(12) STANDARD PATENT (11) Application No. **AU 2012215440 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Isoxazoline derivatives for controlling invertebrate pests

(51) International Patent Classification(s)
C07D 413/04 (2006.01)
A01N 43/80 (2006.01)
C07D 413/14 (2006.01)
C07D 417/04 (2006.01)
C07D 417/14 (2006.01)

(21) Application No: **2012215440** (22) Date of Filing: **2012.02.09**

(87) WIPO No: **WO12/107533**

(30) Priority Data

(31) Number	(32) Date	(33) Country
00247/2011	**2011.02.10**	**CH**

(43) Publication Date: **2012.08.16**
(44) Accepted Journal Date: **2015.08.27**

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(56) Related Art
WO 2010/070068 A2
WO 2007/075459 A2

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 August 2012 (16.08.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/107533 A1

(51) International Patent Classification:
C07D 413/04 (2006.01) ***C07D 417/14*** (2006.01)
C07D 413/14 (2006.01) ***A01N 43/80*** (2006.01)
C07D 417/04 (2006.01)

(21) International Application Number: PCT/EP2012/052241

(22) International Filing Date: 9 February 2012 (09.02.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
00247/2011 10 February 2011 (10.02.2011) CH

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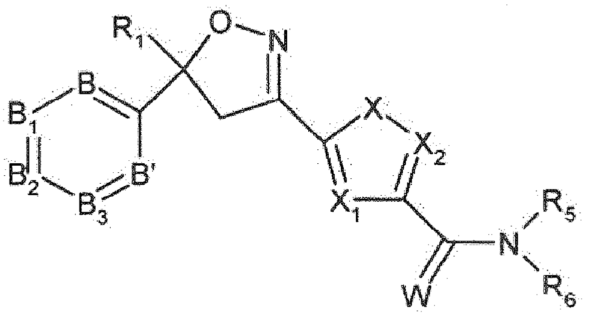
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, 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.

(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, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, 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, 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))*

Published:
— *with international search report (Art. 21(3))*

(54) Title: ISOXAZOLINE DERIVATIVES FOR CONTROLLING INVERTEBRATE PESTS



(I)

(57) Abstract: The invention relates to new isoxazoline compounds of formula (I), wherein the variables have the meaning as indicated in the claims; in free form and in salt form; and optionally the enantiomers and geometrical isomers thereof. The compounds of formula (I) are useful in the control of parasites, in particular ectoparasites, in and on warmblooded animals.

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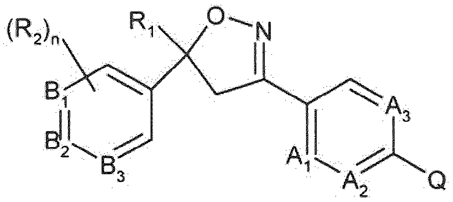
ISOXAZOLINE DERIVATIVES FOR CONTROLLING INVERTEBRATE PESTS

FIELD OF THE INVENTION

This invention relates to novel isoxazolines, their N-oxides and salts, processes for their manufacture, their use in the control of ectoparasites, especially insects and acari, on non-human animals, especially productive livestock and domestic animals, and furthermore pesticidal compositions which contain one or more of these compounds.

BACKGROUND OF THE INVENTION

PCT Patent Publication WO 2007/075459 discloses isoxazoline derivatives of Formula (A) as plant insecticides



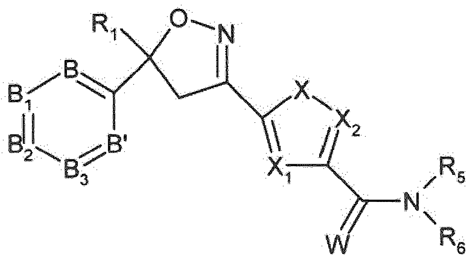
(A)

wherein, inter alia, each of A_1, A_2 and B_1-B_3 are $C(R_3)$, A_3 is N, R_1 is haloalkyl and Q is a heterocyclic radical.

The compounds are mainly used in the control of invertebrate pests in agronomic environments. Many products are commercially available for these purposes, but the need continues for new compounds that are more effective, less costly, less toxic, environmentally safer or have different modes of action. It now has been surprisingly found that novel derivatives with a modified heterocyclic side chain have superior properties in the control of pests.

SUMMARY OF THE INVENTION

This present invention is directed to a compound of formula



(I)

including all geometric and stereoisomers, N-oxides, and salts thereof, and compositions containing them and their use for controlling parasites, wherein

X, is $S(O)_m$, O or NR_4 and X_1 and X_2 are each independently of the other CR_3 or N,

m is an integer from 0 to 2;

B and B' are each independently a group CR_2';

B_1, B_2 and B_3 are each independently selected from the group consisting of CR_2' and N;

R_2' is H or R_2;

each R_2 is independently of the other halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-haloalkylsulfinyl, C_1-C_6-alkylsulfonyl, C_1-C_6-haloalkylsulfonyl, N-mono- or N,N-di-C_1-C_6-alkylamino, C_1-C_6 alkoxycarbonyl, cyano (-CN) or nitro (-NO_2);

R_1 is halogen, cyano, C_1-C_6-alkyl, C_1-C_6-haloalkyl or C_1-C_6-haloalkoxy;

each R_3 is independently H, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_3-C_6-cycloalkyl, C_3-C_6-halocycloalkyl, hydroxy, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl-sulfinyl, C_1-C_6-haloalkylsulfinyl, C_1-C_6-alkylsulfonyl, C_1-C_6-haloalkylsulfonyl, amino, N-mono- or N,N-di-C_1-C_6-alkylamino, C_1-C_6-alkoxycarbonyl, cyano, nitro or unsubstituted or halogen-, C_1-C_6-alkyl-, C_1-C_6-haloalkyl-, hydroxy-, C_1-C_6-alkoxy-, C_1-C_6-haloalkoxy-, amino-, cyano- or nitro-substituted phenyl, pyridyl or pyrimidyl;

R_4 is H, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_4-C_7-alkylcycloalkyl, C_4-C_7-cycloalkylalkyl, C_2-C_8-alkoxyalkyl, C_1-C_6-alkylcarbonyl or C_1-C_6-alkoxycarbonyl;

R_5 and R_6 are each independently of the other H, cyano, hydroxy, nitro, amino, aminocarbonyl, a group $-N=CR_7R_8$ or sulfonamido; or are C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_4-C_7-alkylcycloalkyl, C_4-C_7-cycloalkylalkyl, C_1-C_6-alkoxy, N-mono- or N,N-di-C_1-C_6-alkylamino, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, C_1-C_6-alkoxycarbonyl, C_2-C_6-alkanoyl, C_1-C_6-alkylcarbonylamino, N-mono- or N,N-di-C_1C_6-alkylaminocarbonyl or N-mono- or N,N, di-C_1-C_4-alkylsulfonamido which are each unsubstituted or are substituted in the alkyl, alkenyl or alkynyl moiety by halogen, hydroxy, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_6-alkylamino, C_3-C_6-cycloalkylamino, COOH, C_1-C_6-alkoxycarbonyl, C_2-C_6-alkanoyl, C_1-C_6-alkylcarbonylamino, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido, a group $-C(W')NR_7R_8$ or a radical Q'; or are a radical Q;

or R_5 and R_6 together are a group $=C-NR_7R_8$ or $=C-NR_7(OR_8)$; or

R_5 and R_6 together with the N-atom to which they are attached, form a 3- to 7-membered ring which optionally contains a further heteroatom selected from the group consisting of N,

S and O, and which ring is further unsubstituted or mono- or polysubstituted by C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, hydroxy, halogen, cyano or nitro;
Q and Q' are each independently a 4-, 5- or 6-membered heterocyclic ring, or a C_6-C_{10}-carbocyclic ring system or a 8-, 9- or 10-membered fused hetero-bicyclic ring system, each of them being aromatic or not, and each of them being unsubstituted or mono- or polysubstituted by halogen, hydroxy, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_6-alkylamino, C_3-C_6-cycloalkylamino, COOH, C_1-C_6-alkoxycarbonyl, C_2-C_6-alkanoyl, C_1-C_6-alkylcarbonyl-amino, aminocarbonyl, N-mono- or N,N-di-C_1C_6-alkylaminocarbonyl, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido, a group –C(W')NR_7R_8 or a radical Q";
Q" is a 4-, 5- or 6-membered heterocyclic ring or a C_6-C_{10}-carbocyclic ring system, each of them being aromatic or not, and each of them being unsubstituted or mono- or polysubstituted by halogen, hydroxy, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_6-alkylamino, C_3-C_6-cycloalkylamino, COOH, C_1-C_6-alkoxycarbonyl, C_2-C_6-alkanoyl, C_1-C_6-alkylcarbonyl-amino, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido or a group –C(W')NR_7R_8;
R_7 and R_8 are independently of the other H, cyano, hydroxy, amino, aminocarbonyl, sulfonamido or nitro; or are C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_4-C_7-alkylcycloalkyl or C_4-C_7-cycloalkylalkyl, C_1-C_6-alkoxy, N-mono- or N,N-di-C_1-C_6-alkylamino, C_1-C_6-alkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, C_1-C_6-alkoxycarbonyl, C_2-C_6-alkanoyl, C_1-C_6-alkylcarbonylamino, N-mono- or N,N-di-C_1C_6-alkylaminocarbonyl, or N-mono- or N,N, di-C_1-C_4-alkylsulfonamido, which may each be unsubstituted or substituted in the alkyl, alkenyl or alkynyl moiety by halogen, hydroxy, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkylsulfinyl, C_1-C_6-alkylsulfonyl, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_6-alkylamino, C_3-C_6-cycloalkylamino, COOH, C_1-C_6-alkoxycarbonyl, C_2-C_6-alkanoyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, N-mono- or N,N-di-C_1C_6-alkylaminocarbonyl, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido or a radical Q";
and W and W' are each independently of the other O or S.

This invention also provides a composition comprising a compound of formula (I), an N-oxide or a salt thereof, and at least one additional component selected from the group consisting of a surfactant, a solid diluent and a liquid diluent.

In one embodiment, this invention also provides a composition for controlling parasites, in particular ectoparasites, comprising a biologically effective amount of a compound of formula (I), an N-oxide or a salt thereof, and at least one additional component selected from the group consisting of a surfactant, a solid diluent and a liquid diluent, said composition optionally further comprising a biologically effective amount of at least one additional biologically active compound or agent.

This invention further provides the composition described above in the form of a bait composition wherein the solid diluent and/or the liquid diluent comprises one or more food materials, said composition optionally comprising an attractant and/or a humectant.

This invention further provides a trap device for controlling parasites, in particular ectoparasites, comprising said bait composition and a housing adapted to receive said bait composition, wherein the housing has at least one opening sized to permit the parasites to pass through the opening. so the invertebrate pest can gain access to said bait composition from a location outside the housing, and wherein the housing is further adapted to be placed in or near a locus of potential or known activity for the parasites pest.

This invention also provides a method for controlling parasites comprising contacting the parasites or their environment with a biologically effective amount of a compound of formula (I), an N-oxide or a salt thereof, (e.g., as a composition described herein). This invention also relates to such method wherein the parasites or their environment are contacted with a composition comprising a biologically effective amount of a compound of formula (I), an N-oxide or a salt thereof, and at least one additional component selected from the group consisting of a surfactant, a solid diluent and a liquid diluent, said composition optionally further comprising a biologically effective amount of at least one additional biologically active compound or agent.

This invention also provides a composition for protecting an animal from an parasitic pest comprising a parasiticidally effective amount of a compound of formula (I) an N-oxide or a salt thereof, and at least one carrier. The present invention further provides the composition described above in a form for oral administration. This invention also provides a method for protecting an animal from a parasitic pest comprising administering to the animal a parasiticidally effective amount of a compound of formula (I), an N-oxide or a salt thereof.

DETAILS OF THE INVENTION

In the above recitations, the term "alkyl", used either alone or in compound words such as "alkylthio" or "haloalkyl" includes straight-chain or branched alkyl, such as, methyl, ethyl, n-propyl, i-propyl, or the different butyl, pentyl or hexyl isomers.

The radical (alk) denotes, for example, straight-chain or branched C_1-C_6-alkylene, for example methylene, 1,1- or 1,2-ethylene or straight-chain or branched propylene, butylene, pentylene or hexylene. (alk) is preferably straight-chain or branched C_1-C_4-alkylene, more preferably C_1-C_2-alkylene, most preferably methylene, or 1,2-ethylene and in particular methylene.

"Alkenyl" includes straight-chain or branched alkenes such as ethenyl, 1-propenyl, 2-propenyl, and the different butenyl, pentenyl and hexenyl isomers. "Alkenyl" also includes polyenes such as 1,2-propadienyl and 2,4-hexadienyl.

"Alkynyl" includes straight-chain or branched alkynes such as ethynyl, 1-propynyl, 2-propynyl and the different butynyl, pentynyl and hexynyl isomers. "Alkynyl" can also include moieties comprised of multiple triple bonds such as 2,5-hexadiynyl.

"Alkoxy" includes, for example, methoxy, ethoxy, n-propyloxy, isopropyloxy and the different butoxy, pentoxy and hexyloxy isomers. "Alkylthio" includes branched or straight-chain alkylthio moieties such as methylthio, ethylthio, and the different propylthio, butylthio, pentylthio and hexylthio isomers.

"Alkylsulfinyl" includes both enantiomers of an alkylsulfinyl group. Examples of "alkylsulfinyl" include $CH_3S(O)$-, $CH_3CH_2S(O)$-, $CH_3CH_2CH_2S(O)$-, $(CH_3)_2CHS(O)$- and the different butylsulfinyl, pentylsulfinyl and hexylsulfinyl isomers.

Examples of "alkylsulfonyl" include $CH_3S(O)_2$-, $CH_3CH_2S(O)_2$-, $CH_3CH_2CH_2S(O)_2$-, $(CH_3)_2CHS(O)_2$-, and the different butylsulfonyl, pentylsulfonyl and hexylsulfonyl isomers.

"N-alkylamino", "N,N-di-alkyamino", and the like, are defined analogously to the above examples.

"Cycloalkyl" includes, for example, cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. The term "alkylcycloalkyl" denotes alkyl substitution on a cycloalkyl moiety and includes, for example, ethylcyclopropyl, i-propylcyclobutyl, 3-methylcyclopentyl and 4-methy]cyclohexyl. The term "cycloalkylalkyl" denotes cycloalkyl substitution on an alkyl moiety. Examples of "cycloalkylalkyl" include cyclopropylmethyl, cyclopentylethyl, and other cycloalkyl moieties bonded to straight-chain or branched alkyl groups.

The term "halogen", either alone or in compound words such as "haloalkyl", includes fluorine, chlorine, bromine or iodine. Further, when used in compound words such as "haloalkyl", said alkyl may be partially or fully substituted with halogen atoms which may be the same or different. Examples of "haloalkyl" include F_3C-, $ClCH_2$-, CF_3CH_2- and CF_3CCl_2-. The terms "halocycloalkyl", "haloalkoxy", "haloalkylthio", and the like, are defined analogously to the term "haloalkyl". Examples of "haloalkoxy" include CF_3O-, CCl_3CH_2O-, $HCF_2CH_2CH_2O$- and CF_3CH_2O-. Examples of "haloalkylthio" include CCl_3S-, CF_3S-, CCl_3CH_2S- and $ClCH_2CH_2CH_2S$-. Examples of "haloalkylsulfinyl" include $CF_3S(O)$-, $CCl_3S(O)$-, $CF_3CH_2S(O)$- and $CF_3CF_2S(O)$-. Examples of "haloalkylsulfonyl" include $CF_3S(O)_2$-, $CCl_3S(O)_2$-, $CF_3CH_2S(O)_2$- and $CF_3CF_2S(O)_2$-.

"Alkylcarbonyl" denotes a straight-chain or branched alkyl moieties bonded to a C(=O) moiety. Examples of "alkylcarbonyl" include $CH_3C(=O)$-, $CH_3CH_2CH_2C(=O)$- and $(CH_3)_2CHC(=O)$-. Examples of "alkoxycarbonyl" include $CH_3OC(=O)$-, $CH_3CH_2OC(=O)$, $CH_3CH_2CH_2OC(=O)$-, $(CH_3)_2CHOC(=O)$- and the different butoxy- or pentoxycarbonyl isomers, for example tert.-butoxycarbonyl (Boc).

The total number of carbon atoms in a substituent group is indicated by the "C_i-C_j" prefix where i and j are integers. For example, C_1-C_4 alkylsulfonyl designates methylsulfonyl through butylsulfonyl; C_2-alkoxyalkyl designates CH_3OCH_2; C_3-alkoxyalkyl designates, for example, $CH_3CH(OCH_3)$, $CH_3OCH_2CH_2$ or $CH_3CH_2OCH_2$; and C_4-alkoxyalkyl designates the various isomers of an alkyl group substituted with an alkoxy group containing a total of four carbon atoms, examples including $CH_3CH_2CH_2OCH_2$ and $CH_3CH_2OCH_2CH_2$-.

When a compound is substituted with a substituent bearing a subscript that indicates the number of said substituents can exceed 1, said substituents (when they exceed 1) are independently selected from the group of defined substituents, e.g., $(R_2)_n$, n is 1 or 2. "Aromatic" indicates that each of the ring atoms is essentially in the same plane and has ap-orbital perpendicular to the ring plane, and in which $(4n + 2)$ π electrons, where n is a positive integer, are associated with the ring to comply with Hückel's rule.

The terms "heterocyclic ring" or "heterocycle" denote a ring in which at least one atom forming the ring backbone is not carbon, e.g., nitrogen, oxygen or sulfur. Typically a heterocyclic ring contains no more than 4 nitrogens, no more than 2 oxygens and no more than 2 sulfurs. Unless otherwise indicated, a heterocyclic ring can be a saturated, partially unsaturated, or fully unsaturated ring. When a fully unsaturated heterocyclic ring satisfies Hückel's rule, then said ring is also called a "heteroaromatic ring", "aromatic heterocyclic ring". Unless otherwise indicated, heterocyclic rings and ring systems can be attached through any available carbon or nitrogen by replacement of a hydrogen on said carbon or nitrogen.

R_1 is preferably C_1-C_4-haloalkyl or C_1-C_4-haloalkoxy, more preferably C_1-C_3-haloalkyl, even more preferably C_1-C_2-alkyl substituted with F, and in particular CF_3.

Each R_2 is independently of the other preferably halogen, C_1-C_6-haloalkyl, C_1-C_6 haloalkoxy or cyano, more preferably halogen, CF_3, OCF_3 or cyano, especially halogen, for example chlorine or fluorine, and in particular chlorine.

B and B' are each independently preferably a radical CH or CR_2, wherein R_2 is halogen, in particular each a radical CH.

B_1, B_2 and B_3 are each independently of the other preferably a group CR_2', wherein R_2' is H or R_2, and for R_2 the above-given meanings and preferences apply. One preferred embodiment relates to a compound of formula (I), wherein one of the radicals B_1, B_2 and B_3 is CH and the two other ones are each independently a radical CR_2, wherein R_2 is halogen, for example chlorine or fluorine, and in particular chlorine; within this embodiment it is particularly preferred, that B_2 is CH and B_1 and B_3 are each independently CCl or CF. Another preferred embodiment relates to a compound of formula (I), wherein all three radicals B_1, B_2 and B_3 are independently a radical CR_2, wherein R_2 is halogen, for example chlorine or fluorine, and in particular chlorine.

Each R_3 is independently of the other preferably H, halogen, hydroxy, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, N-mono- or N,N-di-C_1-C_6-alkylamino, cyano or nitro, more preferably H, halogen, hydroxy, C_1-C_2-alkyl, C_1-C_2-haloalkyl, cyclopropyl or C_1-C_2-alkoxy, even more preferably H, hydroxy, C_1-C_2-alkyl or C_1-C_2-alkoxy, most preferably H or C_1-C_2-alkyl, for example H or methyl, and especially methyl.

R_4 is preferably H, C_1-C_4-alkyl, C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-cycloalkyl, C_1-C_4-alkoxy-C_1-C_4-alkyl or C_1-C_4-alkylcarbonyl, more preferably H, C_1-C_2-alkyl, C_2-C_3-alkenyl, C_2-C_4-alkynyl, C_3-C_6-cycloalkyl, C_1-C_2-alkoxy-C_1-C_2-alkyl or C_1-C_2-alkylcarbonyl, and in particular H, C_1-C_2-alkyl, ethenyl, ethynyl, cyclopropyl, C_1-C_2-alkoxy-C_1-C_2-alkyl, acetyl or propionyl.

The variable m is, for example 0, 1 or 2, in particular 0.

The variable X is preferably S or O, for example S, and in particular O.

X_1 or X_2 are each independently of the other preferably a group CR_3, wherein for R_3 the above-given meanings and preferences apply. X_1 is most preferably the group CH. X_2 is most preferably the group $C(CH_3)$.

Preferably X is S or O, and X_1 and X_2 are each independently a radical CR_3, wherein for R_3 the above given meanings and preferences apply. More preferably, X is S or O, X_1 is CH, and X_2 is CR_3 , wherein for R_3 the above given meanings and preferences apply. In particular, X is O, X_1 is CH and X_2 is $C(CH_3)$.

W and W' are each independently of the other preferably O.

R_5 is preferably, H, C_1-C_6-alkyl, C_2-C_6-alkanoylcarbonyl or C_2-C_6-alkoxycarbonyl, more preferably, H, C_1-C_2-alkyl, C_2-C_4-alkanoylcarbonyl or C_2-C_4-alkoxycarbonyl, and in particular H.

R_7 and R_8 are each independently of the other preferably H; C_2-C_4-alkenyl; C_2-C_4-alkynyl; C_3-C_6-cycloalkyl; or C_1-C_6-alkyl which is unsubstituted or substituted by halogen, C_1-C_4-alkoxy, C_1-C_2-alkylthio, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_4alkylamino, pyridyl, pyrimidyl thiazolyl, or pyridyl, pyrimidyl or thiazolyl which is each mono- or disubstituted by halogen, cyano, C_1-C_2-alkyl or C_1-C_2-haloalkyl. R_7 and R_8 are each independently of the other especially preferably H; C_1-C_6-alkyl which is unsubstituted or substituted by halogen C_1-C_2-alkoxy, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_2-alkylamino, pyridyl, pyrimidyl or thiazolyl; C_2-C_4-alkenyl; C_2-C_4-alkynyl; or C_3-C_6-cycloalkyl.

R_7 is most preferably H or C_1-C_4-alkyl, in particular H, methyl or ethyl.
R_8 is most preferably C_1-C_4-alkyl which is unsubstituted or substituted by halogen, cyano or pyridyl, or is C_2-C_4-alkynyl or C_3-C_4-cycloalkyl. Particularly preferred meanings of R_8 are cyclopropyl, C_2-C_4-alkynyl or C_1-C_4-alkyl which is unsubstituted or substituted by halogen or cyano, especially cyclopropyl, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-cyanoalkyl or propynyl .

According to one embodiment of the invention, Q and Q' each may be a C_6-C_{10}-carbocyclic ring system, for example phenyl, naphthyl, tetrahydronaphthyl, indanyl, indenyl, hydrindanyl or octahydro-pentalen, in particular phenyl, which is each unsubstituted or substituted by one or more same or different substituents selected from the group of substituents as mentioned above. Q and Q' as carbocyclic ring radical are each preferably phenyl which is substituted by 1 to 4, preferably 1 to 3 and in particular 1 or 2 same or different substituents selected from the group consisting of halogen, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-haloalkylsulfinyl, C_1-C_4-alkylsulfonyl, C_1-C_4-haloalkylsulfonyl, cyano, nitro, C_1-C_4-alkoxycarbonyl, sulfonamido, C_2-C_3-alkanoyl and unsubstituted or halogen-, C_1-C_4-alkyl-, C_1-C_4-haloalkyl-, C_1-C_4-alkoxy-, C_1-C_4-haloalkoxy-, cyano- or nitro-substituted phenyl, benzyl, benzoyl and phenoxy. Q and Q' as carbocyclic ring radical are each more preferably phenyl, which is substituted by 1 to 3, in particular 1 or 2, same or different substituents selected from the group consisting of halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, C_1-C_2-haloalkylthio, cyano, nitro, and unsubstituted or halogen-, C_1-C_2-alkyl-, C_1-C_2-haloalkyl-, C_1-C_2-alkoxy-, C_1-C_2-haloalkoxy-, cyano- or nitro-substituted phenyl and phenoxy.

According to another embodiment of the invention, Q and Q' are each a 4-, 5- or 6-membered heterocyclic ring, which may be saturated or preferably unsaturated, and which is unsubstituted or substituted with one or more substituents selected from the group of substituents as defined before.

Preferred substituents of the heterocyclic ring Q and Q' are, for example, C_1-C_4-alkyl, C_1-C_4-haloalkyl, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-alkylsulfinyl, C_1-C_4-alkylsulfonyl, cyano, nitro, C_1-C_4-alkoxycarbonyl, sulfonamido, N-mono- or N,N-di-C_1-C_4-alkylamino, C_2-C_3-alkanoyl and unsubstituted Even more preferred substituents of the heterocyclic ring Q and Q' are each selected from the group consisting of halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, and C_1-C_4-alkoxycarbonyl, in particular C_1-C_2-alkyl, C_1-C_2-haloalkyl and C_1-C_4-alkoxycarbonyl.

A suitable heterocyclic ring Q and Q' is, for example, a 5- or 6-membered heteroaromatic ring having from 1 to 4, preferably from 1 to 3 same or different heteroatoms selected from the group consisting of N, O and S, which is further unsubstituted or substituted by one or more substituents as defined before for Q and Q' including the preferences given therefore. The heterocyclic radical Q and Q' is each independently preferably substituted by 0 to 3, in particular 0, 1 or 2 substituents from the group as defined before for Q and Q'.

Examples of a 5- or 6-membered unsaturated aromatic heterocyclic ring radical Q and Q' are thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl, which are each unsubstituted or substituted as mentioned before including the preferences.

Preferred unsaturated aromatic heterocyclic ring radicals Q and Q' are 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1- or 4-pyrazolyl, 2-, 4- or 5-thiazolyl, 1,2,4-triazol-3- or -4-yl, 1,2,3-triazin-1- or 2-yl, 2- 3- or 4-pyridyl or 4- or 5-pyrimidinyl, each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, and C_1-C_4-alkoxycarbonyl.

Particularly preferred aromatic heterocyclic ring radicals Q and Q' are 2-thiazoyl, 2- 3- or 4-pyridyl or 4- or 5-pyrimidinyl, each unsubstituted or substituted by C_1-C_2-alkyl, C_1-C_2-haloalkyl and C_1-C_4-alkoxycarbonyl.

A further group of suitable heterocyclic radicals Q and Q' comprises, for example, a 4-, 5- or 6-membered heteroaliphatic having from 1 to 4, preferably from 1 to 3 same or different heteroatoms selected from the group consisting of N, O and S, which is further unsubstituted or substituted by one or more substituents as defined before for Q and Q' including the preferences given therefore.

Examples of heteroaliphatic rings Q and Q' include thietanyl, tetrahydrofuranyl, tetrahydrothiophenyl, pyrrolidinyl, 1,3-dioxolanyl, 1,2- or 1,3-oxazolidinyl, tetrahydropyranyl, piperidinyl, tetrahydrothiopyranyl, morpholinyl, 1,3- or 1,4-dioxanyl, which may be substituted as mentioned before for Q and Q' including the preferences.

A preferred heteroaliphatic ring radical Q and Q' is thietanyl, or tetrahydrofuranyl, which is unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

Particularly preferred heteroaliphatic ring radicals Q and Q' are thietan-3-yl, tetrahydrofuran-2-yl and tetrahydrofuran-3-yl.

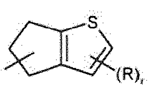
According to a preferred embodiment of the invention, Q and Q' are each 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1- or 4-pyrazolyl, 2-, 4- or 5-thiazolyl, 1,2,4-triazol-3- or -4-yl, 1,2,3-triazin-1- or 2-yl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, thietanyl, or tetrahydrofuranyl, which is each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

A particularly preferred radical Q and Q' is 2-thiazoyl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, thietan-3-yl, tetrahydrofuran-2-yl or tetrahydrofuran-3-yl, which is each unsubstituted or substituted by C_1-C_2-alkyl, C_1-C_2-haloalkyl and C_1-C_4-alkoxycarbonyl.

A suitable fused hetero-bicyclic ring system comprises, for example a 5- or 6-membered heterocyclic ring having from 1 to 4, preferably from 1 to 3 same or different heteroatoms selected from the group consisting of N, O and S, to which is attached an annulated ring; in addition said fused bicyclic system is further unsubstituted or substituted by one or more substituents as defined before for Q including the preferences given. Those rings can be saturated ring or unsaturated rings.

Examples of fused hetero-bicyclic ring systems Q and Q' are illustrated in Exhibit 3 below.

Exhibit 3



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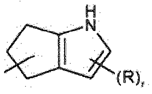

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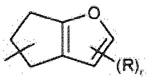

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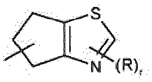

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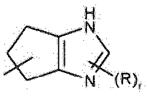

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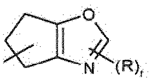

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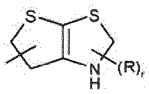

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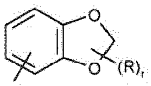

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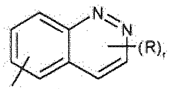

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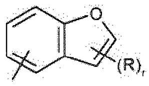

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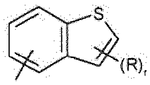

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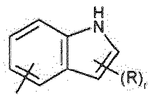

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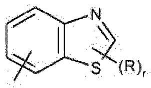

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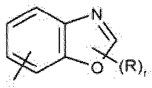

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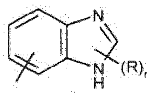

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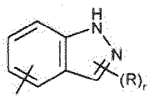

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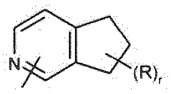

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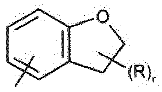

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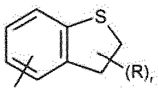

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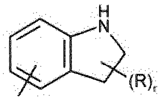

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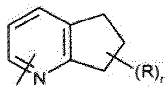

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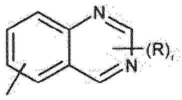

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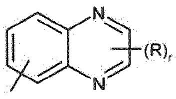

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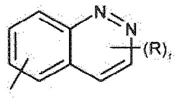

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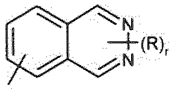

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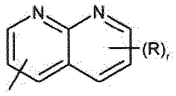

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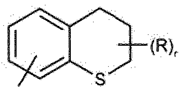

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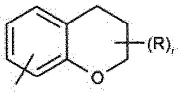

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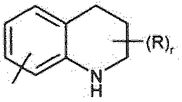

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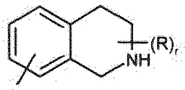

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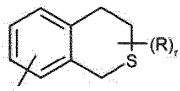

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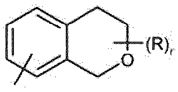

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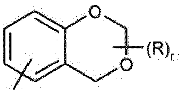

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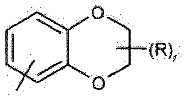

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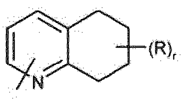

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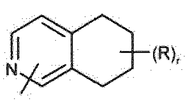

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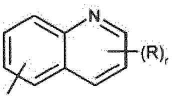

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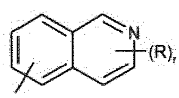


Q-133

wherein R is any substituent as defined before for Q and Q' including the preferences given, and r is an integer from 0 to 4, limited by the number of available positions on each Q group. In addition, when the attachment point between $(R)_r$ and the Q group is illustrated as floating, $(R)_r$ can be attached to any available carbon atom or nitrogen atom of the Q group.

Q" independently has the meaning of Q' as heterocyclic ring or C_6-C_{10}-carbocyclic ring system, with the exception that Q" is not substituted by another radical Q", including the above-given preferences.

R_6 is preferably C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_4-C_7-alkylcycloalkyl or C_4-C_7-cycloalkylalkyl, which is each unsubstituted or are substituted in the alkyl, alkenyl or alkynyl moiety by halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, cyano, amino, N-mono- or N,N-di-C_1-C_4-alkylamino, COOH, C_1-C_4-alkoxycarbonyl, N-C_1-C_4-alkylcarbonylamino, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido, a group $-C(O)NR_7R_8$ or a radical Q'; or is a radical Q;
or R_6 together with R_5 is a group $=C-NR_7R_8$ or $=C-NR_7(OR_8)$; wherein R_7 is H or C_1-C_4-alkyl; R_8 is H; C_2-C_4-alkenyl; C_2-C_4-alkynyl; C_3-C_6-cycloalkyl; or C_1-C_6-alkyl which is unsubstituted or substituted by halogen, C_1-C_4-alkoxy, C_1-C_2-alkylthio, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_4alkylamino, pyridyl, pyrimidyl thiazolyl, or pyridyl, pyrimidyl or thiazolyl which is each mono- or disubstituted by halogen, cyano, C_1-C_2-alkyl or C_1-C_2-haloalkyl; and Q and Q' are each thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl, thietanyl, or tetrahydrofuranyl, which are each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

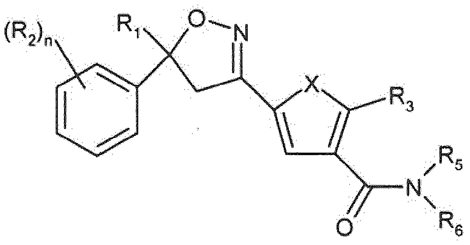
R_6 is even more preferably C_1-C_4-alkyl, which is unsubstituted or are substituted in the alkyl moiety by halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, cyano, COOH, C_1-C_4-alkoxycarbonyl, a group $-C(O)NR_7R_8$ or a radical Q'; or is a radical Q; or R_6 together with R_5 is a group $=C-NR_7R_8$ or $=C-NR_7(OR_8)$, wherein R_7 is H or C_1-C_2-alkyl; R_8 is C_2-C_4-alkenyl; C_2-C_4-alkynyl; C_3-C_6-cycloalkyl; or C_1-C_4-alkyl which is unsubstituted or substituted by halogen, cyano or pyridyl; and Q and Q' are each 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1- or 4-pyrazolyl, 2-, 4- or 5-thiazolyl, 1,2,4-triazol-3- or -4-yl, 1,2,3-triazin-1- or 2-yl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, thietanyl, or tetrahydrofuranyl, which is each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

R_6 is most preferably C_1-C_4-alkyl, which is unsubstituted or are substituted in the alkyl moiety by halogen, C_1-C_2-alkoxy, C_1-C_2-alkylthio, cyano, COOH, C_1-C_2-alkoxycarbonyl, a group –C(O)NR_7R_8 or a radical Q'; or is a radical Q; or R_6 together with R_5 is a group =C–N(C_1-C_2-alkyl)$_2$ or =C–NH(OC_1-C_2alkyl), wherein R_7 is H, R_8 is C_2-C_4-alkynyl, C_3-C_4-cycloalkyl or C_1-C_4-alkyl which is unsubstituted or substituted by halogen or cyano, and Q and Q' are each 2-thiazolyl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, 3-thietanyl, or 2- or 3-tetrahydrofuranyl, which is each unsubstituted or substituted by C_1-C_2-alkyl or C_1-C_2-haloalkyl.

A preferred embodiment of the present invention relates to a compound of formula (I) above, wherein B and B' are each CH, B_1 and B_3 are each independently CCl or CF, B_2 is CH, CCl or CF, R_1 is CF_3, X is O or S, in particular O, X_1 is CH, X_2 is C(CH_3), and for R_5 and R_6 each the above-given meanings and preferences apply.

A further preferred embodiment of the present invention relates to a compound of formula (I) above, wherein B and B' are each CH, B_1 and B_3 are each independently CCl or CF, B_2 is CH, CCl or CF, R_1 is CF_3, X is O, X_1 is CH, X_2 is C(CH_3), R_5 is H, and R_6 is C_1-C_4-alkyl, which is unsubstituted or are substituted in the alkyl moiety by halogen, C_1-C_2-alkoxy, C_1-C_2-alkylthio, cyano, COOH, C_1-C_2-alkoxycarbonyl, a group –C(O)NR_7R_8 or a radical Q'; or is a radical Q; or R_6 together with R_5 is a group =C–N(C_1-C_2-alkyl)$_2$ or =C–NH(OC_1-C_2alkyl), wherein R_7 is H, R_8 is C_2-C_4-alkynyl, C_3-C_4-cycloalkyl or C_1-C_4-alkyl which is unsubstituted or substituted by halogen or cyano, and Q and Q' are each 2-thiazolyl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, 3-thietanyl, or 2- or 3-tetrahydrofuranyl, which is each unsubstituted or substituted by C_1-C_2-alkyl or C_1-C_2-haloalkyl.

According to a another preferred embodiment of the invention there is provided a compound of formula



(Ia)

including all geometric and stereoisomers, N-oxides, and salts thereof, wherein for R_1, R_2, R_3, R_5, R_6 and X each the above-given meanings and preferences apply and n is an integer from 0 to 4, preferably from 1 to 3, and in particular of 2 or 3.

In particular, n is an integer from 1 to 3; R_1 is C_1-C_3-haloalkyl; each R_2 is independently selected from the group consisting of halogen, C_1-C_6-haloalkyl, C_1-C_6-haloalkoxy and cyano; X is S or O; R_3 is H or C_1-C_2-alkyl; R_5 is H or C_1-C_2-alkyl; R_6 is C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_4-C_7-alkylcycloalkyl or C_4-C_7-cycloalkylalkyl, which is each unsubstituted or are substituted in the alkyl, alkenyl or alkynyl moiety by halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, cyano, amino, N-mono- or N,N-di-C_1-C_4-alkylamino, COOH, C_1-C_4-alkoxycarbonyl, N-C_1-C_4-alkylcarbonylamino, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido, a group $-C(O)NR_7R_8$ or a radical Q'; or R_6 is a radical Q; or R_6 together with R_5 is a group $=C-NR_7R_8$ or $=C-NR_7(OR_8)$; R_7 is H or C_1-C_4-alkyl; R_8 is H; C_2-C_4-alkenyl; C_2-C_4-alkynyl; C_3-C_6-cycloalkyl; or C_1-C_6-alkyl which is unsubstituted or substituted by halogen, C_1-C_4-alkoxy, C_1-C_2-alkylthio, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_4alkylamino, pyridyl, pyrimidyl thiazolyl, or pyridyl, pyrimidyl or thiazolyl which is each mono- or disubstituted by halogen, cyano, C_1-C_2-alkyl or C_1-C_2-haloalkyl; and Q and Q' are each thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl, thietanyl, or tetrahydrofuranyl, which are each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

A particularly preferred embodiment of the invention relates to a compound of formula (Ia) above, wherein n is an integer of 2 or 3; R_1 is CF_3; each R_2 is independently halogen; X is S or O; R_3 is H or C_1-C_2-alkyl; R_5 is H; and R_6 is C_1-C_4-alkyl, which is unsubstituted or substituted in the alkyl moiety by halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, cyano, COOH, C_1-C_4-alkoxycarbonyl, a group $-C(O)NR_7R_8$ or a radical Q'; or R_6 is a radical Q; or R_6 together with R_5 is a group $=C-NR_7R_8$ or $=C-NR_7(OR_8)$;

R_7 is H or C_1-C_2-alkyl; R_8 is C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-cycloalkyl, or C_1-C_4-alkyl which is unsubstituted or substituted by halogen, cyano or pyridyl; and Q and Q' are each 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1- or 4-pyrazolyl, 2-, 4- or 5-thiazolyl, 1,2,4-triazol-3- or -4-yl, 1,2,3-triazin-1- or 2-yl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, thietanyl, or tetrahydrofuranyl, which is each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

A further particularly preferred embodiment of the invention relates to a compound of formula (Ia) above, wherein n is an integer of 2 or 3; R_1 is CF_3; each R_2 is independently halogen; X is S or O; R_3 is H or C_1-C_2-alkyl; R_5 is H; R_6 is C_1-C_4-alkyl, which is unsubstituted or are substituted in the alkyl moiety by halogen, C_1-C_2-alkoxy, C_1-C_2-alkylthio, cyano, COOH, C_1-C_2-alkoxycarbonyl, a group $-C(O)NR_7R_8$ or a radical Q'; or R_6 is a radical Q; or R_6 together with R_5 is a group $=C-N(C_1\text{-}C_2\text{-alkyl})_2$ or $=C-NH(OC_1\text{-}C_2\text{alkyl})$; R_7 is H; R_8 is C_2-C_4-alkynyl, C_3-C_4-cycloalkyl or C_1-C_4-alkyl which is unsubstituted or substituted by halogen or cyano; and Q and Q' are each 2-thiazolyl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, 3-thietanyl, or 2- or 3-tetrahydrofuranyl, which is each unsubstituted or substituted by C_1-C_2-alkyl or C_1-C_2-haloalkyl.

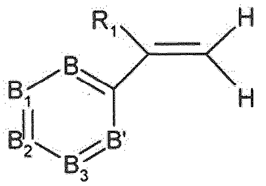
Still a further preferred embodiment of the invention relates to a compound of formula (Ia) above, wherein n is an integer of 2 or 3; R_1 is CF_3; each R_2 is independently halogen; X is O; R_3 is methyl; and for R_5 and R_6 each the above-given meanings and preferences apply. An especially preferred embodiment of the invention relates to a compound of formula (Ia) above, wherein n is an integer of 2 or 3; R_1 is CF_3; each R_2 is independently halogen; X is O; R_3 is methyl; R_5 is H; R_6 is C_1-C_4-alkyl, which is unsubstituted or are substituted in the alkyl moiety by halogen, C_1-C_2-alkoxy, C_1-C_2-alkylthio, cyano, COOH, C_1-C_2-alkoxycarbonyl, a group $-C(O)NR_7R_8$ or a radical Q'; or R_6 is a radical Q; or R_6 together with R_5 is a group $=C-N(C_1\text{-}C_2\text{-alkyl})_2$ or $=C-NH(OC_1\text{-}C_2\text{alkyl})$; R_7 is H; R_8 is C_2-C_4-alkynyl, C_3-C_4-cycloalkyl or C_1-C_4-alkyl which is unsubstituted or substituted by halogen or cyano; and Q and Q' are each 2-thiazolyl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, 3-thietanyl, or 2- or 3-tetrahydrofuranyl, which is each unsubstituted or substituted by C_1-C_2-alkyl or C_1-C_2-haloalkyl.

Compounds of this invention can exist as one or more stereoisomers. The various stereoisomers include enantiomers, diastereomers, atropisomers and geometric isomers. One skilled in the art will appreciate that one stereoisomer may be more active and/or may exhibit beneficial effects when enriched relative to the other stereoisomer(s) or when separated from the other stereoisomer(s). Additionally, the skilled artisan knows how to separate, enrich, and/or to selectively prepare said stereoisomers. The compounds of the invention may be present as a mixture of stereoisomers, individual stereoisomers, or as an optically active form.

One skilled in the art will appreciate that not all nitrogen containing heterocyclic rings can form N-oxides since the nitrogen requires an available lone pair for oxidation to the oxide; one skilled in the art will recognize those nitrogen containing heterocyclic rings which can form N~oxides. One skilled in the art will also recognize that tertiary amines can form N-oxides. Synthetic methods for the preparation of N-oxides of heterocyclic rings and tertiary amines are very well known by one skilled in the art including the oxidation of heterocyclic rings and tertiary amines with peroxy acids such as peracetic and m-chloroperbenzoic acid (MCPBA), hydrogen peroxide, alkyl hydroperoxides such as t-butyl hydroperoxide, sodium perborate, and dioxiranes such as dimethyl dioxirane These methods for the preparation of N-oxides have been extensively described and reviewed m the literature.

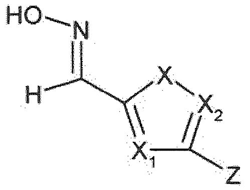
One skilled in the art recognizes that because of the environment and under physiological conditions salts of chemical compounds are in equilibrium with their corresponding nonsalt forms, salts share the biological utility of the nonsalt forms. Thus a wide variety of salts of the compounds of formula (I) are useful for control of invertebrate pests (i.e. are veterinarily or agriculturally suitable). The salts of the compounds of formula (I) include acid-addition salts with inorganic or organic acids such as hydrobromic, hydrochloric, nitric, phosphoric, sulfuric, acetic, butyric, fumaric, lactic, maleic, malonic, oxalic, propionic, salicylic, tartaric, 4-toluenesulfonic "or valeric acids. When a compound of formula (I) contains an acidic moiety such as a carboxylic acid or phenol, salts also include those formed with organic or inorganic bases such as pyridine, triethylamine or ammonia, or amides, hydrides, hydroxides or carbonates of sodium, potassium, lithium, calcium, magnesium or barium. Accordingly, the present invention comprises compounds selected from formula (I), N-oxides and veterinary acceptable and agriculturally suitable salts thereof.

The compounds of the present invention made be prepared, for example, in analogy to the processes as outined in WO 2007/75459 on pages 29-31. Accordingly, the compounds of formula (I) or (Ia) may be prepared, for example, by cycloaddition of a compound of formula



(II)

with a nitrile oxide derived from an oxime of formula

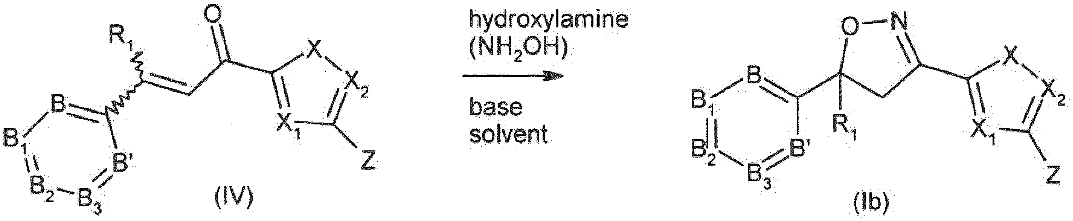


(III),

wherein B, B', B_1-B_3, R_1, X, X_1 and X_2 each have the above-given meaning, Z is Br, I, COOH, $COOC_1$-C_6-alkyl or –C(W)- NR_5R_6, wherein W, R_5 and R_6 each have the above-given meaning, and, if Z is Br, I, COOH or $COOC_1$-C_6-alkyl, converting said radical to a radical –C(W)- NR_5R_6.

The reaction typically proceeds through the intermediacy of an in situ generated hydroxamyl chloride. In a typical procedure a chlorinating reagent such as sodium hypochlorite, N-chlorosuccinimide, or chloramine-T is combined with the oxime in the presence of the styrene. Depending on the conditions amine bases such as pyridine or triethylamine may be necessary. The reaction can be run in a wide variety of solvents including tetrahydrofuran, diethyl ether, methylene chloride, dioxane, and toluene with optimum temperatures ranging from room temperature to the reflux temperature of the solvent.

The compounds of formula (I) or (Ia) may also be prepared by a process in analogy of WO2009/025983, wherein a compound of formula (VI) is contacted with hydroxylamine and a base to form an isoxazole of formula (I)



wherein B, B', B_1-B_3, R_1, X, X_1 and X_2 each have the above-given meaning, Z is Br, I, COOH, $COOC_1$-C_6-alkyl or –C(W)- NR_5R_6, wherein W, R_5 and R_6 each have the above-given meaning, and, if Z is Br, I, COOH or $COOC_1$-C_6-alkyl, converting said radical to a radical –C(W)- NR_5R_6.

The reaction may be performed as described in WO2009/025983 on pages 29-31. In addition, synthetic routes to prepare the intermediate of formula (IV) are likewise disclosed in WO2009/025983 on pages 31-34.

Another process for the preparation of a compound of formula (Ib) above, wherein Z is COOH or $COOC_1$-C_6-alkyl, includes a functional group transformations from a corresponding compound of the formula (Ib), wherein Z is Br or I, which is known in the art; a suitable method comprises halogen-metal exchange (the metal being, for example, Li or Mg) followed by a quench with CO_2 or $(CN)CO_2(C_1$-C_6-alkyl) respectively. The reaction is typically carried out at low temperature, for example at a temperature of from -80°C to 0°C in a solvent such as diethylether or THF.

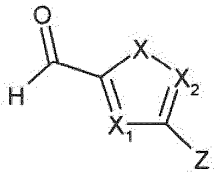
Another process for the preparation of a compound of formula (Ib), wherein Z is a group COOH, is the hydrolysis or saponification of a corresponding compound of the formula (Ib), wherein Z is $COOC_1$-C_6-alkyl or CN; the latter compound is obtainable from a corresponding compound of the formula (Ib), where Z is Br or I, for example, with zinc cyanide or copper cyanide with or without palladium catalyst.

Another process for the preparation of a compound of the formula (I) or (Ia), wherein Z is a group –C(W)-NR_5R_6, includes well known functional group transformations from a corresponding compound of the formula (Ib), wherein Z is Br or I, such as aminocarbonylation with an amino compound HNR_5R_6 and CO. The reaction is typically carried out in the presence of a palladium catalyst under CO atmosphere. Many catalysts are useful for this type of transformation, a typical catalyst being tetrakis(triphenylphosphine)palladiurn(0). Solvents such as 1,2.dimethoxyethane, N,N-dimethylacetamide or toluene are suitable. The method can be conducted over a wide range of temperatures, for example from about 25°C to about 150°C, especially from 60 to 110°C.

Another process for the preparation of a compound of the formula (I) or (Ia), wherein Z is a group –C(W)-NR_5R_6, includes well known functional group transformations from a corresponding compound of the formula (Ib), wherein Z is COOH like amide coupling with well known reagents (for example EDCI, HOBT, PyBOP, PyBrOP) with an amino compound HNR_5R_6 or activation of COOH to an acyl halide (Cl for example with oxalyl chloride or thionyl chloride) and subsequent coupling with an amino compound HNR_5R_6.

The compounds of formula (II) are known, for example, from WO 2006/49459 or may be prepared in analogy to the methods disclosed therein.

The compounds of formula (III) may be prepared, for example, by first of all protecting the aldehyde group of a compound of formula



IIIa,

wherein X, X_1 and X_2 are each as described above and Y is a leaving group, such as halogen, tosylate, triflate or nitro, for example, by converting it to a cyclic acetal, then introducing a suitable radical Z replacing Y by methods known from textbooks of organic chemistry, afterwards deprotecting the aldehyde and converting it to a hydroxyimino compound of formula III in a manner as known from WO 2007/75459.

The compounds of the formula (I) according to the invention are notable for their broad activity spectrum and are valuable active ingredients for use in pest control. They are particularly suitable in the control of ectoparasites and to a certain extent also for controlling endoparasites on and in animals and in the hygiene field, whilst being well tolerated by warm-blooded animals.

Animals in the context of the invention are understood to include warm-blooded animals including farm animals, such as cattle, horses, pigs, sheep and goats, poultry such as chickens, turkeys, guinea fowls and geese, fur-bearing animals such as mink, foxes, chinchillas, rabbits and the like, as well as companion animals such as ferrets, guinea pigs, rats, hamster, cats and dogs, and also humans.

In the context of the present invention, ectoparasites are understood to be in particular insects, acari (mites and ticks), and crustaceans (sea lice). These include insects of the following orders: Lepidoptera, Coleoptera, Homoptera, Hemiptera, Heteroptera, Diptera, Dictyoptera, Thysanoptera, Orthoptera, Anoplura, Siphonaptera, Mallophaga, Thysanura, Isoptera, Psocoptera and Hymenoptera. However, the ectoparasites which may be mentioned in particular are those which trouble humans or animals and carry pathogens, for example flies such as Musca domestica, Musca vetustissima, Musca autumnalis, Fannia canicularis, Sarcophaga carnaria, Lucilia cuprina, Lucilia sericata, Hypoderma bovis, Hypoderma lineatum, Chrysomyia chloropyga, Dermatobia hominis, Cochliomyia hominivorax, Gasterophilus intestinalis, Oestrus ovis, biting flies such as Haematobia irritans irritans, Haematobia irritans exigua, Stomoxys calcitrans, horse-flies (Tabanids) with the subfamilies of Tabanidae such as Haematopota spp. (e.g. Haematopota pluvialis) and Tabanus spp, (e.g.Tabanus nigrovittatus) and Chrysopsinae such as Chrysops spp. (e.g. Chrysops caecutiens); Hippoboscids such as Melophagus ovinus (sheep ked); tsetse flies, such as Glossinia spp,; other biting insects like midges, such as Ceratopogonidae (biting midges), Simuliidae (Blackflies), Psychodidae (Sandflies); but also blood-sucking insects, for example mosquitoes, such as Anopheles spp, Aedes spp and Culex spp, fleas, such as Ctenocephalides felis and Ctenocephalides canis (cat and dog fleas), Xenopsylla cheopis, Pulex irritans, Ceratophyllus gallinae, Dermatophilus penetrans, blood-sucking lice (Anoplura) such as Linognathus spp, Haematopinus spp, Solenopotes spp, Pediculus humanis; but also chewing lice (Mallophaga) such as Bovicola (Damalinia) ovis, Bovicola (Damalinia) bovis and other Bovicola spp. . Ectoparasites also include members of the order Acarina, such as mites (e.g. Chorioptes bovis, Cheyletiella spp., Dermanyssus gallinae, Ortnithonyssus spp., Demodex canis, Sarcoptes scabiei, Psoroptes ovis and Psorergates spp. and ticks. Known representatives of ticks are, for example, Boophilus, Amblyomma, Anocentor, Dermacentor, Haemaphysalis, Hyalomma, Ixodes, Rhipicentor, Margaropus, Rhipicephalus, Argas, Otobius and Ornithodoros and the like, which preferably infest warm-blooded animals including farm animals, such as cattle, horses, pigs, sheep and goats, poultry such as chickens, turkeys, guineafowls and geese, fur-bearing animals such as mink, foxes, chinchillas, rabbits and the like, as well as companion animals such as ferrets, guinea pigs, rats, hamster, cats and dogs, but also humans.

The compounds of the formula (I) according to the invention are also active against all or individual development stages of animal pests showing normal sensitivity, as well as those showing resistance to widely used parasiticides. This is especially true for resistant insects and members of the order Acarina. The insecticidal, ovicidal and/or acaricidal effect of the active substances of the invention can manifest itself directly, i.e. killing the pests either immediately or after some time has elapsed, for example when moulting occurs, or by destroying their eggs, or indirectly, e.g. reducing the number of eggs laid and/or the hatching rate, good efficacy corresponding to a pesticidal rate (mortality) of at least 50 to 60%. Compounds of the formula (I) can also be used against hygiene pests, especially of the order Diptera of the families Muscidae, Sarcophagidae, Anophilidae and Culicidae; the orders Orthoptera, Dictyoptera (e.g. the family Blattidae (cockroaches), such as Blatella germanica, Blatta orientalis, Periplaneta americana) and Hymenoptera (e.g. the families Formicidae (ants) and Vespidae (wasps).

Surprisingly, the compounds of formula (I) are also effective against ectoparasites of fishes, especially the sub-class of Copepoda (e.g. order of Siphonostomatoida (sea lice), whilst being well tolerated by fish.

The compounds of formula (I) can also be used against hygiene pests, especially of the order *Diptera* of the families *Sarcophagidae, Anophilidae* and *Culicidae*; the orders *Orthoptera, Dictyoptera* (e.g. the family *Blattidae*) and *Hymenoptera* (e.g. the family *Formicidae*).

Compounds of the formula (I) also have sustainable efficacy on parasitic mites and insects of plants. In the case of spider mites of the order *Acarina*, they are effective against eggs, nymphs and adults of *Tetranychidae* (*Tetranychus spp.* and *Panonychus spp.*).

They have high activity against sucking insects of the order *Homoptera*, especially against pests of the families *Aphididae, Delphacidae, Cicadellidae, Psyllidae, Loccidae, Diaspididae* and *Eriophydidae* (e.g. rust mite on citrus fruits); the orders *Hemiptera, Heteroptera* and *Thysanoptera*, and on the plant-eating insects of the orders *Lepidoptera, Coleoptera, Diptera* and *Orthoptera*

They are similarly suitable as a soil insecticide against pests in the soil.

The compounds of formula (I) are therefore effective against all stages of development of sucking insects and eating insects on crops such as cereals, cotton, rice, maize, soya, potatoes, vegetables, fruit, tobacco, hops, citrus, avocados and other crops.

The compounds of formula I are also effective against plant nematodes of the species *Meloidogyne, Heterodera, Pratylenchus, Ditylenchus, Radopholus, Rizoglyphus* etc.

Certain compounds of the formula (I) seem to be also effective against certain species of helminths.

Helminths are commercially important because they cause serious diseases in mammals and poultry, e.g. in sheep, pigs, goats, cattle, horses, donkeys, camels, dogs, cats, rabbits, guinea-pigs, hamsters, chicken, turkeys, guinea fowls and other farmed birds, as well as exotic birds. Typical nematodes are: Haemonchus, Trichostrongylus, Ostertagia, Nematodirus, Cooperia, Ascaris, Bunostonum, Oesophagostonum, Charbertia, Trichuris, Strongylus, Trichonema, Dictyocaulus, Capillaria, Heterakis, Toxocara, Ascaridia, Oxyuris, Ancylostoma, Uncinaria, Toxascaris, Parascaris and Dirofilaria. The trematodes include, in particular, the family of Fasciolideae, especially Fasciola hepatica.

The good pesticidal activity of the compounds of formula (I) according to the invention corresponds to a mortality rate of at least 50-60% of the pests mentioned, more preferably to a mortality rate over 90%, most preferably to 95-100%. The compounds of formula (I) are preferably employed internally and externally in unmodified form or preferably together with the adjuvants conventionally used in the art of formulation and may therefore be processed in a known manner to give, for example, liquid formulations (e.g. spot-on, pour-on, spray-on, emulsions, suspensions, solutions, emulsifiable concentrates, solution concentrates), semi-solid formulations (e.g. creams, ointments, pastes, gels, liposomal preparations) and solid preparations (e.g. food additives tablets including e. g. capsules, powders including soluble powders, granules, or embeddings of the active ingredient in polymeric substances, like implants and microparticles). As with the compositions, the methods of application are selected in accordance with the intended objectives and the prevailing circumstances.

The formulation, i.e. preparations containing the active ingredient of formula (I), or combinations of these active ingredients with other active ingredients, and optionally a solid, semi-solid or liquid adjuvant, are produced in a manner known per se, for example by intimately mixing, kneading or dispersing the active ingredients with compositions of excipients, whereby the physiological compatibility of the formulation excipients must be taken into consideration.

The solvents in question may be: alcohols (aliphatic and aromatic), such as benzylalcohol, ethanol, propanol, isopropanol or butanol, fatty alcohols, such as oleyl alcohol and glycols and their ethers and esters, such as glycerin, propylene glycol, dipropylene glycol ether, ethylene glycol, ethylene glycol monomethyl or -ethyl ether and butyl dioxytol, carbonates, such as propylene carbonate, ketones, such as cyclohexanone, isophorone or diacetanol alcohol and polyethylene glycols, such as PEG 300. In addition, the compositions may comprise strong polar solvents, such as N-methyl-2-pyrrolidone, dimethyl sulfoxide or dimethylformamide, or water, fatty acid esters, such as ethyl oleate or isopropylpalmitate, vegetable oils, such as rape, castor, coconut, or soybean oil, synthetic mono-, di-, triglycerides like e.g. glyceryl monostearate and medium chain triglycerides and also, if appropriate, silicone oils. The mentioned ingredients may also serve as carrier for particulate application froms.

As ointment base resp. structure building ingredients the following excipients may be used: Petroleum based substances, such as Vaseline or paraffines, bases made from wool fat, like e.g. lanolin or lanolin alcohols, polyethylene glycols like e.g. macrogols and lipid bases like e.g. phospholipids or triglycerids, such as hydrogenated vegetable oils.

The use of emulsifiers, wetting agents and spreading agents may also be required, in general, lecithins like soy lecithin, salts of fatty acids with alkaline earth and alkali metals, alkyl sulfates like sodium cetylstearyl sulphate, cholates, fatty alcohols like cetyl alcohol, sterols like cholestesterol, polyoxyethylene sorbitan fatty acid esters like polysorbate 20, sorbitan fatty acid esters like sorbitan mono laureate, fatty acid esters and fatty alcohol ethers of polyoxyethylene like poloxyl oleyl ether, polyoxypropylene polyoxyethylene block copolymers as e.g. Pluronic™ , saccharose esters like saccharose distearate, polyglyceryl fatty acid esters like polyglycerol oleate and fatty acid esters like e.g. ethyl oleate or isopropylmyristate.

The formulations may also include gelifying and stiffening agents, like e.g. polyacrylic acid derivatives, cellulose ethers, polyvinyl alcohols, polyvinylpyrrolidons and fine disperse silicium dioxide.

As polymeric agents with controlled release properties, may be applied derivatives made by e.g. polylactic acid, polylactic coglycolic acid, poly orthoester, polyethylene carbonate, poly anhydrids and starch and PVC based matrices.

The addition of penetration enhancers like ketones, sulfoxides, amides, fatty acid esters and fatty alcohols may be necessary.

Also preservatives like sorbic acid, benzyl alcohol and parabenes, and antioxidants as e.g. alpha tocopherol may be added.

The active ingredient or combinations of the active ingredient may also applied in capsules, like hard gelatine capsules or soft capsules.

The binders for tablets and boli may be chemically modified polymeric natural substances that are soluble in water or in alcohol, such as starch, cellulose or protein derivatives (e.g. methyl cellulose, carboxymethyl cellulose, ethylhydroxyethyl cellulose, proteins such as zein, gelatin and the like), as well as synthetic polymers, such as polyvinyl alcohol, polyvinyl pyrrolidone etc. The tablets also contain fillers (e.g. starch, microcrystalline cellulose, sugar, lactose etc.), lubricants (e.g. magnesium stearate), glidants (e.g. colloidal silicon dioxide) and disintegrants (e.g. cellulose derivatives) and acid resistant coatings, like e.g. acrylic acid esters.

The compounds of formula (I) according to the invention may be used alone or in combination with other biocides. They may be combined with pesticides having the same sphere of activity e.g. to increase activity, or with substances having another sphere of activity e.g. to broaden the range of activity. It can also be sensible to add so-called repellents. For example, in case of a compound of formula (I) having a particular efficacy as adulticide, i.e. since it is effective in particular against the adult stage of the target parasites, the addition of a pesticide which instead attack the juvenile stages of the parasites may be very advantageous, or vice versa. In this way, the greatest part of those parasites that produce great economic damage will be covered. Moreover, this action will contribute substantially to avoiding the formation of resistance. Many combinations may also lead to synergistic effects, i.e. the total amount of active ingredient can be reduced, which is desirable from an ecological point of view. Preferred groups of combination partners and especially preferred combination partners are named in the following, whereby combinations may contain one or more of these partners in addition to a compound of formula (I).

Suitable partners in the mixture may be biocides, e.g. the insecticides and acaricides with a varying mechanism of activity, which are named in the following and have been known to the person skilled in the art for a long time, e.g. chitin synthesis inhibitors, growth regulators; active ingredients which act as juvenile hormones; active ingredients which act as adulticides; broad-band insecticides, broad-band acaricides and nematicides; and also the well known anthelminthics and insect- and/or acarid-deterring substances, said repellents or detachers. Non-limitative examples of suitable insecticides and acaricides are mentioned in WO 2009/071500, compounds Nos. 1-284 on pages 18-21. Non-limitative examples of suitable anthelminthics are mentioned in WO 2009/071500, compounds (A1) – (A31) on page 21. Non-limitative examples of suitable repellents and detachers are mentioned in WO 2009/071500, compounds (R1) –(R3) on page 21 and 22. Non-limitative examples of suitable synergists are mentioned in WO 2009/071500, compounds (S1) –(S3) on page 22.

The said partners in the mixture are best known to specialists in this field. Most are described in various editions of the Pesticide Manual, The British Crop Protection Council, London, and others in the various editions of The Merck Index, Merck & Co., Inc., Rahway, New Jersey, USA or in patent literature.

As a consequence of the above details, a further aspect of the present invention relates to a combination preparation for the control of parasites on warm-blooded animals, characterised in that it contains, in addition to a compound of formula (I), at least one further active ingredient having the same or different sphere of activity and at least one physiologically acceptable carrier. The present invention is not restricted to two-fold combinations.
As a rule, the insecticidal and acaricidal compositions according to the invention contain 0.1 to 99 % by weight, especially 0.1 to 95 % by weight of one or more active ingredients of formula (I), 99.9 to 1 % by weight, especially 99.8 to 5 % by weight of a solid or liquid admixture, including 0 to 25 % by weight, especially 0.1 to 25 % by weight of a surfactant.
Application of the compositions according to the invention to the animals to be treated may take place topically, perorally, parenterally or subcutaneously, the composition being present, for example, in the form of solutions, emulsions, suspensions, (drenches), powders, tablets, boli, capsules, chewable treats, collars, eartags and pour-on formulations.
Preferred topical formulations are understood to refer to a ready-to-use solution in form of a spot-on, pour-on or spray-on formulation often consisting of a dispersion or suspoemulsion or a combination of active ingredient and spreading auxiliaries. The expression spot-on or pour-on method is understood to refer to a ready-to-use concentrate intended to be applied topically and locally on the animal. This sort of formulation is intended to be applied directly to a relatively small area of the animal, preferably on the animal's back and breech or at one or several points along the line of the back and breech. It is applied as a low volume of about 0.05 to 1 ml per kg, preferably about 0.1 ml per kg, with a total volume from 0.1 to 100 ml per animal, preferably limited to a maximum of about 50 ml. However, it goes without saying that the total volume has to be adapted to the animal that is in need of the treatment and will clearly be different, for example, in young cats and in cattle. These pour-on and spot-on formulations are designed to spread all around the animal giving protection or treatment to almost any part of the animal. Even so the administration is carried out by applying a swab or spray of the pour-on or spot-on formulation to a relatively small area of the coat, one observes that from the active substance is dispersed almost automatically over wide areas of

the fur owing to the spreading nature of the components in the formulation and assisted by the animal's movements.

Pour-on or spot-on formulations suitably contain carriers, which promote rapid dispersement over the skin surface or in the coat of the host animal, and are generally regarded as spreading oils. Suitable carriers are e.g. oily solutions; alcoholic and isopropanolic solutions such as solutions of 2-octyldodecanol or oleyl alcohol; solutions in esters of monocarboxylic acids, such as isopropyl myristate, isopropyl palmitate, lauric acid oxalate, oleic acid oleyl ester, oleic acid decyl ester, hexyl laurate, oleyl oleate, decyl oleate, capric acid esters of saturated fat alcohols of chain length C_{12}-C_{18}; solutions of esters of dicarboxylic acids, such as dibutyl phthalate, diisopropyl isophthalate, adipic acid diisopropyl ester, di-n-butyl adipate or also solutions of esters of aliphatic acids, e.g. glycols. It may be advantageous for a dispersing agent to be additionally present, such as one known from the pharmaceutical or cosmetic industry. Examples are 2-pyrrolidone, 2-(N-alkyl)pyrrolidone, acetone, polyethylene glycol and the ethers and esters thereof, propylene glycol or synthetic triglycerides.
The oily solutions include e.g. vegetable oils such as olive oil, groundnut oil, sesame oil, pine oil, linseed oil or castor oil. The vegetable oils may also be present in epoxidised form. Paraffins and silicone oils may also be used.

A pour-on or spot-on formulation generally contains 1 to 98.9 % by weight of a compound of formula (I), 0.1 to 80 % by weight of dispersing agent and 1 to 98.9 % by weight of solvent. The pour-on or spot-on method is especially advantageous for use on herd animals such as cattle, horses, sheep or pigs, in which it is difficult or time-consuming to treat all the animals orally or by injection. Because of its simplicity, this method can of course also be used for all other animals, including individual domestic animals or pets, and is greatly favoured by the keepers of the animals, as it can often be carried out without the specialist presence of the veterinarian.

Whereas it is preferred to formulate commercial products as concentrates, the end user will often use dilute formulations. However, this depends on the mode of administration. Orally administered products are most often used in diluted form or as feed additives, whereas commercial pour-on and spot-on formulations are normally ready-to-use concentrates.

Such compositions may also contain further additives, such as stabilisers, anti-foaming agents, viscosity regulators, binding agents or tackifiers, as well as other active ingredients, in order to achieve special effects.

Insecticidal and acaricidal compositions of this type, which are used by the end user, similarly form a constituent of the present invention.

In each of the processes according to the invention for pest control or in each of the pest control compositions according to the invention, the active ingredients of formula (I) can be used in all of their steric configurations or in mixtures thereof.

The invention also includes a method of prophylactically protecting animals, especially productive livestock, domestic animals and pets, against parasitic helminths, which is characterised in that the active ingredients of formula (I) or the active ingredient formulations prepared therefrom are administered to the animals as an additive to the feed, or to the drinks or also in solid or liquid form, orally or by injection or parenterally. The invention also includes the compounds of formula (I) according to the invention for usage in one of the said processes.

The following examples serve merely to illustrate the invention without restricting it, the term active ingredient representing any substance as described in the preparation examples.
In particular, preferred formulations are made up as follows:
(% = percent by weight)
Formulation examples

1. Granulate	a)	b)
(i) active ingredient	5 %	10 %
kaolin	94 %	-
highly dispersed silicic acid	1 %	-
attapulgite	-	90 %

The active ingredient is dissolved in methylene chloride, sprayed onto the carrier and the solvent subsequently concentrated by evaporation under vacuum. Granulates of this kind can be mixed with the animal feed.

(ii) active ingredient	3 %
polyethylene glycol (mw 200)	3 %
kaolin	94 %

(mw = molecular weight)

The finely ground active ingredient is evenly applied in a mixer to the kaolin which has been moistened with polyethylene glycol. In this way, dust-free coated granules are obtained.

2. Tablets or boli

I	active ingredient	33.00 %
	methylcellulose	0.80 %
	silicic acid, highly dispersed	0.80 %
	corn starch	8.40 %
II	lactose, cryst.	22.50 %
	corn starch	17.00 %
	microcryst. cellulose	16.50 %
	magnesium stearate	1.00 %

I Methyl cellulose is stirred into water. After the material has swollen, silicic acid is stirred in and the mixture homogeneously suspended. The active ingredient and the corn starch are mixed. The aqueous suspension is worked into this mixture and kneaded to a dough. The resulting mass is granulated through a 12 M sieve and dried.

II All 4 excipients are mixed thoroughly.

III The preliminary mixes obtained according to I and II are mixed and pressed into tablets or boli.

3. Injectables

A. Oily vehicle (slow release)

(i)	active ingredient	0.1-1.0 g
	groundnut oil	ad 100 ml
(ii)	active ingredient	0.1-1.0 g
	sesame oil	ad 100 ml

Preparation: The active ingredient is dissolved in part of the oil whilst stirring and, if required, with gentle heating, then after cooling made up to the desired volume and sterile-filtered through a suitable membrane filter with a pore size of 0.22 μm.

B Water-miscible solvent (average rate of release)

(i)	active ingredient	0.1-1.0 g
	4-hydroxymethyl-1,3-dioxolane (glycerol formal)	40 g
	1,2-propanediol	ad 100 ml
(ii)	active ingredient	0.1-1.0 g
	glycerol dimethyl ketal	40 g
	1,2-propanediol	ad 100 ml

Preparation: The active ingredient is dissolved in part of the solvent whilst stirring, made up to the desired volume and sterile-filtered through a suitable membrane filter with a pore size of 0.22 µm.

C. Aqueous solubilisate (rapid release)

(i)	active ingredient	0,1-1,0 g
	polyethoxylated castor oil (40 ethylene oxide units)	10 g
	1,2-propanediol	20 g
	benzyl alcohol	1 g
	aqua ad inject.	ad 100 ml
(ii)	active ingredient	0.1-1.0 g
	polyethoxylated sorbitan monooleate (20 ethylene oxide units)	8 g
	4-hydroxymethyl-1,3-dioxolane (glycerol formal)	20 g
	benzyl alcohol	1 g
	aqua ad inject.	ad 100 ml

Preparation: The active ingredient is dissolved in the solvents and the surfactant, and made up with water to the desired volume. Sterile filtration through an appropriate membrane filter of 0.22 µm pore size.

4. Pour on

(i)	active ingredient	5 g
	isopropyl myristate	10 g
	isopropanol	ad 100 ml
(ii)	active ingredient	2 g
	hexyl laurate	5 g
	medium-chained triglyceride	15 g
	ethanol	ad 100 ml

(iii)	active ingredient	2 g
	oleyl oleate	5 g
	N-methyl-pyrrolidone	40 g
	isopropanol	ad 100 ml

5. Spot on

(i)	active ingredient	0-15 g
	diethyleneglycol monoethylether	ad 100 ml
(ii)	active ingredient	10-15 g
	octyl palmitate	10 g
	isopropanol	ad 100 ml
(iii)	active ingredient	10-15 g
	isopropanol	20 g
	benzyl alcohol	ad 100 ml

6. Spray on

(i)	active ingredient	1 g
	isopropanol	40 g
	propylene carbonate	ad 100 ml
(ii)	active ingredient	1 g
	propylene glycol	10 g
	isopropanol	ad 100 ml

The aqueous systems may also preferably be used for oral and/or intraruminal application. The compositions may also contain further additives, such as stabilisers, e.g. where appropriate epoxidised vegetable oils (epoxidised coconut oil, rapeseed oil, or soybean oil); antifoams, e.g. silicone oil, preservatives, viscosity regulators, binders, tackifiers, as well as fertilisers or other active ingredients to achieve special effects.

Further biologically active substances or additives, which are neutral towards the compounds of formula (I) and do not have a harmful effect on the host animal to be treated, as well as mineral salts or vitamins, may also be added to the described compositions.

The following examples serve to illustrate the invention. The letter 'h' stands for hour. The starting materials are known and partially commercially available or may be produced in analogy to methods known per se.

Analysis of the purified samples is in each case done using a Waters Autopurification (HPLC/MS) system with a reversed phase column (Daisogel SP-120-ODS-AP 5µm, 150X3mm) from Bischoff, Leonberg, Germany. The samples are characterized by m/z and retention time. The above-given retention times relate in each case to the use of a solvent system comprising two different solvents, solvent A: H_2O + 0.01% HCOOH, and solvent B: CH_3CN + 0.01% HCOOH). Said two solvents A and B are employed at a flow rate of 2.00 ml/min with a time-dependent gradient as given in the Table:

Method A: column Daisogel SP-120-ODS-AP 5µm, 150X3mm) from Bischoff, Leonberg, Germany, flow rate of 2.00 mL/min with a time-dependent gradient as given in the Table:

Time [min]	A [%]	B [%]
0.5	90	10
1.0	74	26
1.5	60	40
2.0	47	53
2.5	36	64
3.0	26	74
3.5	19	81
4.0	13	87
4.25	10	90
4.5	8	92
4.75	7	93
5.0	6	94
5.5	5	95
6.5	5	95

Method B: column Waters XTerra MS C18 5µm, 50X4.6mm (Waters), flow rate of 3.00 mL/min with a time-dependent gradient as given in the Table:

Time [min]	A [%]	B [%]
0	90	10
0.5	90	10
2.5	5	95
2.8	5	95
2.9	90	10
3.0	90	10

Example 1

This example illustrates the preparation of *N*-(2-((cyanomethyl)amino)-2-oxoethyl)-5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylthiophene-3-carboxamide. (Compound 1.32 in Table 1)

Step A: DIPEA (80 mL) and amino acetonitrile hydrochloride (11.6 g) are added to a solution of *N*-(*tert*-butoxycarbonyl)glycine (20.0 g) and TBTU (40.3 g) in dichloromethane (350 mL) at 0°C. After 18 hours at room temperature, the reaction is quenched with water and extracted three times with dichloromethane. The combined organic phases are washed with a saturated solution of $NaHCO_3$ and a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product is purified by column chromatography on silica gel (ethyl acetate/heptane, 3:2 then 2:1) to yield *tert*-butyl (2-((cyanomethyl)amino)-2-oxoethyl)carbamate (22.2 g).

Step B: Methanesulfonic acid (2.9 mL) is added dropwise to a solution of *tert*-butyl (2-((cyanomethyl)amino)-2-oxoethyl)carbamate (8.73 g) in dichloromethane (360 mL) and THF (90 mL). After 4 hours at room temperature, the reaction mixture is concentrated *in vacuo*. The crude solid is suspended in diethyl ether and filtered to yield 2-amino-N-(cyanomethyl)acetamide methanesulfonate salt (7.9 g) as a white solid.

Step C: Bromine (9.7 mL) is added dropwise to a solution of 1-(5-methylthiophen-2-yl)ethanone (26.6 g) and sodium acetate (17.2 g) in water (100 mL). After 18 hours at room temperature, the reaction mixture is quenched with sodium thiosulfate (1M) and extracted three times with ethyl acetate. The combined organic phases are washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo* to yield 1-(4-bromo-5-methylthiophen-2-yl)ethanone (41.3 g) as a brownish oil. The crude product is used without further purification.

Step D: LiH (3.20 g) is added to a solution of 3',5'-dichloro-2,2,2-trifluoroacetophenone (56.0 g) and 1-(4-bromo-5-methylthiophen-2-yl)ethanone (41.0 g) in THF (500 mL). After 5 hours at 60°C MTBE is added (500 mL) and the reaction mixture is slowly poured onto water (500 mL) at 0°C. The phases are separated and aqueous phase is extracted twice with MTBE. The combined organic phases are washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo* to yield 110 g of 1-(4-bromo-5-

methylthiophen-2-yl)-3-(3,5-dichlorophenyl)-4,4,4-trifluoro-3-hydroxybutan-1-one. The crude product is used without further purification.

Step E: Trifluoroacetic anhydride (38.0 mL) is added dropwise to a solution of 1-(4-bromo-5-methylthiophen-2-yl)-3-(3,5-dichlorophenyl)-4,4,4-trifluoro-3-hydroxybutan-1-one (87.0 g) and triethylamine (53.0 mL) in dichloromethane (1000 mL) at 0°C. After 18 hours at room temperature, the reaction is diluted with a saturated aqueous solution of $NaHCO_3$ and extracted three times with dichloromethane. The combined organic phases are washed with water, dried over $MgSO_4$ and concentrated *in vacuo* to yield (*E/Z*)-1-(4-bromo-5-methylthiophen-2-yl)-3-(3,5-dichlorophenyl)-4,4,4-trifluorobut-2-en-1-one (95.0 g) as a brown oil. The crude product is used without further purification.

Step F: NaOH (18.0 g) and hydroxylamine hydrochloride (13.0 g) are added to a solution of (*E/Z*)- 1-(4-bromo-5-methylthiophen-2-yl)-3-(3,5-dichlorophenyl)-4,4,4-trifluorobut-2-en-1-one (84.0 g) in ethanol (1000 mL). After 18 hours at room temperature the reaction mixture is concentrated *in vacuo* and diethyl ether and water are added. The phases are separated and the aqueous phase is extracted twice with diethyl ether. The combined organic phases are washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product is purified by column chromatography on silica gel (dichloromethane/ heptane, 1:9, 1:4) to yield 3-(4-bromo-5-methylthiophen-2-yl)-5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazole (47.0 g) as a beige solid. M.p. : 110-112°C.

Step G: Zinc cyanide (1.2 g) is added to $Pd(PPh_3)_4$ (1.2 g) and 3-(4-bromo-5-methylthiophen-2-yl)-5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazole (4.6 g) in DMF (12 mL). The reaction mixture is heated at 120°C in a sealed tube in a microwave oven for 1 hour and then allowed to cool to room temperature. Water and ethyl acetate are added and the suspension is filtered through a pad of celite. The phases are separated and the aqueous layer is extracted twice with ethyl acetate. The combined organic phases are washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product is purified on a semi-preparative HPLC to yield 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylthiophene-3-carbonitrile (2.2 g) as a beige solid.

Step H: KOH 8 M (4.1 mL) is added to a solution of 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylthiophene-3-carbonitrile (2.2 g) in ethylene glycol (14 mL). The reaction mixture is heated at 100°C in a sealed tube in a microwave oven for 1 hour. After cooling to room temperature the mixture is diluted with water and HCl 2 M (20 mL) is added carefully. The mixture is extracted three times with ethyl acetate. The combined organic phases are washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product is purified by column chromatography on silica gel (ethyl acetate) and then crystallized with diisopropyl ether to yield 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylthiophene-3-carboxylic acid (1.7 g) as a beige solid.

Step I: Thionyl chloride (0.1 mL) is added to a solution of 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylthiophene-3-carboxylic acid (170 mg) in toluene (1.7 mL). After 30 minutes at reflux, the reaction mixture is cooled down and concentrated *in vacuo*. The crude product is dissolved in dichloromethane (3 mL) and 2-amino-*N*-(cyanomethyl)acetamide methanesulfonate salt (100 mg) and DIPEA (*N,N*-diisopropylethylamine, 0.2 mL) are added. After 18 hours at room temperature, the reaction mixture is diluted with ethyl acetate. The organic phase is washed with water and with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The residue is crystallized with ethyl acetate to yield *N*-(2-((cyanomethyl)amino)-2-oxoethyl)-5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylthiophene-3-carboxamide (130 mg) as a colorless solid. MS (HPLC/MS): 519 (MH^+). Retention time: 1.81 min. M.p. : 158-161°C.

Example 2

This example illustrates the preparation of 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methyl-*N*-(2-oxo-2-((2,2,2-trifluoroethyl)amino)ethyl)furan-3-carboxamide. (Compound 1.19 in Table 1)

Step A: DIPEA (15 ml) is added to a solution of *N*-(*tert*-butoxycarbonyl)glycine (5.0 g), PYBOP (benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate, 16.3 g) and 2,2,2-trifluorethylamine (2.47 ml) in dichloromethane (48 ml). After 24 hours at room temperature, the reaction is quenched with water and extracted three times with dichloromethane. The combined organic phases are washed with HCl (2M), Na_2CO_3 (1M) and a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product is purified by column chromatography (450 g) eluting with a mixture of ethyl acetate and hexane (2:3 to 3:2) to yield [(2,2,2-trifluoro-ethylcarbamoyl)-methyl]-carbamic acid *tert*-butyl ester (3.89 g).

Step B: Trifluoracetic acid (23.4 ml) is added dropwise to a solution of [(2,2,2-trifluoro-ethylcarbamoyl)-methyl]-carbamic acid *tert*-butyl ester (3.89 g) in dichloromethane (75 ml). After 18 hours at room temperature, the reaction mixture is concentrated *in vacuo*. The crude oil is purified by crystallization in diethylether to yield (2,2,2-trifluoro-ethylcarbamoyl)-methyl-ammonium trifluoroacetate (4.12 g) as a white solid.

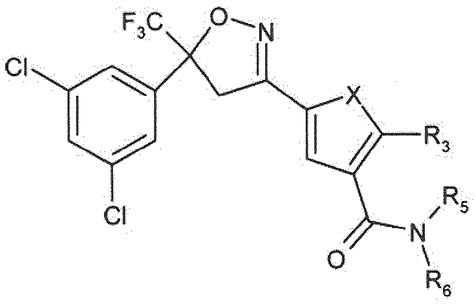
Step C: Hydroxylamine (50% in H_2O, 1.82 mL) is added to a solution of methyl 5-formyl-2-methylfuran-3-carboxylate (5.0 g) in methanol (75 mL). After 3 hours at room temperature, the reaction is concentrated *in vacuo*. The residue is partitioned between ethyl acetate and water. The aqueous phase is extracted three times with ethyl acetate. The combined organic phases are washed with water and with a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo* to yield methyl 5-((hydroxyimino)methyl)-2-methylfuran-3-carboxylate. The crude product is used without further purification.

Step D: A solution of methyl 5-((hydroxyimino)methyl)-2-methylfuran-3-carboxylate (3.0 g) in dichloromethane (18 mL) is added to a solution of 1,3-dichloro-5-(1-trifluoromethyl-vinyl)-benzene (3.95 g), chlorox (4%, 44 mL) and triethylamine (0.23 mL) in dichloromethane (70 mL) at 0°C. After 2 hours, the reaction mixture is filtered and water is added. The phases are separated and the aqueous phase is extracted twice with dichloromethane. The organic phases are combined, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product is purified on a semi-preparative HPLC to yield methyl 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylfuran-3-carboxylate (3.13 g) as a light yellow solid. MS (HPLC/MS): 422 (MH^+). Retention time: 2.19 min.

Step E: LiOH (1.06 g) is added to a solution of methyl 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylfuran-3-carboxylate (3.1 g) in a mixture of THF and water (75 mL, 1:1). After 18 hours at room temperature, water and HCl (2N) are added to the reaction mixture until pH 1-2 is obtained. The mixture is then extracted three times with ethyl acetate. The organic phases are combined, washed with water and a saturated aqueous solution of NaCl, dried over $MgSO_4$ and concentrated *in vacuo* to yield 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylfuran-3-carboxylic acid (2.8 g) as a yellow solid. The crude product is used without further purification.

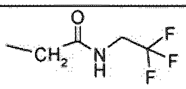
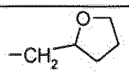
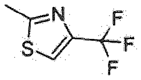
Step F: DIPEA (0.12 mL) is added to a solution of (2,2,2-trifluoro-ethylcarbamoyl)-methyl-ammonium trifluoroacetate (100 mg, from Step B above), PYBOP (150 mg), and 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methylfuran-3-carboxylic acid (100 mg) in dichloromethane (2 mL) at 0°C. After 18 hours at room temperature the reaction mixture is concentrated *in vacuo*. The crude product is purified on a semi-preparative reversed phase HPLC to yield 5-(5-(3,5-dichlorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-2-methyl-*N*-(2-oxo-2-((2,2,2-trifluoroethyl)amino)ethyl)furan-3-carboxamide (63 mg) as a beige solid. MS (HPLC/MS): 546 (MH+). Retention time: 1.84 min. M.p. : 172-174°C.

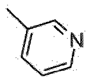
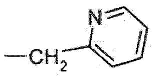
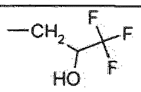
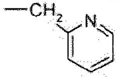
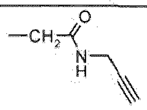
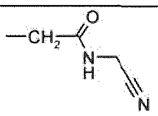
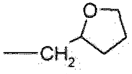
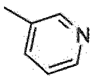
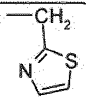
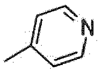
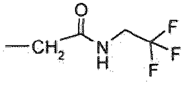
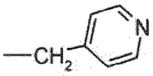
The substances named in the following Table 1 are prepared analogously to the above-described methods. The compounds are of formula

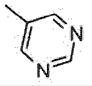
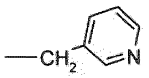
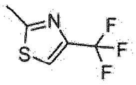
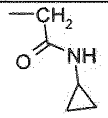
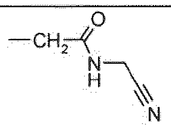
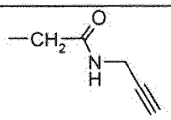
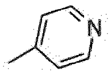


wherein the meaning of X, R_3, R_5 and R_6 are given in Table 1.

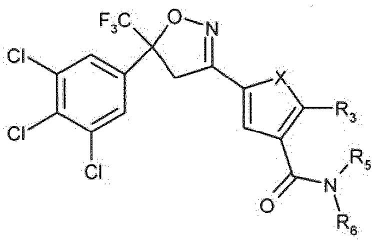
Table 1:

Cpd No.	X	R_3	R_5	R_6	Anal. Method	EM_{calc}	m/z	R_t [min]	M.p. [°C]
1.1	S	Me	H		A	561	562	4.04	197-199
1.2	S	Me	H		A	506	507	2.26	oil
1.3	S	Me	H		A	573	572	5.17	oil

1.4	S	Me	H		A	499	500	3.63	166-168
1.5	S	Me	H		A	513	514	3.60	212-214
1.6	S	Me	H		A	534	535	4.13	oil
1.7	S	Me	H	H	A	422	423	2.79	oil
1.8	S	Me	-	=C-N(Me)2	A	477	478	4.15	oil
1.9	S	Me	-	=C-NH(OMe)	A	479	478	4.61	oil
1.10	O	Me	H	-CH_2CF_3	A	488	489	4.26	oil
1.11	O	Me	H		A	497	498	3.83	171-173
1.12	O	Me	H		B	501	502	1.74	148-150
1.13	O	Me	H		B	502	5.3	1.71	98-100
1.14	O	Me	H		B	490	-	1.02	resin
1.15	O	Me	H		B	483	484	1.03	resin
1.16	O	Me	H		B	503	504	1.87	foam
1.17	O	Me	H		B	476	477	1.83	130-132
1.18	O	Me	H		B	483	484	1.35	resin
1.19	O	Me	H		B	545	546	1.84	172-174
1.20	O	Me	H	Me	B	420	421	2.25	oil
1.21	O	Me	H		B	478	479	2.02	foam
1.22	O	Me	H		B	497	498	1.33	resin
1.23	O	Me	H	CH_2CO_2Me	B	478	479	1.85	resin

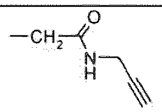
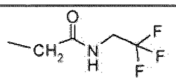
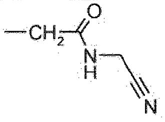
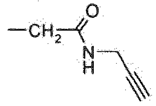
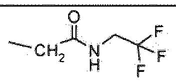
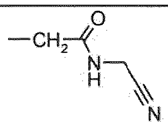
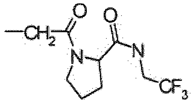
1.24	O	Me	H		B	484	485	1.84	resin
1.25	O	Me	H		B	497	498	1.42	resin
1.26	O	Me	H	$-CH_2CO_2H$	B	464	463	1.69	foam
1.27	O	Me	H		B	557	558	1.90	resin
1.28	O	Me	H	$-CH_2CH_2SMe$	B	480	481	1.98	resin
1.29	O	Me	H	$-CH_2CONHEt$	B	491	492	1.71	resin
1.30	O	Me	H	$-CH_2CONHMe$	B	477	478	1.63	resin
1.31	O	Me	H		B	503	504	1.71	foam
1.32	S	Me	H		B	518	519	1.81	158-161
1.33	S	Me	H		B	517	518	1.85	170-172
1.34	S	Me	H		B	492	493	1.96	161-166
1.35	S	Me	H	$-CH_3$	B	436	437	1.93	143-145
1.36	S	Me	H		B	499	500	1.44	foam
1.37	S	Me	H	$-CH_2CH_2SMe$	B	496	497	2.12	134-136
1.38	S	Me	H		B	494	495	2.15	resin
1.39	S	Me	H	$-CH_2CONHEt$		507			
1.40	S	Me	H	$-CH_2CONHMe$		493			

The substances named in the following Table 2 are prepared analogously to the above-described methods. The compounds are of formula



wherein the meaning of X, R_3, R_5 and R_6 are given in Table 2.

Table 2:

Cpd No.	X	R_3	R_5	R_6	Anal. Method	EM_{calc}	m/z	R_t [min]	M.p. [°C]
2.1	S	Me	H		A	551	552	3.96	
2.2	S	Me	H			595			
2.3	S	Me	H			552			
2.4	S	Me	H	$-CH_2CONHEt$		541			
2.5	O	Me	H	$-CH_2CONHMe$		527			
2.6	O	Me	H		B	535	536	1.87	117-122
2.7	O	Me	H		B	579	580	1.96	122-128
2.8	O	Me	H		B	536	537	1.82	117-122
2.9	O	Me	H	$-CH_2CONHEt$	B	525	526	1.82	n/d
2.10	O	Me	H	$-CH_2CONHMe$		511			
2.11	O	Me	H	-OH	B	456	457	1.78	foam
2.12	O	Me	$-CH_2CH_2CH_2CH_2-$		B	494	495	2.09	foam
2.13	O	Me	$-CH_2CH_2N(Me)CH_2CH_2-$		B	523	524	1.40	foam
2.14	O	Me	$-CH_2CH_2OCH_2CH_2-$		B	510	511	1.97	oil
2.15	O	Me	H	$-NHCOO^tBu$	B	555	556	2.06	n/d
2.16	O	Me	H			619	620	4.60	foam
2.17	O	Me	H	-OMe	B	470	471	1.95	foam
2.18	O	Me	H	$-OCH_2CHCH_2$	B	496	497	2.06	foam

Biological Examples:

1. Activity *in vitro* against *Ctenocephalides felis* (Cat flea).

A mixed adult population of fleas is placed in a suitably formatted 96-well plate allowing fleas to access and feed on treated blood via an artificial feeding system. Fleas are fed on treated blood for 24 hours, after which the compound effect is recorded. Insecticidal activity is determined on the basis of the number of dead fleas recovered from the feeding system.

Compound 1.1, 1.2, 1.7, 1.10-1.14, 1.16-1.22, 1.24, 1.25, 1.28, 1.34, 1.37, 2.6-2.9, 2.12, 2.15, 2.16, 2.18 showed more than 80% (EC_{80}) efficacy at 10ppm.

2. Activity *in vitro* against *Rhipicephalus sanguineus* (Dog tick).

A clean adult tick population is used to seed a suitably formatted 96-well plate containing the test substances to be evaluated for antiparasitic activity. Each compound is tested by serial dilution in order to determine its minimal effective dose (MED). Ticks are left in contact with the test compound for 10 minutes and are then incubated at 28°C and 80% relative humidity for 7 days, during which the test compound effect is monitored. Acaricidal activity is confirmed if adult ticks are dead.

In this test the following examples showed more than 80% (EC_{80}) efficacy at 640ppm: 1.2, 1.11-1.15, 1.17, 1.19-1.22, 1.24, 1.25, 1.27-1.30, 1.32, 1.35, 1.37, 2.6-2.9, 2.12, 2.14, and 2.16.

3. Activity *in vivo* against *Rhipicephalus sanguineus* nymphs on Mongolian gerbils (Meriones unguiculatus) (spray application)

On day 0, gerbils are treated with the test compound at a given dose by spray application. On day +1 (+2), the animals are infested with nymphs of *R.sanguineus*. Ticks are left on the animals until full repletion. Seven days after infestation nymphs dropped off fully engorged are collected and counted. Efficacy in killing is expressed as a tick number reduction in comparison with a placebo treated group, using the Abbot's formula.

In this test the following examples showed more than 80% (EC_{80}) efficacy at the dose indicated in Table 3.

Table 3:

Compound No.	Dose mg/kg	Efficacy in killing %
1.12	3.2	97
1.13	3.2	94
1.19	10	100
1.29	3.2	91
1.30	3.2	92
1.32	100	85
2.6	3.2	99
2.7	3.2	90
2.8	3.2	99

4. Activity *in vivo* against *Ctenocephalides felis* (cat flea) on Mongolian gerbils (Meriones unguiculatus) (per oral application)

On day 0, gerbils are treated orally by gavage with the test compound formulated at a given dose. Immediately after treatment, they are infested with a mixed adult population of cat fleas. Evaluation of efficacy is performed 48h infestation by counting the numbers of live fleas recovered from the gerbils. Efficacy is expressed as comparison with a placebo treated group using the Abbot's formula.

In this test the following examples showed more than 80% (EC_{80}) efficacy at the dose indicated in Table 4.

Table 4:

Compound No.	Dose mg/kg	Efficacy in killing %
1.1	32	100
1.12	1.0	98
1.19	3.2	99

5. Activity *in vivo* against *Ctenocephalides felis* (cat flea) on Mongolian gerbils (*Meriones unguiculatus*) (spray application)

On day 0, gerbils are treated with the test compound at a given dose by spray application. On day +1, the animals are infested with a mixed adult population of cat fleas. Evaluation of efficacy is performed 24h and 48h infestation by counting the numbers of live fleas recovered from the gerbils. Efficacy is expressed as comparison with a placebo treated group using the Abbot's formula.

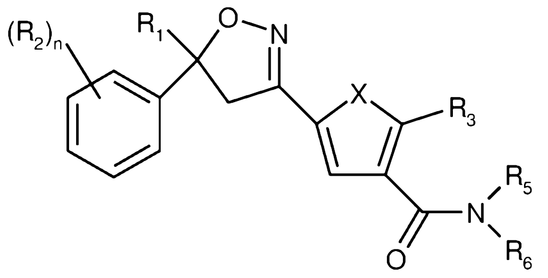
In this test the following examples showed more than 80% (EC_{80}) efficacy at the dose indicated in Table 5.

Table 5:

Compound No.	**Dose mg/kg**	**Efficacy in killing %**
1.12	3.2	96
1.13	10	100
1.19	10	94
1.29	10	89
1.30	3.2	85
1.32	32	96
2.6	1.0	90
2.7	3.2	84
2.9	3.2	97

Claims

1. A compound of formula



(Ia),

or a stereoisomer or a salt thereof, wherein n is an integer from 1 to 3; R_1 is C_1-C_3-haloalkyl; each R_2 is independently selected from the group consisting of halogen, C_1-C_6-haloalkyl, C_1-C_6-haloalkoxy and cyano; X is S or O; R_3 is H or C_1-C_2-alkyl; R_5 is H or C_1-C_2-alkyl; R_6 is C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, C_4-C_7-alkylcycloalkyl or C_4-C_7-cycloalkylalkyl, which is each unsubstituted or are substituted in the alkyl, alkenyl or alkynyl moiety by halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, cyano, amino, N-mono- or N,N-di-C_1-C_4-alkylamino, COOH, C_1-C_4-alkoxy-carbonyl, N-C_1-C_4-alkylcarbonylamino, sulfonamido, N-mono- or N,N, di-C_1-C_4-alkylsulfonamido, a group –C(O)NR_7R_8 or a radical Q'; or R_6 is a radical Q; or R_6 together with R_5 is a group =C–NR_7R_8 or =C–$NR_7(OR_8)$; R_7 is H or C_1-C_4-alkyl; R_8 is H; C_2-C_4-alkenyl; C_2-C_4-alkynyl; C_3-C_6-cycloalkyl; or C_1-C_6-alkyl which is unsubstituted or substituted by halogen, C_1-C_4-alkoxy, C_1-C_2-alkylthio, cyano, nitro, amino, N-mono- or N,N-di-C_1-C_4alkylamino, pyridyl, pyrimidyl thiazolyl, or pyridyl, pyrimidyl or thiazolyl which is each mono- or disubstituted by halogen, cyano, C_1-C_2-alkyl or C_1-C_2-haloalkyl; and Q and Q' are each thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, triazolyl, thiadiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl and triazinyl, thietanyl, or tetrahydrofuranyl, which are each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxy-carbonyl.

2. A compound of formula (Ia) according to claim 1, wherein n is an integer of 2 or 3; R_1 is CF_3; each R_2 is independently halogen; X is S or O; R_3 is H or C_1-C_2-alkyl; R_5 is H; and R_6 is C_1-C_4-alkyl, which is unsubstituted or substituted in the alkyl moiety by halogen, hydroxy, C_1-C_4-alkoxy, C_1-C_4-haloalkoxy, C_1-C_4-alkylthio, C_1-C_4-haloalkylthio, cyano, COOH, C_1-C_4-alkoxycarbonyl, a group –C(O)NR_7R_8 or a radical Q'; or R_6 is a radical Q; or R_6 together with

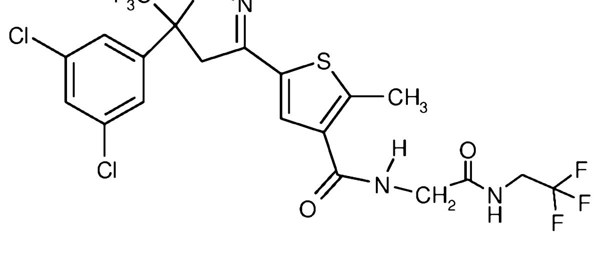
R_5 is a group $=C–NR_7R_8$ or $=C–NR_7(OR_8)$; R_7 is H or C_1-C_2-alkyl; R_8 is C_2-C_4-alkenyl, C_2-C_4-alkynyl, C_3-C_6-cycloalkyl, or C_1-C_4-alkyl which is unsubstituted or substituted by halogen, cyano or pyridyl; and Q and Q' are each 1-, 2- or 3-pyrrolyl, 1-, 2-, 4- or 5-imidazolyl, 1- or 4-pyrazolyl, 2-, 4- or 5-thiazolyl, 1,2,4-triazol-3- or -4-yl, 1,2,3-triazin-1- or 2-yl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, thietanyl, or tetrahydrofuranyl, which is each unsubstituted or substituted by halogen, C_1-C_2-alkyl, C_1-C_2-haloalkyl, C_1-C_2-alkoxy, C_1-C_2-haloalkoxy, cyano, nitro, or C_1-C_4-alkoxycarbonyl.

3. A compound of formula (Ia) according to claim 1, wherein n is an integer of 2 or 3; R_1 is CF_3; each R_2 is independently halogen; X is S or O; R_3 is H or C_1-C_2-alkyl; R_5 is H; R_6 is C_1-C_4-alkyl, which is unsubstituted or are substituted in the alkyl moiety by halogen, C_1-C_2-alkoxy, C_1-C_2-alkylthio, cyano, COOH, C_1-C_2-alkoxycarbonyl, a group $–C(O)NR_7R_8$ or a radical Q'; or R_6 is a radical Q; or R_6 together with R_5 is a group $=C–N(C_1\text{-}C_2\text{-alkyl})_2$ or $=C–NH(OC_1\text{-}C_2\text{alkyl})$; R_7 is H; R_8 is C_2-C_4-alkynyl, C_3-C_4-cycloalkyl or C_1-C_4-alkyl which is unsubstituted or substituted by halogen or cyano; and Q and Q' are each 2-thiazolyl, 2- 3- or 4-pyridyl, 4- or 5-pyrimidinyl, 3-thietanyl, or 2- or 3-tetrahydrofuranyl, which is each unsubstituted or substituted by C_1-C_2-alkyl or C_1-C_2-haloalkyl.

4. A compound according to any one of claims 1 to 3, wherein X is O.

5. A compound according to any one of claims 1 to 4, wherein R_3 is methyl.

6. A compound according to claim 1, which is of formula



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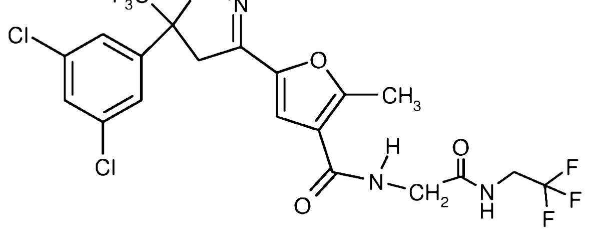

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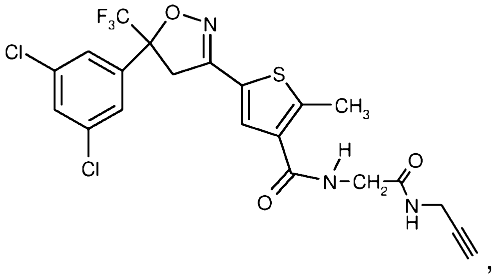
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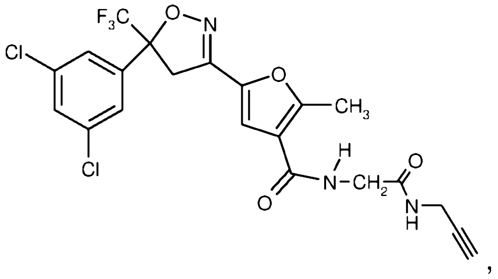
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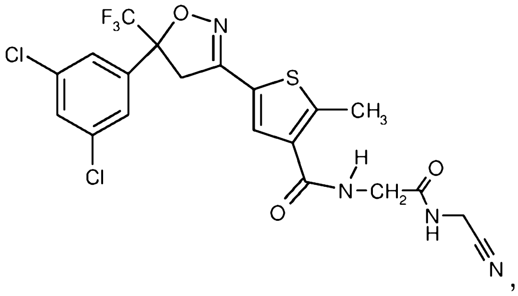
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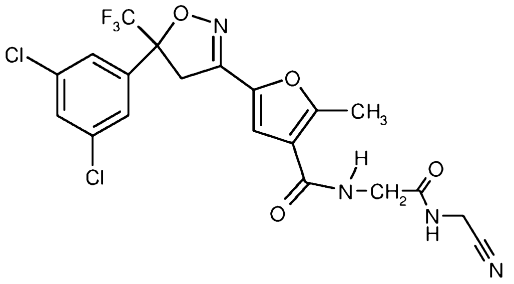
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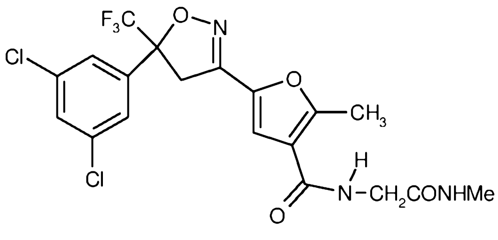
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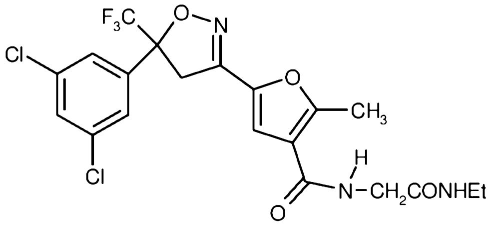
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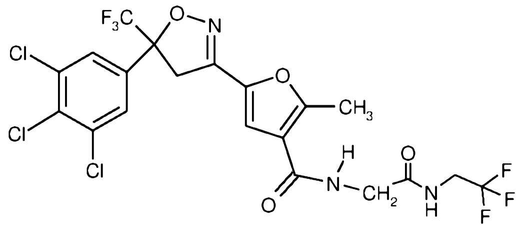

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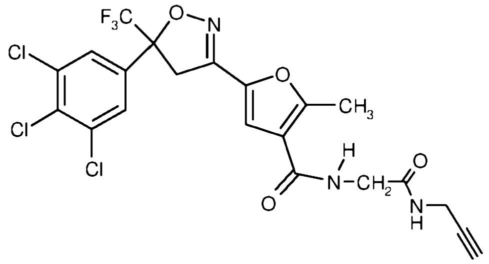

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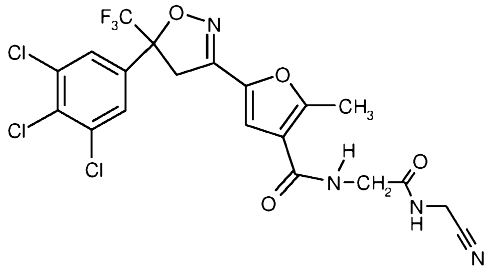

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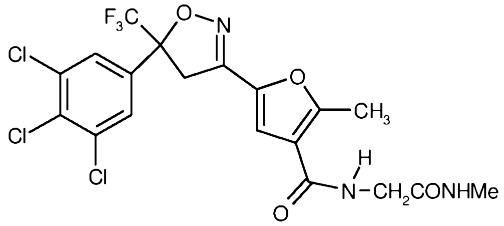

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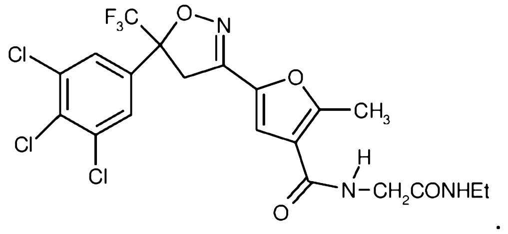

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7. Composition for the control of parasites, comprising as active ingredient at least one compound of the formula (Ia) according to any one of claims 1 to 6, in addition to a carrier and/or a dispersant.

8. Method of controlling parasites in and on warm-blooded animals, which comprises applying to the animals a pharmaceutical effective amount of at least one compound of formula (I) according to any one of claims 1 to 6.

9. Use of a compound of formula (I) according to any one of claims 1 to 6 in the control of parasites.

10. Use of a compound of formula (I) according to any one of claims 1 to 6 in a process for controlling parasites in and on warm-blooded animals.

11. Use of an effective amount of a compound of formula (I) according to any one of claims 1 to 6 in the preparation of a pharmaceutical composition for the control of parasites in and on warm-blooded animals.

Novartis Tiergesundheit AG

Patent Attorneys for the Applicant/Nominated Person

SPRUSON & FERGUSON