H or N;
 R₁ is methyl, ethyl, n-propyl, i-propyl or cyclopropylmethyl;
 R_{2a} is halogen, trifluoromethyl, cyano or cyclopropyl which can be monosubstituted by cyano;
 R₃ is hydrogen or trifluoromethyl;
 R₅ is methyl or ethyl; and X and R₈ are as defined under formula I in claim 1.

20 9. A compound of formula I according to claim 1 represented by the compounds of formula (I-1a)



wherein

A is N or CH;
 R₁ is C₁-C₄alkyl;
 R_{2a} is C₁-C₄haloalkyl;
 R₃ is hydrogen, halogen, C₂-C₆alkenyl, C₁-C₄haloalkyl or C₃-C₆cycloalkyl; or

-124-

R₃ is phenyl which can be mono- or di-substituted by substituents selected from the group consisting of cyano, halogen, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₄haloalkoxy and C₁-C₄haloalkyl; or

R₃ is pyrazolyl, which can be mono-substituted by C₁-C₄haloalkyl; or

R₃ is pyridinyl which can be mono- or di-substituted by substituents selected from the group consisting

5 of C₁-C₄alkyl, C₁-C₄haloalkyl and halogen; or

R₃ is pyrimidinyl which can be mono-substituted by C₁-C₄alkoxy;

R₄ is C₁-C₆alkyl or C₁-C₆haloalkyl, preferably 1,1,1-trifluoroethyl;

R₄ is C₁-C₄alkyl mono-substituted by cyano, C₁-C₄alkylsulfanyl, phenyl, C₁-C₄alkoxy, C₁-C₄alkoxy C₁-C₄alkoxy or C₃-C₆cycloalkyl; or

10 R₄ is C₂-C₆alkenyl or C₂-C₆alkynyl; or

R₄ is C₂-C₆alkenyl substituted by phenyl;

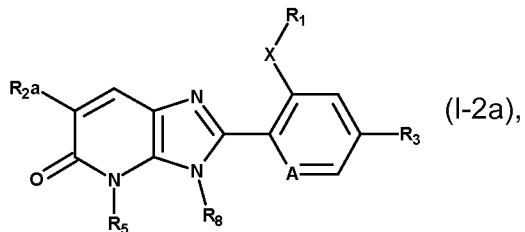
R₄ is benzyl which can be mono-substituted by C₁-C₄alkoxy;

R₈ is C₁-C₄alkyl; preferably methyl; and

X is S or SO₂.

15

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



20

wherein

A is N or CH;

R₁ is C₁-C₄alkyl;

25 R_{2a} is hydrogen, halogen or C₁-C₄haloalkyl;

R₃ is C₁-C₄haloalkyl, phenyl or phenyl substituted by C₁-C₄haloalkyl;

R₅ is C₁-C₄alkyl;

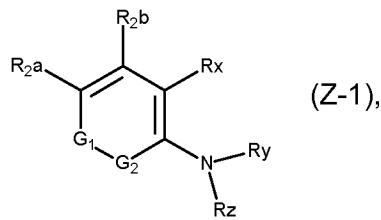
R₈ is C₁-C₄alkyl; and

X is S or SO₂.

30

11. A compound of formula Z-1

-125-



wherein G_1 , G_2 , R_{2a} , and R_{2b} are as defined under formula I in claim 1;

Rx is NO_2 or NH_2 ;

5 Ry is hydrogen and

Rz is C_1 - C_4 alkyl.

12. A pesticidal composition, which comprises at least one compound of formula I according to claim 1 or, where appropriate, a tautomer thereof, in each case in free form or in agrochemically utilizable salt form, as active ingredient and at least one auxiliary.

13. A method for controlling pests, which comprises applying a composition according to claim 12 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.

15

14. A method for the protection of plant propagation material from the attack by pests, which comprises treating the propagation material or the site, where the propagation material is planted, with a composition according to claim 12.

20 15. A substrate selected from nonwoven and fabric material comprising a composition according to claim 12.