HU000034042T2

(19) **HU**

(11) Lajstromszám: **E 034 042**

(13) **T2**

MAGYARORSZÁG
Szellemi Tulajdon Nemzeti Hivatala

EURÓPAI SZABADALOM
SZÖVEGÉNEK FORDÍTÁSA

(21) Magyar ügyszám: **E 11 761595**
(22) A bejelentés napja: **2011. 09. 28.**

(96) Az európai bejelentés bejelentési száma:
EP 20110761595
(97) Az európai bejelentés közzétételi adatai:
EP 2621903 A1 **2012. 04. 05.**
(97) Az európai szabadalom megadásának meghirdetési adatai:
EP 2621903 B1 **2017. 03. 01.**

(51) Int. Cl.: ***C07D213/74*** *(2006.01)*
A61K 31/47 *(2006.01)*
C07D215/46 *(2006.01)*
A61K 31/435 *(2006.01)*
A61K 33/10 *(2006.01)*

(86) A nemzetközi (PCT) bejelentési szám:
PCT/EP 11/066806
(87) A nemzetközi közzétételi szám:
WO 12041873

(30) Elsőbbségi adatok:

388466 P	**2010. 09. 30.**	**US**
10181553	**2010. 09. 29.**	**EP**

(72) Feltaláló(k):
BERGER, Michael, 55270 Schwabenheim (DE)
KERN, Christopher, 55270 Schwabenheim (DE)
ECK, Marko, 55270 Schwabenheim (DE)
SCHRÖDER, Jörg, 55270 Schwabenheim (DE)

(73) Jogosult(ak):
Intervet International B.V., 5831 AN Boxmeer (NL)

(74) Képviselő:
Sworks Nemzetközi Szabadalmi Ügyvivői Iroda Kft., Budapest

(54) **N-Heteroaril vegyületek**

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 621 903 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
01.03.2017 Bulletin 2017/09

(21) Application number: **11761595.5**

(22) Date of filing: **28.09.2011**

(51) Int Cl.:
C07D 213/74 *(2006.01)* ***C07D 215/46*** *(2006.01)*
A61K 31/435 *(2006.01)* ***A61K 31/47*** *(2006.01)*
A61K 33/10 *(2006.01)*

(86) International application number:
PCT/EP2011/066806

(87) International publication number:
WO 2012/041873 (05.04.2012 Gazette 2012/14)

(54) **N-HETEROARYL COMPOUNDS**

N-HETEROARYLVERBINDUNGEN

COMPOSÉS N-HÉTÉROARYLÉS

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

(30) Priority: **30.09.2010 US 388466 P**
29.09.2010 EP 10181553

(43) Date of publication of application:
07.08.2013 Bulletin 2013/32

(73) Proprietor: **Intervet International B.V.**
5831 AN Boxmeer (NL)

(72) Inventors:
- **BERGER, Michael**
  55270 Schwabenheim (DE)
- **KERN, Christopher**
  55270 Schwabenheim (DE)
- **ECK, Marko**
  55270 Schwabenheim (DE)
- **SCHRÖDER, Jörg**
  55270 Schwabenheim (DE)

(74) Representative: **Intervet International B.V.**
Hertford Road
Hoddesdon, Hertfordshire EN11 9BU (GB)

(56) References cited:
EP-A2- 1 900 772
WO-A1-2004/035591
CN-A- 101 284 812

EP 2 621 903 B1

Description

FIELD OF THE INVENTION

[0001] This invention relates to novel N-heteroaryl compounds that are useful as medicaments, the preparation of such compounds and the use of such compounds. The medicament can preferably be used for the treatment of parasitic infections such as helminth infections and especially for the treatment of parasitoses, such as caused by helminth infections. This invention also relates to uses of the compounds to make medicaments and treatments comprising the administration of the compounds to animals in need of the treatments. Moreover this invention relates to pharmaceutical compositions and kits comprising the compounds.

BACKGROUND OF THE INVENTION

[0002] Parasitic diseases in animals cause substantial suffering and economic losses throughout the world. Thus, treatment of parasitic infections remains an important global endeavor. The causative organisms include helminths, such as nematodes, cestodes, and trematodes. These organisms can infect, for example, the stomach, intestinal tract, lymphatic system, muscle tissues, kidney, liver, lungs, heart, and brain of animals.

[0003] There are many known drugs (or"anthelmintic agents") available to treat various helminith parasite infections, see, *e.g.,* McKellar, Q.A., et al., "Veterinary anthelmintics: old and new," Review: Trends in Parasitology, 20(10), 456-61 (October 2004). These anthelmintic agents treat specifically either nematode, cestode or trematode infections or have a broader anthelmintic spectrum. An example of an anthelmintic agent with sole effect on cestodes (tapeworms) is praziquantel. Some primary nematicidal compounds like fenbendazole, mebendazole, oxfendazole, albendazole have a broader spectrum than nematodes and treat cestode infections as well. Closantel, rafoxanide and triclabendazole are examples of specific compounds for the treatment of trematode infections (flukes).

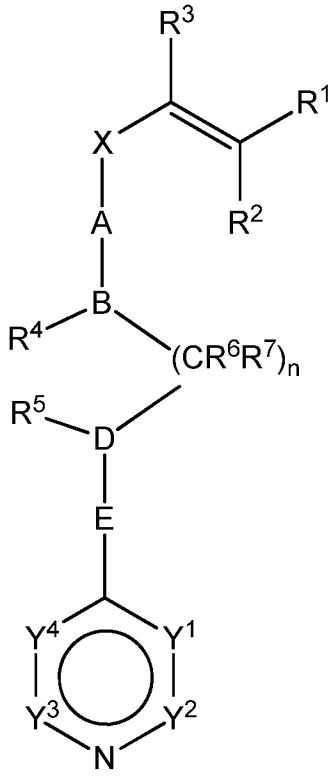
[0004] While many parasitic infections can be treated with known drugs, evolutionary development of resistance by the parasites can render such drugs obsolete over time, see, *e.g.,* Jabbar, A., et al., "Anthelmintic resistance: the state of play revisited," Life Sciences, 79, 2413-31 (2006). In addition, known drugs may have other deficiencies, such as limited spectrum of activity and the need for repeated treatments.

[0005] In WO 2008/028689 A1 certain N-(1-phtalazin-1-ylpiperidin-4-yl)-amides are described as EP2 receptor modulators. WO 2008/028691 A1 discloses as EP2 receptors certain N-(1-hetaryl-piperidin-4-yl)(het)arylamides.

[0006] There still exists a need for new medicaments, such as antiparasitic agents to ensure safe, effective, and convenient treatment of a wide range of parasitic helminth infections over a long period of time.

SUMMARY OF THE INVENTION

[0007] Briefly, this invention relates to compounds that can generally be used as a medicament for animals. The compounds correspond in structure to formula (I) or its pharmaceutically acceptable salts, solvates, N-oxides or prodrugs



Formula (I)

, wherein

R^1 is halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, SF_5, C_1-C_6-alkyl sulfonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,

R^2 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6- alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,

R^3 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^4 is hydrogen, C_1-C_6-alkyl or cycloalkyl preferably hydrogen,

R^5 is hydrogen, C_1-C_6-alkyl, cycloalkyl, acyl or C_1-C_6-alkyloxycarbonyl,

R^6 is hydrogen, C_1-C_6-alkyl, cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy, C_1-C_6-alkyloxy or cycloalkyloxy

R^7 is hydrogen, C_1-C_6-alkyl or cycloalkyl

or R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cycloalkyl radicals,

n is an integer from 1 to 3,

X is a carbonyl, thiocarbonyl or sulfonyl group, preferably a carbonyl group,

A is a bond or NR^8, wherein R^8 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

E is a bond or NR^9, wherein R^9 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

B is N or CR^{10}, wherein R^{10} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

D is N or CR^{11}, wherein R^{11} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl,

Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

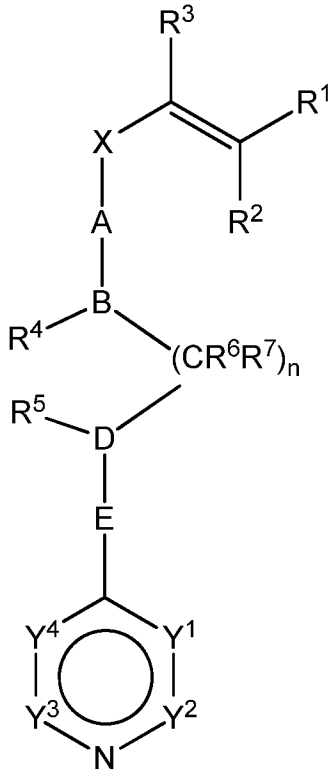
Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio" C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system,
and wherein at least one of B and D is a nitrogen atom.

[0008] This invention also relates to compounds according to formula (I a) or its pharmaceutically acceptable salts, solvates or N-oxides



Formula (I a)

, wherein

R^1 is hydrogen, halogen, C_1-C_6-alkyl, cycloalkyl, C_1-C_6-alkyloxy, cycloalkyloxy, C_1-C_6-alkylthio, cycloalkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, cycloalkyloxy C_1-C_6-alkyl, C_1-C_6-alkyloxy cycloalkyl, cycloalkyloxy cycloalkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, cycloalkylthio C_1-C_6-alkyl, C_1-C_6-alkylthio cycloalkyl, cycloalkylthio cycloalkyl, amino, C_1-C_6-alkylamino, cycloalkylamino, di-(C_1-C_6-alkyl)amino, di-(cycloalkyl)amino, C_1-C_6-alkylamino-C_1-C_6-alkyl, cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-alkylamino-cycloalkyl, cycloalkylamino-cycloalkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-cycloalkyl, di-(cycloalkyl)amino-C_1-C_6-alkyl, di-(cycloalkyl)amino-cycloalkyl, C_1-C_6-alkyl carbonyl, cycloalkylcarbonyl, C_1-C_6-alkyloxy carbonyl, cycloalkoxy carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms, or R^1 is phenyl, furanyl, imidazolinyl, or thiophenyl, wherein each of the rings optionally is substituted by one or more radicals from the group of C_1-C_6-alkyl, cycloalkyl and halogen, preferably fluorine,

R^2 is hydrogen, halogen, C_1-C_6-alkyl, cycloalkyl, C_1-C_6-alkyloxy, cycloalkyloxy, C_1-C_6-alkylthio, cycloalkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, cycloalkyloxy C_1-C_6-alkyl, C_1-C_6-alkyloxy cycloalkyl, cycloalkyloxy cycloalkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, cycloalkylthio C_1-C_6-alkyl, C_1-C_6-alkylthio cycloalkyl, cycloalkylthio cycloalkyl, amino, C_1-C_6-alkylamino, cycloalkylamino, di-(C_1-C_6-alkyl)amino, di-(cycloalkyl)amino, C_1-C_6-alkylamino-C_1-C_6-alkyl, cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-alkylamino-cycloalkyl, cycloalkylamino-cycloalkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-cycloalkyl, di-(cycloalkyl)amino-C_1-C_6-alkyl, di-(cycloalkyl)amino-cycloalkyl, C_1-C_6-alkyl carbonyl, cycloalkylcarbonyl, C_1-C_6-alkyloxy carbonyl, cycloalkoxy carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms, or R^1 is phenyl, furanyl, imidazolinyl, or thiophenyl, wherein each of the rings optionally is substituted by one or more radicals from the group of C_1-C_6-alkyl, cycloalkyl and halogen, preferably fluorine, preferably R^2 is hydrogen,

R^3 is hydrogen, C_1-C_6-alkyl or cycloaolkyl, preferably hydrogen,

R^4 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^5 is hydrogen, C_1-C_6-alkyl, cycloalkyl or acyl,

R^6 is hydrogen, C_1-C_6-alkyl, cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alky-

loxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxyl, C_1-C_6-alkyloxy or cycloalkoxy,

R^7 is hydrogen, C_1-C_6-alkyl or cycyloalkyl,

or R^6 and R^7 together represent an oxo-group or a thioxo-group, or R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cycloalkyl radicals,

n is an integer from 1 to 3,

X is a carbonyl or sulfonyl group, preferably a carbonyl group,

A is a bond or NR^8, wherein R^8 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

E is a bond or NR^9, wherein R^9 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

B is N or CR^{10}, wherein R^{10} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

Dis N or CR^{11}, wherein R^{11} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl

Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycyloalkyl,

Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system,

and wherein at least one of B and D is a nitrogen atom

for treating a helminth infection.

[0009] The compounds of the formula (I) and pharmaceutically acceptable solvates, N-oxides, salts and prodrugs thereof are hereinafter together referred to as "compound(s) according to this invention".

[0010] The use of the compounds according to formula (I a) and pharmaceutically acceptable solvates, N-oxides and salts thereof is hereinafter referred to as "use according to the invention". The compounds according to formula (I a) are hereinafter referred to as "compound(s) corresponding to the use according to the invention".

[0011] This invention is directed, in part, to a novel compound of the formula (I) and pharmaceutically acceptable solvates, N-oxides and salts thereof, and its use as a medicament, preferably a medicament for animals, e.g. for treating parasitic infections such as helminth infections in animals. This invention also is directed, in part, to using at least one compound of the formula (I) and pharmaceutically acceptable solvates, N-oxides and salts thereof to prepare a medicament for treating an infection including diseases caused by such infections (e.g., parasitoses caused by a helminth infection) in animals.

[0012] This invention also is directed, in part, to methods of making the novel N-heteroaryl compounds, and interme-

diates thereof. The preferred embodiments specified in this description for the compounds represent likewise preferred embodiments for the intermediates.

[0013] This invention also is directed, in part, to pharmaceutical compositions. The pharmaceutical compositions comprise a) at least one N-heteroaryl compound according to this invention, and b) at least one excipient, and/or at least one active compound (preferably anthelmintic compound) which differs in structure from the component a).

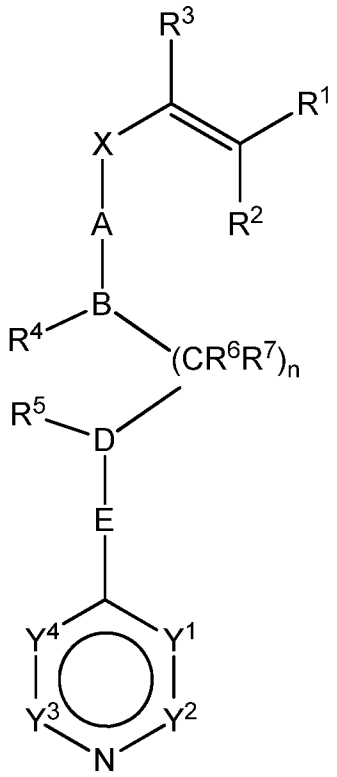
[0014] This invention also is directed, in part, to a kit. The kit comprises at least one N-heteroaryl compound according to this invention. In addition, the kit comprises at least one other component, such as another ingredient (e.g., an excipient or active ingredient), and/or an apparatus for combining the compound with another ingredient, and/or an apparatus for administering the compound, and/or a diagnostic tool.

[0015] Further benefits of Applicants' invention will be apparent to one skilled in the art from reading this specification.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Compounds according to this invention

[0016] The present invention also relates to compounds according to formula (I b) and pharmaceutically acceptable solvates, N-oxides, salts and prodrugs thereof and their use as a medicament.



Formula (Ib)

In the compounds of the formula (I b) the radicals, indices and groups have the following meanings:

R^1 is halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms

R^2 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6- alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atom

R^3 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^4 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^5 is hydrogen, C_1-C_6-alkyl, cyclcoalkyl or acyl

R^6 is hydrogen, C_1-C_6-alkyl, cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy, C_1-C_6-alkyloxy or cycloalkyloxy

R^7 is hydrogen, C_1-C_6-alkyl or cycloalkyl,

or R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cycloalkyl radicals,

n is an integer from 1 to 3

X is is a carbonyl or sulfonyl group, preferably a carbonyl group,

A is a bond or NR^8, wherein R^8 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

E is a bond or NR^9, wherein R^9 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

B is N or CR^{10}, wherein R^{10} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

D is N or CR^{11}, wherein R^{11} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl ,phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system, and wherein at least one of B and D is a nitrogen atom.

[0017] For a compound of formula (Ib), the radicals, indices and groups may have the following additional meaning (leading to compounds referred to here-beneath as "additional comound(s)"):

A first additional compound wherein R^1 is SF_5, a second additional compound wherein X is thiocarbonyl and a third additional compound wherein R^1 is SF_5 and X is thiocarbonyl.

[0018] For a next additional compound of any of the additional compounds mentioned here-above or beneath, R^1 may be a C_1-C_6-alkyl sulfonyl.

[0019] For a next additional compound of any of the additional compounds mentioned here-above or beneath, R^5 is C_1-C_6-alkyloxycarbonyl.

[0020] For next additional compounds of any of the additional compounds mentioned here-above or beneath, Y^1 is C wherein C is substituted by R^{12} which is C_1-C_6-alkenyl, or Cycloalkyl, or Cycloalkyloxy, or Cycloalkylamino, or (C_1-C_6-alkyl)-(Cycloalkyl)amino, or Cycloalkylthio or C_1-C_6-haloalkylthio.

[0021] For next additional compounds of any of the additional compounds mentioned here-above or beneath, Y^2 is C

wherein C is substituted by R^{13} which is C_1-C_6-alkenyl, or Cycloalkyl, or Cycloalkyloxy, or Cycloalkylamino, or (C_1-C_6-alkyl)-(Cycloalkyl)amino, or Cycloalkylthio or C_1-C_6-haloalkylthio.

[0022] For next additional compounds of any of the additional compounds mentioned here-above or beneath, Y^3 is C wherein C is substituted by R^{14} which is C_1-C_6-alkenyl, or Cycloalkyl, or Cycloalkyloxy, or Cycloalkylamino, or (C_1-C_6-alkyl)-(Cycloalkyl)amino, or Cycloalkylthio or C_1-C_6-haloalkylthio.

[0023] For next additional compounds of any of the additional compounds mentioned here-above, Y^4 is C wherein C is substituted by R^{15} which is C_1-C_6-alkenyl, or Cycloalkyl, or Cycloalkyloxy, or Cycloalkylamino, or (C_1-C_6-alkyl)-(Cycloalkyl)amino, or Cycloalkylthio or C_1-C_6-haloalkylthio.

[0024] The compounds accoridng to formula (Ib) and the additional compounds are also included in the terms "compounds according to this invention".

[0025] The present invention also relates to compounds of formula (I) and pharmaceutically acceptable solvates, N-oxides, salts and prodrugs thereof and their use as a medicament. In the compounds of the formula (I) the radicals, indices and groups have the following meanings:

R^1 is halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, SF_5, C_1-C_6-alkyl sulfonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,

R^2 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6- alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms

R^3 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen.

X is a carbonyl, thiocarbonyl or sulfonyl group, preferably a carbonyl group.

R^4 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen.

R^5 is hydrogen, C_1-C_6-alkyl, cycloalkyl, acyl or C_1-C_6-alkyloxycarbonyl.

R^6 is hydrogen, C_1-C_6-alkyl, cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy, C_1-C_6-alkyloxy or cycloalkyloxy. Preferably R^6 is hydrogen, C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), phenyl, phenyl C_1-C_6-alkyl, more preferably R^6 is hydrogen or C_1-C_6-alkyl.

R^7 is hydrogen, C_1-C_6-alkyl or cyclcoalkyl, preferably hydrogen.

[0026] Alternatively R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cycloalkyl radicals.

[0027] If R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group a spiro compound is formed, wherein said C_1-C_3-alkylene groups are preferably ethylene groups. One or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cyclcoalkyl radicals.

[0028] The group $(CR^6R^7)_n$ represents a C_1-C_3-alkylene group, preferably an ethylene group, which is unsubstituted or is substituted by R^7 = C_1-C_6-alkyl and/or by R^6 = C_1-C_6-alkyl, Cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, or phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy or C_1-C_6-alkyloxy, preferably the group $(CR^6R^7)_n$ represents a C_1-C_3-alkylene group, preferably an ethylene group, which is unsubstituted or substituted by C_1-C_6-alkyl.

[0029] The substructure A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a chain of 3 to 7 chain atoms, preferably of 4 to 6 chain atoms. In a preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents an ethylenediamine, propylenediamine or butylenediamine chain, which is unsubstituted or substituted as defined in formula (I) above.

[0030] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a semicarbazide chain with B(R^4), D(R^5) and E being NH, A being a bond, n=1, and R^6 and R^7 forming an oxo-group.

[0031] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a semicarbazide chain with B(R^4), D(R^5) and A being NH, E being a bond, n=1, and $R^6$and R^7 forming an oxo-group.

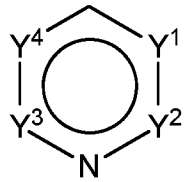
[0032] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a thiosemicarbazide chain with B(R^4), D(R^5) and E being NH, A being a bond, n=1, and $R^6$and R^7 forming a thioxo-group.

[0033] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a thiosemicarbazide chain with B(R^4), D(R^5) and A being NH, E being a bond, n=1, and $R^6$and R^7 forming a thioxo-group.

[0034] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents an ethylamine or propylamine chain with A and E being a bond, B being N, D(R^5) being CH_2, CH(C_1-C_6-alkyl) or C(C_1-C_6-alkyl)$_2$, and n = 1 or 2.

[0035] The integer n is from 1 to 3, and is preferably 2. If n is larger than 1 the CR^6R^7-groups can be identical or different.

[0036] The group of the formula (A) in formula (I) and formula (II)



Formula (A)

represents a mono- or polycyclic heterocyclic ring system. A monocyclic ring system is obtained if the carbon/nitrogen atoms Y^1, Y^2, Y^3 and Y^4 are unsubstituted or substituted but not joined together. A polycyclic ring system is obtained if either Y^1 and Y^2 are joined together or Y^3 and Y^4 are joined together or both Y^1 and Y^2 as well as Y^3 and Y^4 are joined together.

[0037] A ring system formed by joining together Y^1 and Y^2 is a saturated or non-saturated ring system (e.g. an aromatic ring system). The ring system itself is a monocyclic or polycyclic ring system, preferably a monocyclic, bicyclic or tricyclic, preferably a monocyclic or bicyclic ring system. The ring system contains from 4 to 10 ring atoms, preferably from 5 to 8 ring atoms, more preferably from 5 to 6 ring atoms, wherein the number of ring atoms includes Y^1 and Y^2. The ring system optionally contains one or more, preferably one, two or three, more preferably one or two, ring heteroatoms, such as nitrogen, sulfur or oxygen. The ring system is unsubstituted or substituted, preferred substituents are one or more, preferably one, two or three, more preferably one or two, radicals selected from the group of C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkoxycarbonyl and C_1-C_6-alkylthio.

[0038] A ring system formed by joining together Y^3 and Y^4 is a saturated or non-saturated ring system (e.g. an aromatic ring system). The ring system itself is a monocyclic or polycyclic ring system, preferably a monocyclic, bicyclic or tricyclic, preferably a monocyclic or bicyclic ring system. The ring system contains from 4 to 10 ring atoms, preferably from 5 to 8 ring atoms, more preferably from 5 to 6 ring atoms, wherein the number of ring atoms includes Y^3 and Y^4. The ring system optionally contains one or more, preferably one, two or three, more preferably one or two, ring heteroatoms, such as nitrogen, sulfur or oxygen. The ring system is unsubstituted or substituted, preferred substituents are one or more, preferably one, two or three, more preferably one or two, radicals selected from the group of C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkoxycarbonyl and C_1-C_6-alkylthio.

[0039] The mentioning of the preferred embodiments of the ring system formed by joining together Y^1 and Y^2 and/or Y^3 and Y^4 is intended to disclose all combinations of the preferred embodiments, including but not limited to a saturated, monocyclic, bicyclic or tricyclic ring system with 4 to 10 ring atoms, one, two or three ring heteroatoms from the group of nitrogen, sulphur and oxygen, which is unsubstituted or substituted by one or two radicals from the group of C_1-C_6-alkyl, C_1-C_6-alkyloxy and C_1-C_6-alkylthio, or an unsaturated, monocyclic or bicyclic ring system with 5 to 6 ring atoms, one or two ring heteroatoms, which is unsubstituted, etc.

[0040] The group of the formula (A) preferably represents a pyridine (Y^1, Y^2, Y^3 and Y^4 are C), pyrimidine, quinoline, quinazoline, thienopyrimidine, thienopyridine, triazolopyrimidine, pyridopyridine, pyrrolopyridine, pyrazolopyrimidine, pyrazolopyridine, furopyridine, 2,3-dihydrofuropyridine, 2,3-dihydro-1,4-dioxinopyridine, furopyrimidine, pyridazine or cinnoline group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, halogen, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0041] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group, wherein each group is optionally substituted by one or more radicals, preferably

by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0042] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group (preferably a pyridine, pyrimidine or quinoline group), wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0043] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0044] In another preferred embodiment the group of formula (A) is a pyridine or quinoline group, preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0045] In another preferred embodiment the group of formula (A) is a pyrimidine group, which is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio.

[0046] In another preferred embodiment of all of the embodiments of compounds according to the invention as described here-in, in the group of formula (A) no more than one of R^{12}, R^{13}, R^{14} and R^{15} represents a halogen atom, more preferably the group of formula (A) contains no more than one halogen atom in total.

[0047] Preferably at least two of A, B, D and E contain a nitrogen atom. More preferably at least one of A and B and at least one of D and E contains a nitrogen atom, even more preferred one of A and B and one of D and E contains a nitrogen atom.

[0048] In some embodiments each of A, B, D and E contains a nitrogen atom. In other embodiments each of A, B and D, or each of A, B and E, or each of A, D and E, or each of B, D and E contains a nitrogen atom. In still other embodiments each of A and D, or each of B and E, or each of B and D contains a nitrogen atom.

[0049] In some embodiments B is N, D is N and each of A and E is a bond. In other embodiments A is NR^8, B is CR^{10}, D is N, and E is a bond, or A is NR^8, B is N, D is N and E is a bond, or A is a bond, B is N, D is N and E is NR^9, or A is a bond, B is N, D is CR^{11} and E is NR^9, wherein R^8 to R^{11} are as defined above.

[0050] In a preferred compound of formula (I)

R^1 is halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, SF_5, C_1-C_6-alkyl sulfonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,
R^2 is hydrogen,
R^3 is hydrogen,
R^4 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^5 is hydrogen, C_1-C_6-alkyl, acyl or C_1-C_6-alkyloxycarbonyl,
$(CR^6R^7)_n$ is a C_1-C_3-alkylene group, preferably an ethylene group, which is optionally substituted by one or more C_1-C_6-alkyl radicals,
A is a bond or NR^8, wherein R^8 is H or C_1-C_6-alkyl,
E is a bond or NR^9, wherein R^9 is H or C_1-C_6-alkyl,
B is N or CR^{10}, wherein R^{10} is H or C_1-C_6-alkyl,
D is N or CR^{11}, wherein R^{11} is H or C_1-C_6-alkyl,
X is a carbonyl, thiocarbonyl or sulfonyl group, preferably a carbonyl group,
Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cy-

cloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

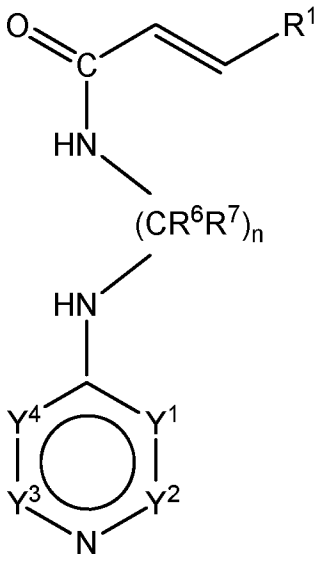
Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system,
and wherein at least one of B and D is a nitrogen atom.

[0051] A preferred compound has the formula (II),



Formula (II)

, wherein

R^1 is C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, or C_1-C_6-alkylthio C_1-C_6-alkyl, wherein each of the carbon-containing radicals is unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms,

R^6 is hydrogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy or C_1-C_6-alkyloxy, preferably R^6 is hydrogen, C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), phenyl, phenyl C_1-C_6-alkyl, more preferably R^6 is hydrogen or C_1-C_6-alkyl, even more preferably hydrogen,
R^7 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
n is 2 or 3, preferably 2,
Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, Cycloalkyl, Cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl,
Y^2 is C or N, preferably C, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, Cycloalkyl, Cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^3 is C or N, preferably C, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, Cycloalkyl, Cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^4 is C or N, preferably C, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a 5- or 6-membered ring system.

[0052] In a preferred compound of the formula (II)

R^1 is C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, or C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkylamino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, wherein each of the carbon-containing radicals unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms,
Y^1 is C or N, wherein C is substituted by R^{12} which is H, or C_1-C_6-alkyl,
Y^2 is C, wherein C is substituted by R^{13} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkyl carbonyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-alkylthio,
Y^3 is C, wherein C is substituted by R^{14} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkyl carbonyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-alkylthio,
Y^4 is C, wherein C is substituted by R^{15} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio,

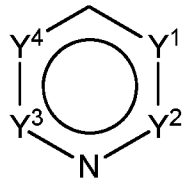
or Y^1 and Y^2 or Y^3 and Y^4 are joined together to form a 5- or 6-membered ring system.

[0053] In a preferred compound of the formula (I) or (II)
R^2 is hydrogen,
R^3 is hydrogen,
R^4 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^5 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^6 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^7 is hydrogen,
X is a carbonyl group,
n is 2,
the group of formula (A) represents a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, more preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, Cycloalkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholi-

nyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl, and
one of A and B and one of D and E contains a nitrogen atom.

[0054] In another preferred compound of the formula (I) or (II)
R^1 is C_1-C_6-alkyl which is unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms.

[0055] In another preferred compound of the formula (II) the group of the formula (A)



Formula (A)

represents a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine, thienopyridine, triazolopyrimidine, pyridopyridine, pyrrolopyridine, pyrazolopyrimidine, pyrazolopyridine, furopyridine, 2,3-dihydrofuropyridine, 2,3-dihydro-1,4-dioxinopyridine, furopyrimidine, pyridazine or cinnoline group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, Cycloalkyl, Cycloalkoxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0056] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0057] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group (preferably a pyridine, pyrimidine or quinoline group), wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0058] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl, and preferably .selected from the group of C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio.

[0059] In another preferred embodiment the group of formula (A) is a pyridine or quinoline group, preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0060] In another preferred embodiment the group of formula (A) is a pyrimidine group, which is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio.

Use according to this invention

[0061] The present invention also relates to compounds of formula (Ia) and pharmaceutically acceptable solvates, N-oxides and salts thereof and their use for treating a helminth infection In the compounds of the formula (Ia) the radicals, indices and groups have the following meanings:

R^1 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, amino, C_1-C_6-alkylamino, di-(C_1-C_6-alkyl)amino, C_1-C_6-alkylamino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_1-C_6-alkyloxy carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms, or R^1 is phenyl, furanyl, imidazolinyl, or thiophenyl, wherein each of the rings optionally is substituted by one or more radicals from the group of C_1-C_6-alkyl and halogen, preferably fluorine,
R^2 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, amino, C_1-C_6-alkylamino, di-(C_1-C_6-alkyl)amino, C_1-C_6-alkylamino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_1-C_6-alkyloxy carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms, or R^2 is phenyl, furanyl, imidazolinyl, or thiophenyl, wherein each of the rings optionally is substituted by one or more radicals from the group of C_1-C_6-alkyl and halogen, preferably fluorine, preferably R^2 is hydrogen,
R^3 is hydrogen or C_1-C_6-alkyl, preferably hydrogen.
X is a carbonyl or sulfonyl group, preferably a carbonyl group.
R^4 is hydrogen or C_1-C_6-alkyl, preferably hydrogen.
R^5 is hydrogen, C_1-C_6-alkyl or acyl, preferably hydrogen.
R^6 is hydrogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy or C_1-C_6-alkyloxy. Preferably R^6 is hydrogen, C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), phenyl, phenyl C_1-C_6-alkyl, more preferably R^6 is hydrogen or C_1-C_6-alkyl.
R^7 is hydrogen or C_1-C_6-alkyl, preferably hydrogen.

[0062] Alternatively R^6 and R^7 together represent an oxo-group or a thioxo-group or R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl radicals.

[0063] If R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group a spiro compound is formed, wherein said C_1-C_3-alkylene groups are preferably ethylene groups. One or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl radicals.

[0064] The group (CR^6R^7)n represents a C_1-C_3-alkylene group, preferably an ethylene group, which is unsubstituted or is substituted by R^7 = C_1-C_6-alkyl and/or by R^6 = C_1-C_6-alkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, or phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy or C_1-C_6-alkyloxy, preferably the group $(CR^6R^7)_n$ represents a C_1-C_3-alkylene group, preferably an ethylene group, which is unsubstituted or substituted by C_1-C_6-alkyl.

[0065] The substructure A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a chain of 3 to 7 chain atoms, preferably of 4 to 6 chain atoms. In a preferred embodiment A-B(R^4)-(CR^6R^77)$_n$-D(R^5)-E represents an ethylenediamine, propylenediamine or butylenediamine chain, which is unsubstituted or substituted as defined in formula (I) above.

[0066] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a semicarbazide chain with B(R^4), D(R^5) and E being NH, A being a bond, n=1, and R^6 and R^7 forming an oxo-group.

[0067] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a semicarbazide chain with B(R^4), D(R^5) and A being NH, E being a bond, n=1, and R^6 and R^7 forming an oxo-group.

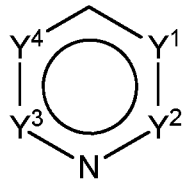
[0068] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a thiosemicarbazide chain with B(R^4), D(R^5) and E being NH, A being a bond, n=1, and R^6 and R^7 forming a thioxo-group.

[0069] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents a thiosemicarbazide chain with B(R^4), D(R^5) and A being NH, E being a bond, n=1, and R^6 and R^7 forming a thioxo-group.

[0070] In another preferred embodiment A-B(R^4)-(CR^6R^7)$_n$-D(R^5)-E represents an ethylamine or propylamine chain with A and E being a bond, B being N, D(R^5) being CH_2, CH(C_1-C_6-alkyl) or C(C_1-C_6-alkyl)$_2$, and n = 1 or 2.

[0071] The integer n is from 1 to 3, and is preferably 2. If n is larger than 1 the CR^6R^7-groups can be identical or different.

[0072] The group of the formula (A) in formula (Ia)



Formula (A)

represents a mono- or polycyclic heterocyclic ring system. A monocyclic ring system is obtained if the carbon/nitrogen atoms Y^1, Y^2, Y^3 and Y^4 are unsubstituted or substituted but not joined together. A polycyclic ring system is obtained if either Y^1 and Y^2 are joined together or Y^3 and Y^4 are joined together or both Y^1 and Y^2 as well as Y^3 and Y^4 are joined together.

[0073] A ring system formed by joining together Y^1 and Y^2 is a saturated or non-saturated ring system (e.g. an aromatic ring system). The ring system itself is a monocyclic or polycyclic ring system, preferably a monocyclic, bicyclic or tricyclic, preferably a monocyclic or bicyclic ring system. The ring system contains from 4 to 10 ring atoms, preferably from 5 to 8 ring atoms, more preferably from 5 to 6 ring atoms, wherein the number of ring atoms includes Y^1 and Y^2. The ring system optionally contains one or more, preferably one, two or three, more preferably one or two, ring heteroatoms, such as nitrogen, sulfur or oxygen. The ring system is unsubstituted or substituted, preferred substituents are one or more, preferably one, two or three, more preferably one or two, radicals selected from the group of C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkoxycarbonyl and C_1-C_6-alkylthio.

[0074] A ring system formed by joining together Y^3 and Y^4 is a saturated or non-saturated ring system (e.g. an aromatic ring system). The ring system itself is a monocyclic or polycyclic ring system, preferably a monocyclic, bicyclic or tricyclic, preferably a monocyclic or bicyclic ring system. The ring system contains from 4 to 10 ring atoms, preferably from 5 to 8 ring atoms, more preferably from 5 to 6 ring atoms, wherein the number of ring atoms includes Y^3 and Y^4. The ring system optionally contains one or more, preferably one, two or three, more preferably one or two, ring heteroatoms, such as nitrogen, sulfur or oxygen. The ring system is unsubstituted or substituted, preferred substituents are one or more, preferably one, two or three, more preferably one or two, radicals selected from the group of C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkoxycarbonyl and C_1-C_6-alkylthio.

[0075] The mentioning of the preferred embodiments of the ring system formed by joining together Y^1 and Y^2 and/or Y^3 and Y^4 is intended to disclose all combinations of the preferred embodiments, including but not limited to a saturated, monocyclic, bicyclic or tricyclic ring system with 4 to 10 ring atoms, one, two or three ring heteroatoms from the group of nitrogen, sulphur and oxygen, which is unsubstituted or substituted by one or two radicals from the group of C_1-C_6-alkyl, C_1-C_6-alkyloxy and C_1-C_6-alkylthio, or an unsaturated, monocyclic or bicyclic ring system with 5 to 6 ring atoms, one or two ring heteroatoms, which is unsubstituted, etc.

[0076] The group of the formula (A) preferably represents a pyridine (Y^1, Y^2, Y^3 and Y^4 are C), pyrimidine, quinoline, quinazoline, thienopyrimidine, thienopyridine, triazolopyrimidine, pyridopyridine, pyrrolopyridine, pyrazolopyrimidine, pyrazolopyridine, furopyridine, 2,3-dihydrofuropyridine, 2,3-dihydro-1,4-dioxinopyridine, furopyrimidine, pyridazine or cinnoline group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, halogen, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0077] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, diox-

olane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0078] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group (preferably a pyridine, pyrimidine or quinoline group), wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0079] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0080] In another preferred embodiment the group of formula (A) is a pyridine or quinoline group, preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0081] In another preferred embodiment the group of formula (A) is a pyrimidine group, which is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio.

[0082] In another preferred embodiment of all embodiments of the use according to the invention, in the group of formula (A) no more than one of R^{12}, R^{13}, R^{14} and R^{15} represents a halogen atom, more preferably the group of formula (A) contains no more than one halogen atom in total.

[0083] Preferably at least two of A, B, D and E contain a nitrogen atom. More preferably at least one of A and B and at least one of D and E contains a nitrogen atom, even more preferred one of A and B and one of D and E contains a nitrogen atom.

[0084] In some embodiments each of A, B, D and E contains a nitrogen atom. In other embodiments each of A, B and D, or each of A, B and E, or each of A, D and E, or each of B, D and E contains a nitrogen atom. In still other embodiments each of A and D, or each of B and E, or each of B and D contains a nitrogen atom.

[0085] In some embodiments B is N, D is N and each of A and E is a bond. In other embodiments A is NR^8, B is CR^{10}, D is N, and E is a bond, or A is NR^8, B is N, D is N and E is a bond, or A is a bond, B is N, D is N and E is NR^9, or A is a bond, B is N, D is CR^{11} and E is NR^9, wherein R^8 to R^{11} are as defined above.

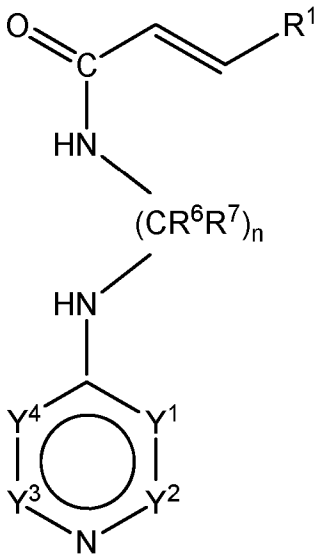
[0086] In a preferred compound of formula (Ia)

R^1 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkylamino, di-(C_1-C_6-alkyl)amino, C_1-C_6-alkylamino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_1-C_6-alkyloxy carbonyl, or C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,
R^2 is hydrogen,
R^3 is hydrogen,
R^4 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^5 is hydrogen, C_1-C_6-alkyl or acyl,
$(CR^6R^7)_n$ is a C_1-C_3-alkylene group, preferably an ethylene group, which is optionally substituted by one or more C_1-C_6-alkyl radicals,
A is a bond or NR^8, wherein R^8 is H or C_1-C_6-alkyl,
E is a bond or NR^9, wherein R^9 is H or C_1-C_6-alkyl,
B is N or CR^{10}, wherein R^{10} is H or C_1-C_6-alkyl,
D is N or CR^{11}, wherein R^{11} is H or C_1-C_6-alkyl,
Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system,
and wherein two of A, B, D and E contain a nitrogen atom and at least one of B and D is a nitrogen atom, preferably B and D represent a nitrogen atom and A and E are a bond.

[0087] A preferred compound for use according to the invention has the formula (II) as depicted immediately herebeneath,



Formula (II)

, wherein

R^1 is C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, or C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkylamino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, wherein each of the carbon-containing radicals is unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms,
R^6 is hydrogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy or C_1-C_6-alkyloxy, preferably R^6 is hydrogen, C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl

C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), phenyl, phenyl C_1-C_6-alkyl, more preferably R^6 is hydrogen or C_1-C_6-alkyl, even more preferably hydrogen,
R^7 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
n is 2 or 3, preferably 2,
Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, phenyl,
Y^2 is C or N, preferably C, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^3 is C or N, preferably C, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^4 is C or N, preferably C, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, phenyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a 5- or 6-membered ring system.

[0088] In a preferred compound of the formula (IIa)

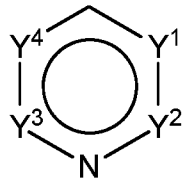
R^1 is C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, or C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkylamino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, wherein each of the carbon-containing radicals unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms,
Y^1 is C or N, wherein C is substituted by R^{12} which is H, or C_1-C_6-alkyl,
Y^2 is C, wherein C is substituted by R^{13} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkyl carbonyl,
Y^3 is C, wherein C is substituted by R^{14} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkyl carbonyl,
Y^4 is C, wherein C is substituted by R^{15} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy,

or Y^1 and Y^2 or Y^3 and Y^4 are joined together to form a 5- or 6-membered ring system.

[0089] In a preferred compound of the formula (I a) or (IIa)
R^2 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^3 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^4 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^5 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^6 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^7 is hydrogen,
X is a carbonyl group,
n is 2,
the group of formula (A) represents a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, more preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl, and
one of A and B and one of D and E contains a nitrogen atom.

[0090] In another preferred compound of the formula (Ia) or (IIa)
R^1 is C_1-C_6-alkyl which is unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms.

[0091] In another preferred compound of the formula (IIa) the group of the formula (A)



Formula (A)

represents a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine, thienopyridine, triazolopyrimidine, pyridopyridine, pyrrolopyridine, pyrazolopyrimidine, pyrazolopyridine, furopyridine, 2,3-dihydrofuropyridine, 2,3-dihydro-1,4-dioxinopyridine, furopyrimidine, pyridazine or cinnoline group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0092] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0093] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine or thienopyridine group (preferably a pyridine, pyrimidine or quinoline group), wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0094] In another preferred embodiment the group of formula (A) is a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl, and preferably .selected from the group of C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio.

[0095] In another preferred embodiment the group of formula (A) is a pyridine or quinoline group, preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each ring is unsubstituted or substituted by C_1-C_6-alkyl.

[0096] In another preferred embodiment the group of formula (A) is a pyrimidine group, which is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, amino, C_1-C_6-alkylamino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio.

Salts, Solvates, N-Oxides and Prodrugs

[0097] A salt of the compounds of the formula (I), (Ia) or (Ib), or another compound may be advantageous due to one or more of the salt's physical properties, such as pharmaceutical stability in differing temperatures and humidities; crystalline properties; and/or a desirable solubility in water, oil, or other solvent. In some instances, a salt may be used as an aid in the isolation, purification, and/or resolution of the compound. Acid and base salts can typically be formed by, for example, mixing the compound with an acid or base, respectively, using various known methods in the art. To the extent a salt of the compound is intended to be administered *in vivo* (*i.e.* to an animal) for a therapeutic benefit, the salt is pharmaceutically acceptable.

[0098] Salts may also be of advantage in the synthesis of the compounds according to this invention. For instance

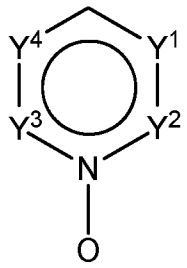
certain intermediates may advantagously be used in form of their salts in the preparation process of the compounds according to this invention.

[0099] In general, an acid addition salt can be prepared by reacting a free base compound with an approximately stoichiometric amount of an inorganic or organic acid. Examples of often suitable inorganic acids for making (pharmaceutically acceptable) salts include hydrochloric, hydrobromic, hydroiodic, nitric, carbonic, sulfuric, and phosphoric acid. Examples of often suitable organic acids for making (pharmaceutically acceptable) salts generally include, for example, aliphatic, cycloaliphatic, aromatic, araliphatic, heterocyclic, carboxylic, and sulfonic classes of organic acids. Specific examples of often suitable organic acids include cholic, sorbic, lauric, acetic, trifluoroacetic, formic, propionic, succinic, glycolic, gluconic, digluconic, lactic, malic, tartaric acid, citric, ascorbic, glucuronic, maleic, fumaric, pyruvic, aspartic, glutamic, aryl carboxylic acid (*e.g.*, benzoic), anthranilic acid, mesylic, stearic, salicylic, p-hydroxybenzoic, phenylacetic, mandelic, embonic (pamoic), alkylsulfonic (*e.g.*, ethanesulfonic), arylsulfonic (*e.g.*, benzenesulfonic), pantothenic, 2-hydroxyethanesulfonic, sulfanilic, cyclohexylaminosulfonic, β-hydroxybutyric, galactaric, galacturonic, adipic, alginic, butyric, camphoric, camphorsulfonic, cyclopentanepropionic, dodecylsulfic, glycoheptanoic, glycerophosphic, heptanoic, hexanoic, nicotinic, 2-naphthalesulfonic, oxalic, palmoic, pectinic, 3-phenylpropionic, picric, pivalic, thiocyanic, tosylic, and undecanoic acid. In some such embodiments, for example, the salt comprises a trifluoroacetate, mesylate, or tosylate salt. In other embodiments, the salt comprises a hydrochloric acid salt.

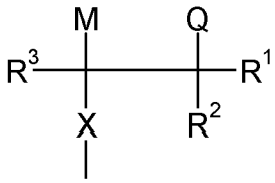
[0100] In general, a base addition salt can be prepared by reacting a free acid compound with an approximately stoichiometric amount of an inorganic or organic base. Examples of base addition salts may include, for example, metallic salts and organic salts. Metallic salts, for example, include alkali metal (group Ia) salts, alkaline earth metal (group IIa) salts, and other physiologically acceptable metal salts. Such salts may be made from aluminum, calcium, lithium, magnesium, potassium, sodium, and zinc. For example, a free acid compound may be mixed with sodium hydroxide to form such a base addition salt. Organic salts may be made from amines, such as trimethylamine, diethylamine, N,N'-dibenzylethylenediamine, chloroprocaine, ethanolamine, diethanolamine, ethylenediamine, meglumine (N-methylglucamine), and procaine. Basic nitrogen-containing groups may be quaternized with agents such as C_1-C_6-alkyl halides (*e.g.*, methyl, ethyl, propyl, and butyl chlorides, bromides, and iodides), dialkyl sulfates (*e.g.*, dimethyl, diethyl, dibuytl, and diamyl sulfates), long chain halides (*e.g.*, decyl, lauryl, myristyl, and stearyl chlorides, bromides, and iodides), arylalkyl halides (*e.g.*, benzyl and phenethyl bromides), and others.

[0101] A solvate of a compound of the formula (I), (Ia) or (Ib), or another compound may be formed by aggregation of said compound of the formula (I) with solvent molecules such as water, alcohols, for example ethanol, aromatic solvents such as toluene, ethers, halogenated organic solvents such as dichloromethane, preferably in a definite proportion by weight.

[0102] An N-oxide of a compound of the formula (I), (Ia) or (Ib), or another compound may be formed by oxidation of an N-atom in an amine or N-heterocycle such as pyridine by oxidation agents such as hydrogen peroxide, peracids or inorganic oxidation agents such as potassium peroxymonosulfate (oxone). In preferred N-oxides a nitrogen atom in the group of formula (A) is oxidized, more preferred are N-oxides wherein the nitrogen atom in the para-position is oxidized:



[0103] This invention also discloses prodrug derivatives of the compounds of
formula (I) and (Ib). The term prodrug refers to compounds that are transformed *in vivo* to yield the parent compound of formula (I) or (Ib). *In vivo* means that in the case of, for example, treatment of a parasitic infection this transformation can occur in the host organism and/or the parasite. Various forms of prodrugs are well known in the art. For example, if the group of formula (A) represents a pyridine, it is possible to form pyridinium salts such as, for example, acyloxyalkylpyridinium salts, which can offer advantages in terms of higher solubility for parenteral dosage forms, which are described in S. K. Davidsen et al., J. of Med. Chem. 37 4423-4429 (1994). Other examples of possible prodrugs are compounds that form the double bond present in formula (I) and (Ib) by elimination from a saturated precursor compound:



[0104] Elimination of MQ will generate compounds of formula (I) or (Ib). If M is hydrogen, this type of elimination is also known in the art as retro-Michael reaction or retro-Michael addition. Examples of such retro-Michael reactions that occur *in vivo* to generate unsaturated compounds are described in, for example, S. C. Alley, Bioconjugate Chem. 19, 759-765 (2008); D. Lopez, Abstracts of Papers, 231st National Meeting, Atlanta, GA, United States, March 26-30, 2006, MEDI-292.

Isomers

[0105] The compounds according to this invention, their intermediates and compounds corresponding to the use according to the invention, may exist in various isomeric forms. A reference to a compound according to this invention, an intermediate thereof or a compound corresponding to the use according to the invention always includes all possible isomeric forms of such compound.

[0106] In some embodiments, such compounds may have two or more isomers, such as optical isomers or conformational isomers. For example, the compounds can have a *cis* or *trans* configuration at the $-CXR^3=CR^1R^2$ double bond. In some preferred embodiments, such compound has the (*E*) configuration, in other embodiments, the compound has the (*Z*) configuration. In a preferred embodiment the compounds have (*E*) configuration. For instance the compounds of the formula (II), the compounds of Table A wherein $R^2 = R^3 = H$ and the compounds of Table B exhibit (*E*) configuration.

[0107] Unless otherwise stated, a compound structure that does not indicate a particular conformation is intended to encompass compositions of all the possible conformational isomers of the compound, as well as compositions comprising fewer than all the possible conformational isomers. In some embodiments, the compound is a chiral compound. In some embodiments, the compound is a non-chiral compound.

Compounds for use in the treatment of helminth infections

[0108] This section pertains to compounds according to the invention and compounds corresponding to the use according to the invention. The compounds and were applicable pharmaceutically acceptable solvates, N-oxides, salts and prodrugs thereof may generally be used as a medicament for animals. In some embodiments of this invention, one or more, preferably one compound according to this invention is administered to treat infections such as parasitic infections (*e.g.* helminth infections) of an animal (or make a medicament to treat infections such as parasitic infections of an animal). In one embodiment one or more, preferably one compound according to this invention is administered to treat parasitoses of an animal (or make a medicament to treat parasitoses of an animal). The use according to the invention is directed to treat helminth infections.

[0109] The term "(parasitic) infection" includes conditions associated with or caused by one or more (parasitic) pathogens; said conditions include clinical conditions (parasitoses) and sub-clinical conditions. The term "treatment of parasitic infection" thus includes both the treatment of parasitoses and the treatment of sub-clinical conditions. The treatment of a parasite infection generally implies the suppression of parasite (*e.g.* helminth) burdens in the animal below that level at which economic loss occurs.

[0110] Sub-clinical conditions are typically conditions not directly leading to clinical symptoms in the parasite infected animal but leading to economic losses. Such economic losses can be *e.g.* by depression of growth in young animals, lower feed efficiency, lower weight gain in meat producing animals, lower milk production in ruminants, lower egg production in laying hens, or lower wool-production in sheep.

[0111] The term "parasitoses" relates to clinically manifest pathologic conditions and diseases associated with or caused by an infection by one or more parasites, such as, for example parasitic gastroenteritis or anemia in ruminants *e.g.* sheep and goats or colic in horses.

[0112] In general, the prevention or treatment of parasitic infection including parasitoses is achieved by administering one or more, preferably one compound according to this invention to treat a parasitic infection such as a helminth infection, the latter treatment being the sole treatment of the use according to the invention.

[0113] Thus the invention provides a method of treating a (parasitic) infection such as a helminth infection, including parasitoses, which comprises administering to the animal an antiparasitically, preferably an anthelmintically, effective amount of one or more compounds according to this invention, or where applicable, a compound corresponding to the use according to the invention. Preferably nematode, cestode or trematode infections are treated, more preferably

nematode infections.

[0114] "Treating (parasitic) infections" includes treating parasitoses and means to partially or completely inhibit the development of (parasitic) infections of an animal susceptible to (parasitic) infection, reduce or completely eliminate the symptoms of infections of an animal having infections, and/or partially or completely cure infections of an animal having infections. This can be achieved by alleviating or reducing pathogen numbers such as parasite numbers in an animal.

[0115] The effect of the compounds according to this invention or the use according to the invention can be *e.g.* ovicidal, larvicidal, and/or adulticidal or a combination thereof. The effect can manifest itself directly, i.e. killing the parasites either immediately or after some time has elapsed, for example when molting occurs, or by destroying their eggs, or indirectly, *e.g.* reducing the number of eggs laid and/or the hatching rate. Alternatively the parasite is not killed but paralyzed and is then dislodged and excreted by the host animal.

[0116] In another aspect the present invention thus provides a pharmaceutical composition comprising an anthelmintically effective amount of one or more, preferably one compound according to this invention or a compound corresponding to the use according to the invention and one or more pharmaceutically acceptable excipients.

[0117] The compounds and pharmaceutical compositions according to this invention are useful in treating parasitic infections such as helminth infections of animals. An "effective amount," is the amount or quantity of a compound that is required to alleviate or reduce parasite numbers in an animal, and/or to inhibit the development of parasite infections in an animal, in whole or in part.

[0118] This amount is readily determined by observation or detection of the pathogen numbers such as parasite numbers both before and after contacting the sample of pathogens such as parasites including their stages with the compound according to this invention, directly and/or indirectly, *e.g.*, by contacting articles, surfaces, foliage, or animals with the compound *e.g.* the parasite count is reduced, after a first administration, by an amount ranging from 5% to about 100%.

[0119] This can be evaluated by counting parasites (especially helminthes) directly after necroscopy of the host animal.

[0120] The reduction of parasite numbers, especially gastrointestinal helminth parasites can be alternatively measured in-directly by faecal egg or differential larval counts. In this case the effective amount of the compound is determined by the reduction of the number of excreted helminth eggs or larvae in the faeces of the treated animal before and after treatment. For an *in vivo* administration the compound according to this invention, is preferably administered to an animal in an effective amount which is synonymous with "pharmaceutically effective amount" or "anthelmintically effective amount".

[0121] A single administration of a compound according to this invention or a compound corresponding to the use according to the invention is typically sufficient to treat a parasitic infection such as a helminth infection, preferably a nematode, cestode or trematode infection, more preferably a nematode infection. Although such a single dose is typically preferred, it is contemplated that multiple doses can be used. When the compound is orally administered, the total dose to treat a disease such as a helminth infection is generally greater than about 0.01 mg/kg (i.e., milligram of compound per kilogram body weight of the treated animal). In some such embodiments, the total dose is from about 0.01 to about 100 mg/kg, from about 0.01 to about 50 mg/kg, from about 0.1 to about 25 mg/kg, or from about 1 to about 20. For sheep, for example, the dose is generally from about 0.5 to about 15 mg/kg, from about 1 to about 10 mg/kg. The same dose range may be suitable for other dosage routes. For example, in some embodiments, the same dose range is used for subcutaneous administration. The desired dose, however, may be less in some instances where the compound according to this invention is administered intravenously.

[0122] If the compound according to this invention or a compound corresponding to the use according to the invention is administered parenterally via an injection, the concentration of the compound in the dosage form preferably is sufficient to provide the desired therapeutically effective amount of the compound in a volume that is acceptable for parenteral administration.

[0123] Factors affecting the preferred dosage may include, for example, the parasite species infection to be treated and the development stages of the parasites, the type (*e.g.*, species and breed), age, size, sex, diet, activity, and condition of the of the infected animal; the dosage route; pharmacological considerations, such as the activity, efficacy, pharmacokinetic, and toxicology profiles of the particular composition administered; and whether the compound being administered as part of a combination of active ingredients. Thus, the preferred amount of the compound can vary, and, therefore, can deviate from the typical dosages set forth above. Determining such dosage adjustments is generally within the skill of those in the art.

[0124] In a preferred embodiment the compounds according to this invention are used to treat a helminth infection, such as an infection caused by one or more helminths selected from the group consisting of a) cestodes: *e.g. Anaplocephala* spp.; *Dipylidium* spp.; *Diphyllobothrium* spp.; *Echinococcus* spp.; *Moniezia* spp.; *Taenia* spp.; b) trematodes *e.g. Dicrocoelium* spp.; *Fasciola* spp.; *Paramphistomum* spp.; *Schistosoma* spp.; or c) nematodes, *e.g. ; Ancylostoma* spp.; *Anecatorspp.*; *Ascaridia* spp.; *Ascaris* spp.; *Brugia* spp.; *Bunostomum* spp.; *Capillaria* spp.; *Chabertia* spp.; *Cooperia* spp.; *Cyathostomum* spp.; *Cylicocyclus* spp.; *Cylicodontophorus* spp.; *Cylicostephanus* spp.; *Craterostomum* spp.; *Dictyocaulus* spp.; *Dipetalonema* spp; *Dirofilaria* spp.; *Dracunculus* spp.; *Enterobius* spp.; *Filaroides* spp.; *Habronema* spp.;

Haemonchus spp.; *Heterakis* spp.; *Hyostrongylus* spp.; *Metastrongylus* spp.; *Meullerius* spp. *Necatorspp.*; *Nematodirus* spp.; *Nippostrongylus* spp.; *Oesophagostomum* spp.; *Onchocerca* spp.; *Ostertagia* spp.; *Oxyuris* spp.; *Parascaris* spp.;*Stephanurus* spp.; *Strongylus* spp.; *Syngamus* spp.; *Toxocara* spp.; *Strongyloides* spp.; *Teladorsagia* spp.; *Toxascaris* spp.; *Trichinella* spp.; *Trichuris* spp.; *Trichostrongylus* spp.; *Triodontophorous* spp.; *Uncinaria* spp., and/or *Wuchereria* spp.;

[0125] It is contemplated that the compounds according to this invention and compounds correspondng to the use according to the invention may be used to treat animals, including humans and non-human animals, especially non-human mammals. Such non-human mammals include, for example, livestock mammals (*e.g.*, swine, livestock ruminats like bovines, sheep, goats, etc.), laboratory mammals (*e.g.*, mice, rats, jirds, etc.), companion mammals (*e.g.*, dogs, cats, equines, etc.), and wild and zoo mammals (*e.g.*, buffalo, deer, etc.). It is contemplated that the compounds also are suitable to treat non-mammals, such as poultry (*e.g.*, turkeys, chickens, ducks, etc.) and fish (*e.g.*, salmon, trout, koi, etc.).

[0126] In some embodiments, one or more, preferably one compound according to this invention or a compound corresponding to the use according to the invention is used to treat an infection by a helminth, such as a nematode, cestode or trematode, preferably a nematode (such as *Haemonchus contortus*), that is resistant to one or more other anthelmintic agents. In some embodiments, the compound according to this invention is active against a helminth, such as a nematode, cestode or trematode, preferably a nematode such as *Haemonchus contortus,* that is resistant to one or more of the following anthelmintics: an avermectin (*e.g.*, ivermectin, selamectin, doramectin, abamectin, and eprinomectin); a milbemycin (moxidectin and milbemycin oxime); a pro-benzimidazole (*e.g.*, febantel, netobimin, and thiophanate); a benzimidazole derivative, such as a thiazole benzimidazole derivative (*e.g.*, thiabendazole and cambendazole) or a carbamate benzimidazole derivative (*e.g.*, fenbendazole, albendazole (oxide), mebendazole, oxfendazole, parbendazole, oxibendazole, flubendazole, and triclabendazole); an imidazothiazole (*e.g.*, levamisole and tetramisole); a tetrahydropyrimidine (morantel and pyrantel), an organophosphate (*e.g.*, trichlorphon, haloxon, dichlorvos, and naphthalophos); a salicylanilide (*e.g.*, closantel, oxyclozanide, rafoxanide, and niclosamide); a nitrophenolic compound (*e.g.*, nitroxynil and nitroscanate); benzoenedisulphonamide (*e.g.*, clorsulon); a pyrazinaisoquinoline (*e.g.*, praziquantel and epsiprantel); a heterocyclic compound (*e.g.*, piperazine, diethylcarbamazine, dichlorophen, and phenothiazine); an arsenical (*e.g.*, thiacetarsamide, melorsamine, and arsenamide); cyclooctadepsipeptide (*e.g.*, emodepside); and a paraherquamide.

[0127] In some such embodiments, for example, the compound according to this invention or a compound corresponding to the use according to the invention is active against a helminth (for example, *Haemonchus contortus*) resistant to an avermectin, such as ivermectin. In other embodiments, the compound according to this invention is alternatively or additionally active against a helminth (for example, *Haemonchus contortus*) resistant to a benzimidazole derivative, such as fenbendazole. In other embodiments, the compound according to this invention is alternatively or additionally active against a helminth (for example, *Haemonchus contortus*) resistant to levamisole. And, in other embodiments, the compound according to this invention is alternatively or additionally active against a helminth (for example, *Haemonchus contortus*) resistant to pyrantel.

[0128] The compounds according to this invention or the compounds corresponding to the use according to the invention may be administered in various dosage forms. The term "dosage form" means that the compounds are formulated into a product suitable for administering to the animal via the envisaged dosage route. Such dosage forms are sometimes referred to herein as formulations or pharmaceutical composition.

[0129] The formulation type chosen for a dosage form in any instance will depend upon the particular purpose envisaged and the physical, chemical and biological properties of the compound according to this invention.

[0130] Dosage forms useful in the current invention can be liquid, semi-solid or solid dosage forms.

[0131] Liquid dosage forms of the compounds are generally solutions, suspensions or emulsions. A solution is a mixture of two or more components that form a single phase that is homogeneous down to the molecular level. A suspension consists of insoluble solid particles dispersed in a liquid medium, with the solid particles accounting for about 0.5% to about 30% of the suspension. The liquid may be aqueous, oily, or both. An emulsion is a heterogeneous dispersion of one immiscible liquid in another; it relies on an emulsifying agent for stability. A dry powder (or granule) for reconstitution is reconstituted as a solution or as a suspension immediately prior to injection. The principal advantage of this dosage form is that it overcomes the problem of instability in solution or suspension.

[0132] One possible dosage route is the oral dosage route, wherein the compound is administered via the mouth. Oral dosage forms suitable for oral administration comprise liquids (*e.g.*drench or drinking water formulations), semi-solids (*e.g.*pastes, gels), and solids (*e.g.*tablets, capsules, powders, granules, chewable treats, premixes and medicated blocks).

[0133] A drench is a liquid oral formulation that is administered directly into the mouth/throat of an animal, especially a livestock animal, by means of a "drench gun" or syringe or another suitable device. When the composition is administered in the animal recipient's drinking water or as a drench, it may be convenient to use a solution or suspension formulation. This formulation can be, for example, a concentrated suspension that is mixed with water or a dry preparation that is

mixed and suspended in the water.

[0134] Semi-solid oral formulations (pastes or gels) are generally administered via an applicator directly into the mouth of an animal or mixed with the feed.

[0135] Solid oral formulations are either administered directly to an animal (tablet, capsule) or mixed with the feed or via medicated feed blocks.

[0136] When the oral formulation is administered via a non-human animal's feed, it may, for example, be fed as a discrete feed or as a chewable treat. Alternatively (or additionally), it may, for example, be intimately dispersed in the animal recipient's regular feed, used as a top dressing, or in the form of solid pellets, paste or liquid that is added to the finished feed. When the oral formulation is administered as a feed additive, it may be convenient to prepare a "premix" in which the oral formulation is dispersed in a liquid or solid carrier. This "premix" is, in turn, dispersed in the animal's feed using, for example, a conventional mixer.

[0137] Several modified-release delivery systems have been developed, that take advantage of the unique anatomy of the ruminant forestomach, i.e. for intra-ruminal administration. An intraruminal bolus is a specific formulation for ruminants (cattle, sheep, goats, buffalos, camelids, deer etc). It is a veterinary delayed release delivery system which remains in the rumeno-reticular sac of a ruminant animal over an extended period of time and in which the therapeutically active substance has a predictable and delayed release pattern. Such intraruminal boluses are usually administered using a balling gun or another suitable device.

[0138] It is contemplated that the compounds according to this invention or compounds corresponding to the use according to the invention may alternatively be administered via non-oral dosage routes, such as topically (*e.g.*, via a spot-on, pour-on or transdermal patch), or parenterally (*e.g.*, subcutaneous injection, intravenous injection, intramuscular injection, etc.).

[0139] For instance the compounds may be administered topically using a transdermal formulation (i.e. a formulation that passes through the skin). Alternatively the compounds may be administered topically via the mucosa.

[0140] Topical dosage forms suitable for topical administration comprise liquids (*e.g.* bath, spray, spot-on), semi-solids (*e.g.* creams, gels), and solids (*e.g.* patches, powders, collars). Typical topical formulations for animals are liquid or semi-liquid dosage forms. Typical formulations for transdermal and mucosal administration include, for example, pour-ons, spot-ons, dips, sprays, mousses, shampoos, powders, gels, hydrogels, lotions, solutions, creams, ointments, dusting powders, dressings, foams, films, skin patches, limb bands, collars, ear tags, wafers, sponges, fibers, bandages, and microemulsions. When a liquid formulation is used topically on skin, it can be administered by, for example, pouring on (pour-on or spot-on), spreading, rubbing, atomizing, spraying, dipping, bathing, or washing.

[0141] The pour-on or spot-on methods, for example, comprise applying the formulation to a specific location of the skin or coat, such as on the neck or backbone of the animal. This may be achieved by, for example, applying a swab or drop of the pour-on or spot-on formulation to a relatively small area of the recipient animal's skin or coat (i.e., generally no greater than about 10% of the animal recipient's skin or coat). In some embodiments, the compound is dispersed from the application site to wide areas of the fur due to the spreading nature of the components in the formulation and the animal's movements while, in parallel, being absorbed through the skin and distributed via the animal recipient's fluids and/or tissues.

[0142] Parenteral formulations and delivery systems for non-oral routes comprise liquids (e.g. solutions, suspensions, emulsions, and dry powders for reconstitution), semi-solids and solids (e.g.implants). The majority of implants that are used in veterinary medicine are compressed tablets or dispersed matrix systems in which the drug is uniformly dispersed within a nondegradable polymer or alternatively extrusion products.

Pharmaceutical compositions

[0143] This invention also is directed to pharmaceutical compositions (or medicaments) comprising one or more, preferably one compound according to this invention. The compositions also may (and preferably will) comprise one or more pharmaceutically acceptable excipients. The following subject matter about pharmaceutical compositions is also applicable to pharmaceutical compositions comprising compounds corresponding to the use according to this invention.

[0144] Pharmaceutical compositions of the present invention may be manufactured by, for example, processes known in the art. These processes include, for example, a variety of known mixing, dissolving, granulating, emulsifying, encapsulating, entrapping, and lyophilizing processes. Optimal formulation depends on, for example, the dosage route (*e.g.* oral, injection, topical).

[0145] Solid dosage forms, for example, may be prepared by, for example, intimately and uniformly mixing the compounds with fillers, binders, lubricants, glidants, disintegrants, flavoring agents (*e.g.*, sweeteners), buffers, preservatives, pharmaceutical-grade dyes or pigments, and controlled release agents.

[0146] Oral dosage forms other than solids may be prepared by mixing the compounds with, for example, one or more solvents, viscosity-enhancing agents, surfactants, preservatives, stabilizers, resins, fillers, binders, lubricants, glidants, disintegrants, co-solvents, sweeteners, flavorings, perfuming agents, buffers, suspending agents, and pharmaceutical-

grade dyes or pigments.

[0147] Contemplated binders include, for example, gelatin, acacia, and carboxymethyl cellulose.

[0148] Contemplated lubricants include, for example, magnesium stearate, stearic acid, and talc.

[0149] Contemplated disintegrants include, for example, corn starch, alginic acid, sodium carboxymethylcellulose, and sodium croscarmellose.

[0150] Contemplated buffers include, for example, sodium citrate, and magnesium and calcium carbonate and bicarbonate.

[0151] Contemplated solvents include, for example, water, petroleum, animal oils, vegetable oils, mineral oil, and synthetic oil. Physiological saline solution or glycols (e.g., ethylene glycol, propylene glycol, or polyethylene glycol) also may be included. The solvent preferably has sufficient chemical properties and quantity to keep the compounds solubilized at temperatures in which the composition is stored and used.

[0152] Contemplated viscosity-enhancing agents include, for example, polyethylene, methylcellulose, sodium carboxymethylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, sodium alginate, carbomer, povidone, acacia, guar gum, xanthan gum, tragacanth, methylcellulose, carbomer, xanthan gum, guar gum, povidone, sodium carboxymethylcellulose, magnesium aluminum silicate, carboxyvinyl polymers, carrageenan, hydroxyethyl cellulose, laponite, water-soluble salts of cellulose ethers, natural gums, colloidal magnesium aluminum silicateor finely divided silica, homopolymers of acrylic acid crosslinked with an alkyl ether of pentaerythritol or an alkyl ether of sucrose, and carbomers.

[0153] Contemplated surfactants include, for example, polyoxyethylene sorbitan fatty acid esters; polyoxyethylene monoalkyl ethers; sucrose monoesters; lanolin esters and ethers; alkyl sulfate salts; and sodium, potassium, and ammonium salts of fatty acids.

[0154] Contemplated preservatives include, for example, phenol, alkyl esters of parahydroxybenzoic acid (*e.g.*, methyl *p*-hydroxybenzoate (or "methylparaben") and propyl *p*-hydroxybenzoate (or "propylparaben")), sorbic acid, o-phenylphenol benzoic acid and the salts thereof, chlorobutanol, benzyl alcohol, thimerosal, phenylmercuric acetate and nitrate, nitromersol, benzalkonium chloride, and cetylpyridinium chloride.

[0155] Contemplated stabilizers include, for example, chelating agents and antioxidants.

[0156] Solid dosage forms also may comprise, for example, one or more excipients to control the release of the compounds. For example, it is contemplated that the compounds may be dispersed in, for example, hydroxypropylmethyl cellulose. Some oral dosage forms (*e.g.*, tablets and pills) also may be prepared with enteric coatings.

[0157] Topical dosage route uses, for example, a concentrated liquid or semi-liquid solution, suspension (aqueous or non-aqueous), emulsion (water-in-oil or oil-in-water), or microemulsion comprising a compounds dissolved, suspended, or emulgated in a pharmaceutically-acceptable liquid vehicle. In such embodiments, a crystallization inhibitor optionally may generally be present.

[0158] Such a pour-on or spot-on formulation can be prepared by dissolving, suspending, or emulsifying the compounds in a suitable skin-fitted solvent or solvent mixture. Other excipients may be included as well, such as, for example, a surfactant, colorant, antioxidant, stabilizer, adhesive, etc. Contemplated solvents include, for example, water, alkanol, glycol, polyethylene glycol, polypropylene glycol, glycerin, benzyl alcohol, phenylethanol, phenoxyethanol, ethyl acetate, butyl acetate, benzyl benzoate, dipropylene glycol monomethyl ether, diethylene glycol monobutyl ether, acetone, methyl ethyl ketone, aromatic and/or aliphatic hydrocarbons, vegetable or synthetic oil, DMF, liquid paraffin, silicone, dimethylacetamide, N-methylpyrrolidone, or 2,2-dimethyl-4-oxy-methylene-1,3-dioxolane.

[0159] In some embodiments, a topical formulation (particularly a pour-on or spot-on formulation) comprises a carrier that promotes the absorption or penetration of the compounds through the skin into the blood stream, other bodily fluids (lymph), and/or body tissue (fat tissue). Contemplated examples of dermal penetration enhancers include, for example, dimethylsulfoxide, isopropyl myristate, dipropylene glycol pelargonate, silicone oil, aliphatic esters, triglycerides, and fatty alcohols.

[0160] Topical formulations also (or alternatively) may comprise, for example, one or more spreading agents. These substances act as carriers that assist in distributing an active ingredient over the animal recipient's coat or skin. They may include, for example, isopropyl myristate, dipropylene glycol pelargonate, silicone oils, fatty acid esters, triglycerides, and/or fatty alcohols. Various spreading oil/solvent combinations also may be suitable, such as, for example, oily solutions, alcoholic and isopropanolic solutions (*e.g.*, solutions of 2-octyl dodecanol or oleyl alcohol), solutions of esters of monocarboxylic acids (*e.g.*, isopropyl myristate, isopropyl palmitate, lauric acid oxalic ester, oleic acid oleyl ester, oleic acid decyl ester, hexyl laurate, oleyl oleate, decyl oleate, and caproic acid esters of saturated fatty alcohols having a carbon chain of 12 to 18 carbons), solutions of esters of dicarboxylic acids (*e.g.*, dibutyl phthalate, diisopropyl isophthalate, adipic acid diisopropyl ester, and di-n-butyl adipate), or solutions of esters of aliphatic acids (*e.g.*, glycols). When the formulation comprises a spreading agent, it also may be advantageous to include a dispersant, such as, for example, pyrrolidin-2-one, N-alkylpyrrolidin-2-one, acetone, polyethylene glycol or ether or ester thereof, propylene glycol, or synthetic triglycerides.

[0161] When formulated in, for example, an ointment, it is contemplated that the compounds may be mixed with, for

example, either a paraffinic or a water-miscible ointment base. When formulated in a cream, it is contemplated that the compounds may be formulated with, for example, an oil-in-water cream base. In some instances, the aqueous phase of the cream base includes, for example at least about 30% (w/w) of a polyhydric alcohol, such as propylene glycol, butane-1,3-diol, mannitol, sorbitol, glycerol, polyethylene glycol, or a mixture thereof.

[0162] Injectable formulations may be prepared according to, for example, the known art using suitable solvents, solubilizing agents, protecting agents, dispersing agents, wetting agents, and/or suspending agents. Contemplated carrier materials include, for example, water, ethanol, butanol, benzyl alcohol, glycerin, 1,3-butanediol, Ringer's solution, isotonic sodium chloride solution, bland fixed oils (*e.g.*, synthetic mono- or diglycerides), vegetable oil (*e.g.*, corn oil), dextrose, mannitol, fatty acids (*e.g.*, oleic acid), dimethyl acetamide, surfactants (*e.g.*, ionic and non-ionic detergents), N-methylpyrrolidone, propylene glycol, and/or polyethylene glycols (*e.g.*, PEG 400). Contemplated solubilizing agents include, for example, polyvinyl pyrrolidone, polyoxyethylated castor oil, polyoxyethylated sorbitan ester, and the like. Contemplated protecting agents include, for example, benzyl alcohol, trichlorobutanol, *p*-hydroxybenzoic acid ester, *n*-butanol, and the like.

[0163] In some embodiments, a parenteral formulation is, for example, prepared from sterile powders or granules having one or more of the carriers materials discussed above for other formulations. The compound is, for example, dissolved or suspended in a liquid comprising water, polyethylene glycol, propylene glycol, ethanol, corn oil, cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, and/or various buffers. The pH generally may be adjusted, if necessary, with a suitable acid, base, or buffer.

[0164] Other inert ingredients may generally be added to the composition as desired. To illustrate, it is contemplated that these may include, for example, lactose, mannitol, sorbitol, calcium carbonate, sodium carbonate, tribasic calcium phosphate, dibasic calcium phosphate, sodium phosphate, kaolin, compressible sugar, starch, calcium sulfate, dextro or microcrystalline cellulose, colloidal silicon dioxide, starch, sodium starch glycolate, crospovidone, microcrystalline cellulose, tragacanth, hydroxypropylcellulose, pregelatinized starch, povidone, ethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and methylcellulose.

[0165] Further aspects regarding formulation of drugs and various excipients are found in, for example, Gennaro, A.R., et al., eds., Remington: The Science and Practice of Pharmacy (Lippincott Williams & Wilkins, 20th Ed., 2000). Another source regarding formulation of drugs and various excipients is found in, for example, Liberman, H. A., et al., eds., Pharmaceutical Dosage Forms (Marcel Decker, New York, N.Y., 1980).

[0166] The concentration of the compounds according to this invention in the applied dosage form may vary widely depending on, for example, the dosage route. In general, the concentration is from about 1 to about 70% (by weight). In some such embodiments, for example, the concentration is from about 1 to about 50% (by weight), or from about 10 to about 50% (by weight). In other embodiments, the concentration is from about 35 to about 65% (by weight), from about 40 to about 60% (by weight), from about 45 to about 55% (by weight), or about 50% (by weight).

[0167] In another aspect the present invention thus provides a pharmaceutical composition comprising an anthelmintically effective amount of one or more, preferably one compound according to this invention and one or more pharmaceutically acceptable excipients.

[0168] The formulation type chosen for a dosage form in any instance will depend upon the particular purpose envisaged and the physical, chemical and biological properties of the compound according to this invention.

[0169] The compounds and pharmaceutical compositions according to this invention are useful in treating parasitic infections such as helminth infections of animals. An "effective amount," is the amount or quantity of a compound that is required to alleviate or reduce parasite numbers in an animal, and/or to inhibit the development of parasite infections in an animal, in whole or in part.

[0170] This amount is readily determined by observation or detection of the pathogen numbers such as parasite numbers both before and after contacting the sample of pathogens such as parasites including their stages with the compound according to this invention, directly and/or indirectly, *e.g.,* by contacting articles, surfaces, foliage, or animals with the compound.

[0171] This can be evaluated by counting parasites (especially helminthes) directly after necroscopy of the host animal.

[0172] The reduction of parasite numbers, especially gastrointestinal helminth parasites can be alternatively measured in-directly by faecal egg or differential larval counts. In this case the effective amount of the compound is determined by the reduction of the number of excreted helminth eggs or larvae in the faeces of the treated animal before and after treatment. For an *in vivo* administration the compound according to this invention, is preferably administered to an animal in an effective amount which is synonymous with "pharmaceutically effective amount" or "anthelmintically effective amount"..

Examples of contemplated combination therapies

[0173] The methods and pharmaceutical compositions of this invention encompass methods wherein a compound according to this invention or a compound corresponding to the use according to the invention is the sole active ingredient

administered to the recipient animal. It is contemplated, however, that the methods and pharmaceutical compositions also encompass combination therapies wherein a compound is administered in combination with one or more other pharmaceutically acceptable active ingredients. The other active ingredient(s) may be, for example, one or more other compounds according to this invention or one or more other compounds corresponding to the use according to the invention. Alternatively (or additionally), the other active ingredient(s) may be one or more pharmaceutically acceptable compounds that are not compounds according to this invention or compounds corresponding to the use according to the invention. The other active ingredient(s) may target the same and/or different parasites and conditions.

[0174] Contemplated active ingredient(s) that may be administered in combination with the compounds include, for example, pharmaceutically acceptable anthelmintics, insecticides and acaricides, insect growth regulators, anti-inflammatories, antiinfectives, anti-protozoals, hormones, dermatological preparations (*e.g.*, antiseptics and disinfectants), and immunobiologicals (*e.g.*, vaccines and antisera) for disease prevention.

[0175] Therefore this invention is also directed to the use as a medicament of combinations comprising a) one or more compounds according to this invention or one or more compounds corresponding to the use according to this invention with b) one or more pharmaceutically acceptable active compounds which differ in structure from component a). The active compounds b) are preferably anthelmintic compounds, more preferably selected from the group consisting of avermectins (*e.g.*, ivermectin, selamectin, doramectin, abamectin, and eprinomectin); milbemycins (moxidectin and milbemycin oxime); pro-benzimidazoles (*e.g.*, febantel, netobimin, and thiophanate); benzimidazole derivatives, such as a thiazole benzimidazole derivative (*e.g.*, thiabendazole and cambendazole) or a carbamate benzimidazole derivatives (*e.g.*, fenbendazole, albendazole (oxide), mebendazole, oxfendazole, parbendazole, oxibendazole, flubendazole, and triclabendazole); an imidazothiazoles (*e.g.*, levamisole and tetramisole); a tetrahydropyrimidine (morantel and pyrantel), organophosphates (*e.g.*, trichlorphon, haloxon, dichlorvos, and naphthalophos); salicylanilides (*e.g.*, closantel, oxyclozanide, rafoxanide, and niclosamide); nitrophenolic compounds (*e.g.*, nitroxynil and nitroscanate); benzenedisulphonamides (*e.g.*, clorsulon); pyrazineisoquinolines (*e.g.*, praziquantel and epsiprantel); heterocyclic compounds (*e.g.*, piperazine, diethylcarbamazine, dichlorophen, and phenothiazine); arsenicals (*e.g.*, thiacetarsamide, melorsamine, and arsenamide); cyclooctadepsipeptides (*e.g.*, emodepside); paraherquamides (*e.g.* derquantel); and amino-acetonitrile compounds (*e.g.* monepantel, AAD 1566); tribendimidine (amidine compound); amidine compounds (*e.g.*, amidantel and tribendimidin), including all pharmaceutically acceptable forms, such as salts, solvates or N-oxides.

[0176] Preferred combinations are comprising a) one compound selected from the group compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables (or salts, solvates, N-oxides or prodrugs.thereof) and b) one compound selected from the group consisting of anthelmintic avermectins (*e.g.*, ivermectin, selamectin, doramectin, abamectin, emamectin and eprinomectin); milbemycins (moxidectin and milbemycin oxime); pro-benzimidazoles (*e.g.*, febantel, netobimin, and thiophanate); benzimidazole derivatives, such as triclabendazole, thiazole benzimidazole derivatives (*e.g.*, thiabendazole and cambendazole), carbamate benzimidazole derivatives (*e.g.*, fenbendazole, albendazole (oxide), mebendazole, oxfendazole, parbendazole, oxibendazole, flubendazole); imidazothiazoles (*e.g.*, levamisole and tetramisole); tetrahydropyrimidines (morantel and pyrantel), organophosphates (*e.g.*, trichlorphon, haloxon, dichlorvos, and naphthalophos); salicylanilides (*e.g.*, closantel, oxyclozanide, rafoxanide, and niclosamide); nitrophenolic compounds (*e.g.*, nitroxynil and nitroscanate); benzenedisulphonamides (*e.g.*, clorsulon); pyrazineisoquinolines (*e.g.*, praziquantel and epsiprantel); heterocyclic compounds (*e.g.*, piperazine, diethylcarbamazine, dichlorophen, and phenothiazine); arsenicals (*e.g.*, thiacetarsamide, melorsamine, and arsenamide); cyclooctadepsipeptides (*e.g.*, emodepside); paraherquamides (*e.g.* derquantel); amino-acetonitrile compounds (*e.g.* monepantel, AAD 1566); tribendimidine (amidine compound); and amidantel (amidine compound); including all pharmaceutically acceptable forms, such as salts.

[0177] Preferred combinations comprise at least one compound selected from the group of compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables (or salts, solvates or N-oxides.thereof) and

abamectin, ivermectin, emamectin, eprinomectin, doramectin, moxidectin, milbemycin oxime; or
closantel, oxyclozanide, rafoxanide, niclosamide; or
nitroxynil, nitroscanate, clorsulon; or
praziquantel and epsiprantel; or
emodepside, derquantel, monepantel.

[0178] Examples of such combinations are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with abamectin.

[0179] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with ivermectin.

[0180] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emamectin.

[0181] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with eprinomectin.

[0182] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with doramectin.

[0183] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with moxidectin.

[0184] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with milbemycin oxime.

[0185] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with closantel.

[0186] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with oxyclozanide.

[0187] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with rafoxanide.

[0188] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with niclosamide.

[0189] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroxynil.

[0190] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroscanate.

[0191] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with clorsulon.

[0192] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with praziquantel.

[0193] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with epsiprantel.

[0194] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emodepside.

[0195] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with derquantel.

[0196] Other examples are combinations of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with monepantel.

[0197] Examples of such combinations are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with abamectin.

[0198] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with ivermectin.

[0199] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emamectin.

[0200] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with eprinomectin.

[0201] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with doramectin.

[0202] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with moxidectin.

[0203] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with milbemycin oxime.

[0204] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with closantel.

[0205] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with oxyclozanide.

[0206] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with rafoxanide.

[0207] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with niclosamide.

[0208] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroxynil.

[0209] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroscanate.

[0210] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with clorsulon.

[0211] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with praziquantel.

[0212] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with epsiprantel.

[0213] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emodepside.

[0214] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with derquantel.

[0215] Other examples are combinations of a salt of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with monepantel.

[0216] Examples of such combinations are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with abamectin.

[0217] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with ivermectin.

[0218] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emamectin.

[0219] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with eprinomectin.

[0220] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with doramectin.

[0221] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with moxidectin.

[0222] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with milbemycin oxime.

[0223] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with closantel.

[0224] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with oxyclozanide.

[0225] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with rafoxanide.

[0226] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with niclosamide.

[0227] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroxynil.

[0228] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroscanate.

[0229] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with clorsulon.

[0230] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with praziquantel.

[0231] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with epsiprantel.

[0232] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emodepside.

[0233] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with derquantel.

[0234] Other examples are combinations of a solvate of one of the compounds A-1 to A-697, Aa-1 to Aa-5, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with monepantel.

[0235] Examples of such combinations are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with abamectin.

[0236] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with ivermectin.

[0237] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emamectin.

[0238] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with eprinomectin.

[0239] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with doramectin.

[0240] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with moxidectin.

[0241] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, , and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with milbemycin oxime.

[0242] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with closantel.

[0243] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with oxyclozanide.

[0244] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with rafoxanide.

[0245] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with niclosamide.

[0246] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroxynil.

[0247] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with nitroscanate.

[0248] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with clorsulon.

[0249] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with praziquantel.

[0250] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with epsiprantel.

[0251] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with emodepside.

[0252] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with derquantel.

[0253] Other examples are combinations of an N-oxide of one of the compounds A-1 to A-697, and B-1 to B-204 of Tables A and B below and variants as mentioned at the bottom of these tables with monepantel.

[0254] The compounds as described in this specification can be combined with pharmaceutically acceptable insecticides or acaricides. Such pharmaceutically acceptable insecticides and acaricides include, for example, acetamiprid, acetoprole, amitraz, amidoflumet, avermectin, azadirachtin, bifenthrin, bifenazate, buprofezin, bistrifluron, chlorfenapyr, chlorfluazuron, chlorantraniliprole, chlorpyrifos, chromafenozide, clothianidin, cyantraniliprole, cyflumetofen, β-cyfluthrin, cyhalothrin, λ-cyhalothrin, cymiazole cypermethrin, cyromazine, deltamethrin, demiditraz, diafenthiuron, diazinon, diflubenzuron, dimefluthrin, dinotefuran, emamectin, esfenvalerate, ethiprole, fenoxycarb, fenpropathrin, fenvalerate, fipronil, flonicamid, flubendiamide, flucythrinate, tau-fluvalinate, flufenoxuron, halofenozide, hexaflumuron, imidacloprid, indoxacarb, lufenuron, metaflumizone, methoprene, metofluthrin, methoxyfenozide, nitenpyram, novaluron, noviflumuron, permethrin,phosmet, profluthrin, protrifenbute, pymetrozine, pyrafluprole, pyrethrin, pyridalyl, pyrifluquinazon, pyriprole, pyriproxyfen, rotenone, ryanodine, spinetoram, spinosad, spirodiclofen, spiromesifen, spirotetramat, sulfoxaflor, tebufenozide, tebufenpyrad, teflubenzuron, tefluthrin, tetrachlorvinphos, tetramethylfluthrin, thiacloprid, thiamethoxam, tolfenpyrad, tralomethrin, and triflumuron. General references discussing antiparasitic agents, such as insecticides and acaricides, include, for example, The Pesticide Manual, 13th Edition, C. D. S. Tomlin, Ed., British Crop Protection Council, Farnham, Surrey, U.K. (2003).

[0255] The compounds as described in tis specification can be combined with pharmaceutically acceptable insect growth regulators. Such pharmaceutically acceptable insect growth regulators include, for example, methoprene, pyriproxyfen, tetrahydroazadirachtin, chlorfluazuron, cyromazine, diflubenzuron, fluazuron, flucycloxuron, flufenoxuron, hexaflumuron, lufenuron, ifenuron, tebufenozide, and triflumuron. These compounds tend to provide both initial and sustained treatment of parasite infections at all stages of insect development, including eggs, on the animal subject, as well as within the environment of the animal subject.

[0256] The compounds as described in this specification can be combined with pharmaceutically acceptable anti-protozoals. Such pharmaceutically acceptable anti-protozoals include, for example, triazintriones like, for example,. toltrazuril and ponazuril and triazindiones such as clazuril, diclazuril and letrazuril.

[0257] In some contemplated embodiments, the compounds are administered with dihydroazole compounds, such as, for example, compounds discussed in WO 2010/75591.

[0258] In some contemplated embodiments, the compounds are administered with anthelminic proteins, such as, for example Bacillus thuringensis crystal proteins *e.g.* described in WO 2010/053517.

[0259] In some contemplated embodiments, the compounds are administered with pyridylmethylamine derivatives, such as, for example, pyridylmethylamine derivatives discussed in European Patent Appl. EP0539588 or Int'l Patent Appl. Publ. WO2007/115643.

[0260] In some contemplated embodiments, the compounds is administered with nodulisporic acids and derivatives thereof, such as, for example, compounds discussed in US Patent 5,399,582; 5,945,317; 5,962,499; 5,834,260; 6,221,894; or 5,595,991; or Int'l Patent Appl. Publ. 1996/29073.

[0261] Other antiparasitic compounds contemplated to be useful in combination therapies with the compounds include, for example, imidazo[1,2-b] pyridazine compounds discussed in US Patent Appl. Publ. No. 2005-0182059; 1-(4-Mono and dihalomethylsulphonylphenyl)-2-acylamino-3-fluoropropanol compounds discussed US Patent 7,361,689; trifluoromethanesulfonanilide oxime ether compounds discussed in US Patent 7,312,248; n-[(phenyloxy)phenyl]-1,1,1-trifluoromethanesulfonamide and n-[(phenylsulfanyl)phenyl]-1,1,1-trifluoromethanesulfonamide compounds discussed in US Patent Appl. Publ. 2006-0281695; and 2-phenyl-3-(1 H-pyrrol-2-yl)acrylonitrile compounds discussed in US Appl. Publ. 2006/0128779; isoxazoline compounds discussed in WO Patent Appl, Publ. 2005-085216, WO 2007-026965, WO 2007-070606, WO 2007-075459, WO 2007-079162, WO 2007-105814, WO 2007-125984, WO 2008-019760, WO 2008-122375, WO 2008-150393, WO 2009-002809, WO 2009-003075, WO 2009-022746, WO 2009-035004, WO 2009-045999, WO 2009-051956, WO 2009-035004.

[0262] In the contemplated combination therapies, the compounds according to this invention may be administered before, simultaneously, and/or after the other active ingredient(s). In addition, the compounds according to this invention may be administered in the same composition as the other active ingredient(s) and/or in separate compositions from the other active ingredient(s). Further, the compounds according to this invention and other active ingredient(s) may be administered via the same and/or different dosage route.

[0263] When the compounds according to this invention are administered in a combination therapy, the weight ratio of the active ingredients may vary widely. Factors influencing this ratio include, for example, the particular compounds; the identity of the other active ingredient(s) be administered in the combination therapy; the dosage route of the compounds and other active ingredient(s); the target condition and pathogen; the type (*e.g.*, species and breed), age, size, sex, diet, activity, and condition of the animal; and pharmacological considerations, such as the activity, efficacy, pharmacokinetic, and toxicology profiles of the compounds and other active ingredient(s). In some contemplated embodiments, for example, the weight ratio of the compounds to the other active ingredient(s) is, for example, is from about 1:3000 to about 3000:1. In some such instances, the weight ratio is from about 1:300 to about 300:1. In other such instances, the weight ratio is from about 1:30 and about 30:1.

[0264] In addition to other active ingredients, it is contemplated that the compounds may be administered with one or more other compounds that beneficially affects (*e.g.* enhances or prolongs) the activity (or other characteristic, such as safety) of the compounds. For example, it is contemplated that the compounds may be administered with one or more synergists, such as, for example, piperonyl butoxide (PBO) and triphenyl phosphate (TPP). Other synergists include, for example, N-(2-ethylhexyl)-8,9,10-trinorborn-5-ene-2,3-dicarboxamide (also known as "ENT 8184" or "MGK 264") and Verbutin (also known as "MB-599").

[0265] This invention also is directed to kits that are, for example, suitable for use in performing the methods of treatment described above. The kit comprises a therapeutically effective amount of one or more compounds of this invention, and an additional component. The additional component(s) may be, for example, one or more of the following: another ingredient (*e.g.*, an excipient or active ingredient), an apparatus for combining the compound of this invention with another ingredient and/or for administering the compound of this invention, or a diagnostic tool.

[0266] The compounds used according to this invention show an excellent activity in treating parasite infections and in addition are acceptable for the animals treated.

[0267] Compounds of the current invention are useful agronomically for protecting field crops from phytophagous invertebrate pests and also nonagronomically for protecting other horticultural crops and plants from phytophagous invertebrate pests.

[0268] Invertebrate pests are insects, acarids, mollusks, fungi and nematodes that cause damage to field crops or other horticultural crops and plants.

[0269] Nonagronomic uses of the compounds of this invention and compositions include control of invertebrate pests in stored grains, beans and other foodstuffs and in textiles such as clothing and carpets. Nonagronomic uses of the compounds of formula (I) and compositions also include invertebrate pest control in ornamental plants, forests, in yards, along roadsides and railroad rights of way, and on turf such as lawns, golf courses and pastures.

[0270] Compounds of this invention will generally be used as an invertebrate pest control active ingredient in a composition, i.e. formulation, with at least one additional component selected from the group consisting of surfactants, solid diluents and liquid diluents, which serves as a carrier. The formulation or composition ingredients are selected to be consistent with the physical properties of the active ingredient, mode of application and environmental factors such as soil type, moisture and temperature.

[0271] Invertebrate pests are controlled in agronomic and nonagronomic applications by applying one or more compounds of formula (I), typically in the form of a composition, in a biologically effective amount, to the environment of the pests, including the agronomic and/or nonagronomic locus of infestation, to the area to be protected, or directly on the pests to be controlled.

[0272] Examples of suitable compositions comprising a compound of the invention include granular compositions wherein the additional active compound is present on the same granule as the compound of the invention or on granules separate from those of the compound of the invention.

[0273] To achieve contact with a compound or composition of the invention to protect a field crop from invertebrate pests, the compound or composition is typically applied to the seed of the crop before planting, to the foliage (*e.g.*, leaves, stems, flowers, fruits) of crop plants, or to the soil or other growth medium before or after the crop is planted.

[0274] One embodiment of a method of contact is by spraying. Alternatively, a granular composition comprising a compound of the invention can be applied to the plant foliage or the soil. Compounds of this invention can also be effectively delivered through plant uptake by contacting the plant with a composition comprising a compound of this invention.

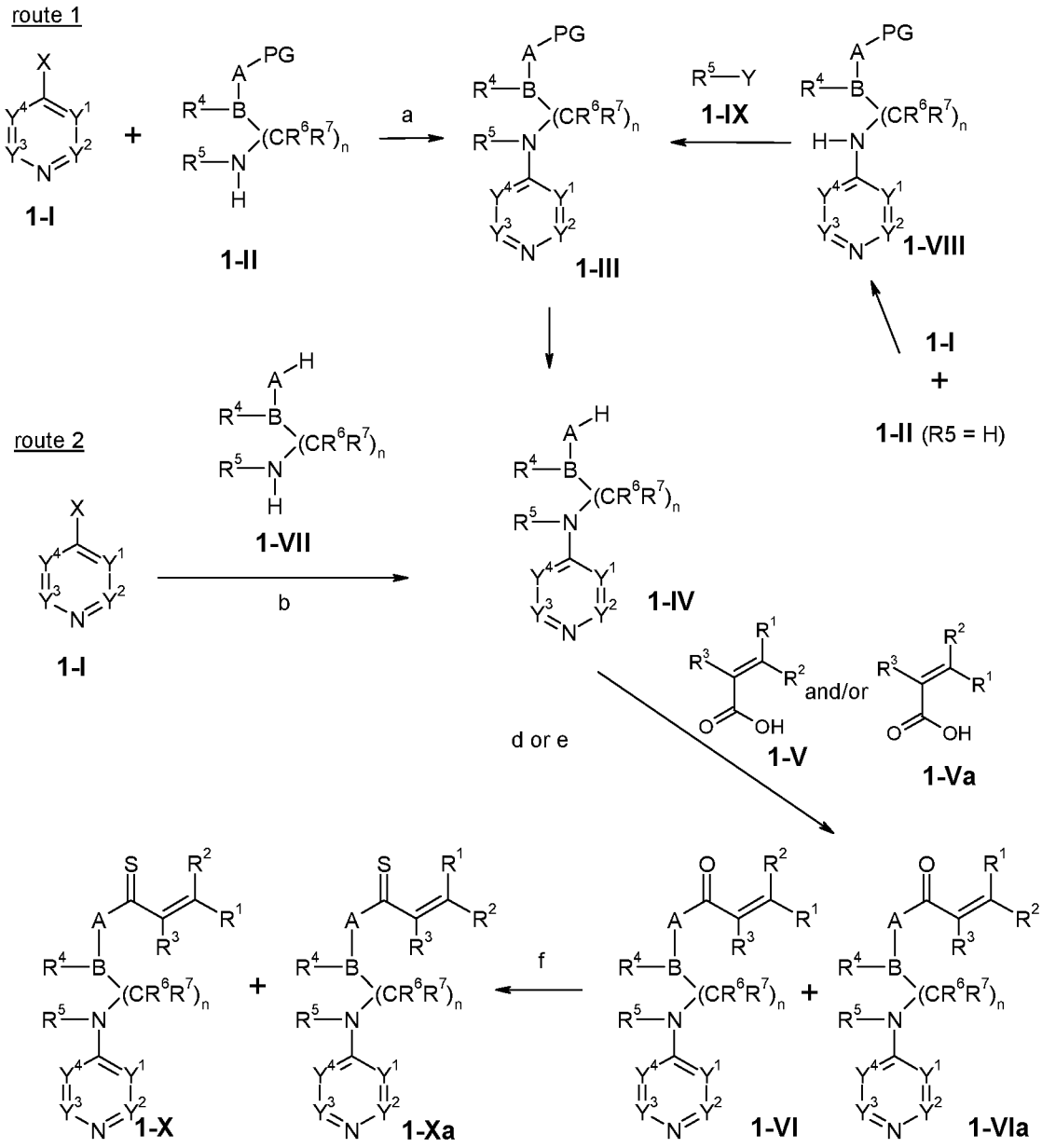
EXAMPLES

[0275] The following examples are merely illustrative, and not limiting to the remainder of the disclosure in any way.

A. General Description of Synthesis of Compounds according to this specification

[0276] The compounds as described in this specification can be obtained by various synthesis routes. A person skilled in the art will choose the synthetic route to obtain compounds as described in this specification depending on the nature of its radicals as defined in Formula (I). This is illustrated in the following schemes, which are merely illustrative but not limiting the disclosure in any way.

Scheme 1:



[0277] Exemplary conditions: a: palladium acetate, 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), caesium carbonate, dioxane; b: 1-methoxy-2-propanol, 110°C d: oxalyl chloride, dichloromethane (DCM), dimethylformamide (DMF) then DCM, triethylamine (TEA); e: 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate (HBTU), diisopropylethylamine , DMF, room temperature; f: Lawesson's reagent, tetrahydrofuran (THF), 130°C.

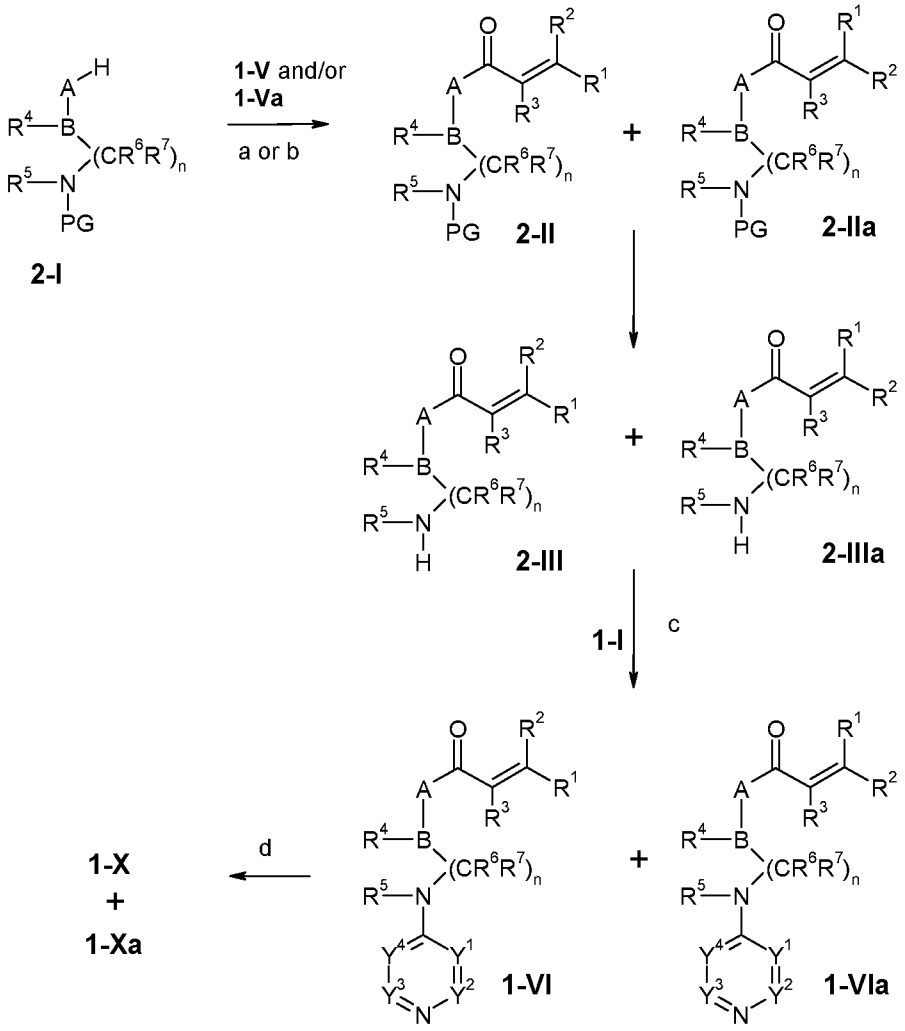
[0278] A compound of general formula **1-VI** can be synthesized as shown in scheme 1: in route 2 a heteroarylcompound **1-I** is reacted with a diamine **1-VII** to give **1-IV. 1-I** contains a suitable leaving group X, which is preferably a halogon like chloro or bromo or a nitro group. The reaction with **1-VII** takes place in an inert solvent like DMF or dimethylacetamide, preferably in a diol-derived solvent like ethyleneglycolmonomethylether or propyleneglycolmonomethylether or 1-methoxy-2-propanol and preferably at elevated temperatures. The reaction might also be done without any solvent with neat reactants. **1-VII** is employed preferably in excess. An additional base might be added. Alternatively, the reaction can be done in pyridine as solvent. The diamine can be protected with a suitable protecting group as in **1-II** of route 1. Suitable protecting groups (PG) for the nitrogen in **1-II** include, but are not limited to, preferably *tert*-butyl carbamate (Boc), benzyl carbamate (Cbz) and the like. A protected diamine **1-II** can be reacted under the same conditions as **1-VII**, alternatively Pd-catalysis can be used employing a Pd-containing molecule like palladium acetate, a phosphorus-containing ligand like BINAP, a base like caesium carbonate or sodium *tert*-butoxide in a solvent like an ether-containing solvent like diethylether, dioxane or tetrahydrofuran, preferably dioxane or an inert solvent like toluene. The protecting group in the

intermediate **1-III** can be removed by suitable methods known to a person skilled in the art; if PG is a Boc-group, for example, the protecting group can be removed by an acid like trifluoroacetic acid or hydrochloric acid to give the amine **1-IV.** Other suitable methods for protection and deprotection are described in, for example, Green and Wuts, Protective Groups in Organic Synthesis, 3rd edition, John Wiley & Sons, New York, 1999**.** If **1-I** and **1-II** are reacted and R^5 is H, the resulting **1-VIII** can be reacted with **1-IX** to give the intermediate **1-III**. **1-IX** contains a suitable leaving group Y, *e.g.* a chloro and is, depending on the nature of the radical R^5 an alkylating or acylating agent that is reacted under conditions known to a person skilled in the art. **1-IV** is acylated with an unsaturated acid derivative **1-V** to give the final product **1-VI**. **1-V** can be accompanied by the isomeric **1-Va,** so that a mixture of **1-V** and **1-Va** is used in the acylation step. In this case a mixture of **1-VI** and **1-VIa** is formed that can be separated by methods known to a person skilled in the art, e.g. by chromatography. Or **1-Va** can be used in a pure form in the acylation step to give **1-VIa**. Thus, if in the following descriptions and schemes the acid **1-V** is mentioned, the same applies for the isomeric acid **1-Va,** either in its pure form or in form of a mixture of **1-V** and **1-Va.** The same applies for reaction products derived from **1-V:** these can be obtained in pure form if the isomerically pure **1-V** or **1-Va** are used in the acylation step, or they can be obtained as a mixture if a mixture of **1-V** and **1-Va** is used and might be separated then by methods known to a person skilled in the art, *e.g.* by chromatography. There are many acylation methods known to a person skilled in the art: **I-V** can be converted to an acid chloride with oxalyl chloride, thionyl chloride or the like which can be isolated or used directly to react with **1-IV** in the presence of a base like triethylamine or diisopropylethylamine to give **1-VI.** The base might also be polymer-supported to ease work-up. The base might be used in excess, the excess might be removed using aqueous work-up or polymer-supported reagents like polymer-supported acid chloride. The acid **I-V** can also be reacted directly with the amine **I-IV** using coupling reagents like N,N,N',N'-tetramethyl-O-(7-azabenzotriazol-1-yl)-uronium hexafluorophosphate (HATU), N,N,N',N'-tetramethyl-O-(1H-benzotriazol-1-yl)-uronium hexafluorophosphate (HBTU), 1-hydroxy-7-azabenzotriazole (HOAt), N,N'-dicyclohexylcarbodiimide (DCC) or the like. Other suitable amide coupling procedures are described in Goodman, M.; Felix, A.; Moroder, L.; Toniolo, C. in volume E22a of Methods of Organic Chemistry (Houben-Weyl), Synthesis of Peptides and Peptidomimetics, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 2002**.** **1-VI** and **1-VIa** can be converted into their thiocarbonyl analogue **1-X** and **1-Xa** by treatment with, for example, Lawesson's reagent under microwave heating. Other methods are described in, for example, Smith, M.B.; March, J.; March's Advanced Organic Chemistry, John Wiley & Sons, Hoboken; New Jersey, 2007, 1277-1280. A compound of general formula **1-VI** can be substituted at Y^1-Y^4. This substituent can already be present in the heteroaryl compound **1-I.** A person skilled in the art will appreciate that it can also be introduced in a compound **1-III**, **1-IV** or **1-VI**. For example, Y^1-Y^4 in **1-I** might be substituted by a potential leaving group like, for example, halogen, which can be replaced by another group, for example a nucleophilic group in, for example, a nucleophilic substitution reaction. Or, for example, Y^1-Y^4 in **1-III** might be substituted by a potential leaving group like, for example, halogen, which can be replaced by another group, for example a nucleophilic group in, for example, a nucleophilic substitution reaction. Or, for example, Y^1-Y^4 in **1-IV** might be substituted by a potential leaving group like, for example, halogen, which can be replaced by another group, for example a nucleophilic group in, for example, a nucleophilic substitution reaction. **1-I** might also be substituted at Y^1-Y^4 with a group that can react with a group present in the reaction partner **1-II** or **1-VII** like, for example, the amino group in **1-II** or **1-VII**. In this case the reacting group in **1-I** can be protected by a protecting group by methods known to a person skilled in the art. For example, **1-I** can be substituted by an acyl group. This acyl group can be protected as, for example, an oxolan prior to the reaction with **1-II** or **1-VII** and deprotected by, for example, aqueous acid after the reaction with **1-II** or **1-VII** as described in, for example, Green and Wuts, Protective Groups in Organic Synthesis, 3rd edition, John Wiley & Sons, New York, 1999**.** The same applies to the following schemes in an analogous way.

[0279] The heteroaryl compound **1-I** can be substituted at the N-Atom with oxygen, thus being a heteroaryl-N-oxid, for example a quinoline-N-oxid or a pyridine-N-oxid. Methods for the synthesis of such heteroaryl-N-oxides are described in, for example, R. Kreher (editor), volume E7a of Methods of Organic Chemistry (Houben-Weyl), Hetarenes II, part 1, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1991**.** A person skilled in the art will appreciate that the synthetic transformations described in scheme 1 result in this case in the corresponding heteroaryl-N-oxides of heteroaryl compounds of general formula **1-VI** and **1-VIa**, for example.

[0280] Intermediates of formula **1-IV** in which Y^1-Y^4 are C, substituted by R^{12}, R^{13}, R^{14} and R^{15} = halogen, C_1-C_6-alkyl, C^1-C^6-haloalkyl, C_1-C_6-alkoxy, C^1-C^6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl or phenyl, and wherein at least one of R^{12} and R^{13} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, B is N, A is N or a bond, n is 2, R^6 and R^7 = H, and R^4 and R^5 are defined as in formula (I) or (II) above, are new and a subject of this invention. In one preferred embodiment R^{12} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, in another preferred embodiment R^{13} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy.

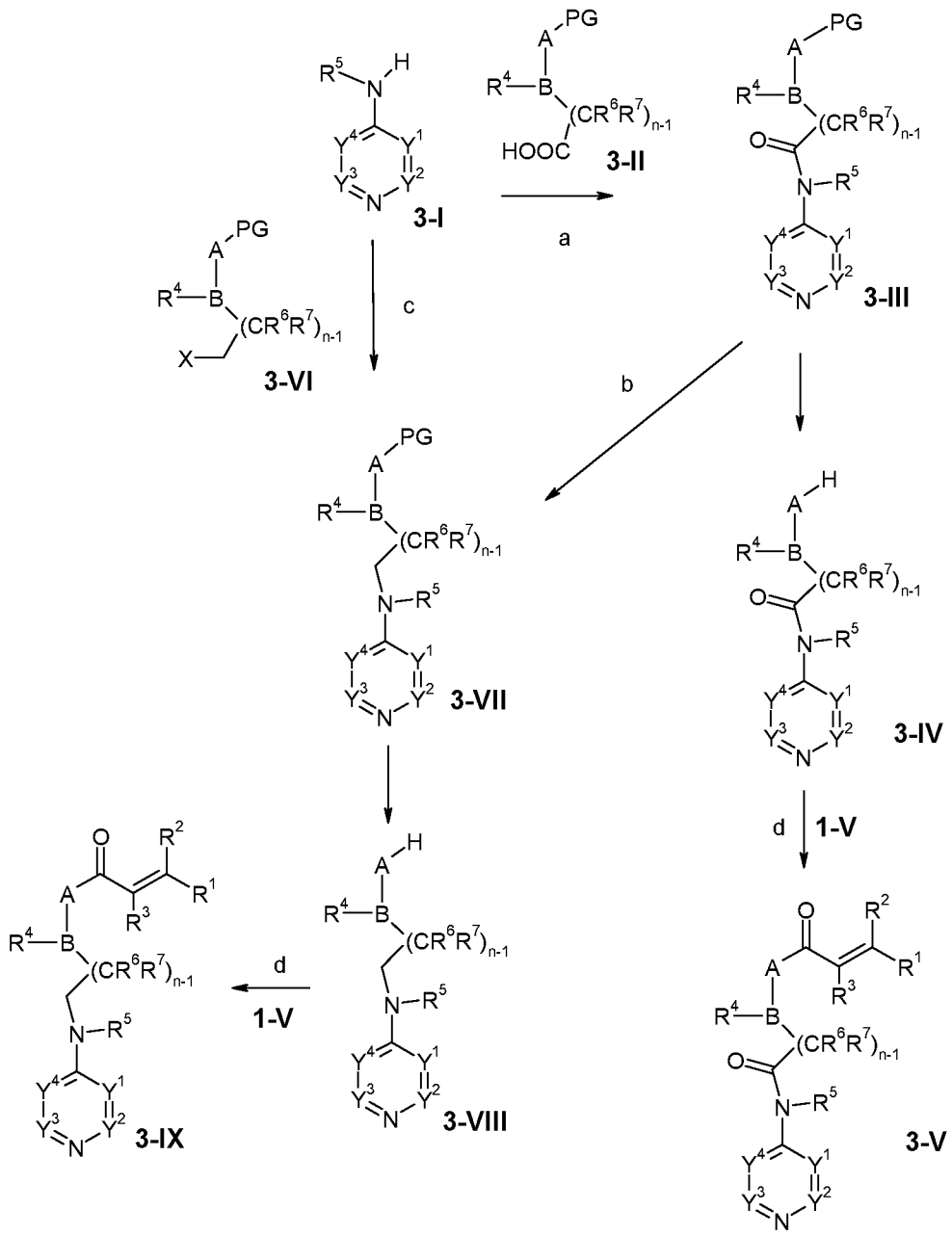
Scheme 2:



[0281] Exemplary conditions: a: oxalyl chloride, DCM, DMF then DCM, triethylamine; b: HBTU, N-ethyl-diisopropylamine (EDIPA), DMF, room temperature; c: palladium acetate, BINAP, caesium carbonate, dioxane; d: Lawesson's reagent, THF, 130°C.

[0282] An alternative synthetic route is shown in scheme 2: the diamine **2-I** is coupled with **1-V** as described for **1-IV** followed by deprotection as described for **1-III** yielding **2-III** which is reacted with **1-I** as described for the reaction of **1-I** with **1-II.**

Scheme 3:



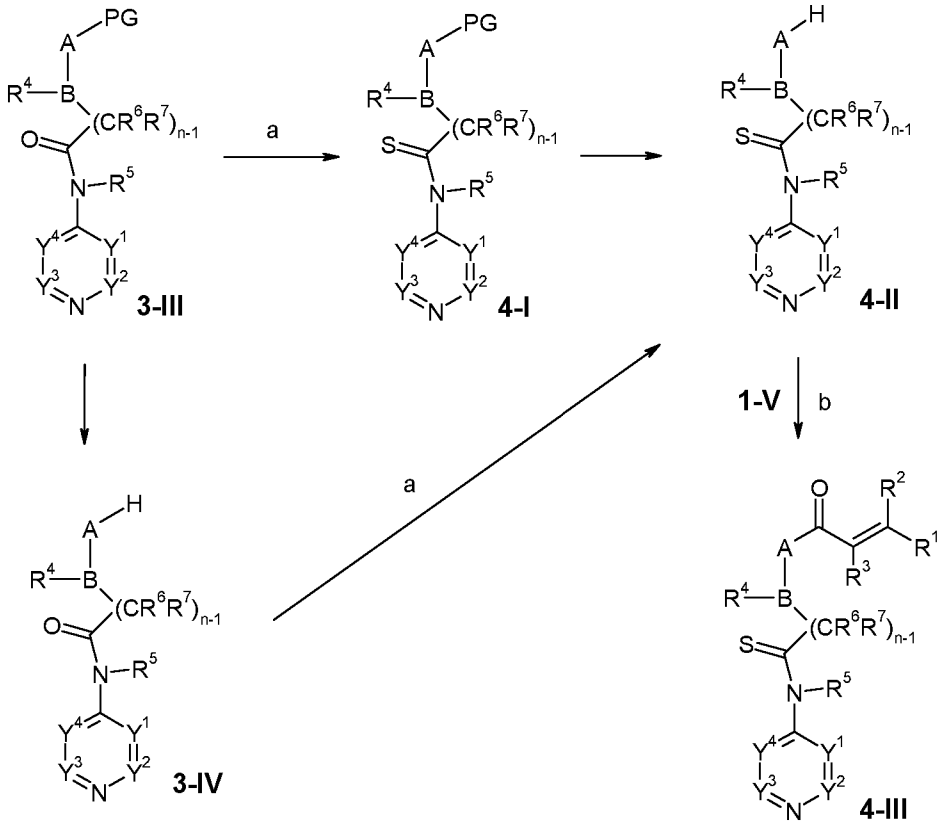
[0283] Exemplary conditions: a: oxalyl chloride, DCM, DMF then DCM, triethylamine b: $LiAlH_4$, THF; c: DCM, triethylamine; d: HBTU, EDIPA , DMF, room temperature

[0284] A compound of general formula **3-V** can be synthesized as shown in scheme 3: A heteroarylaminocompound **3-I** is acylated with an amino acid derivative **3-II** by methods known to a person skilled in the art, some of which have been described in scheme 1. The protecting group (PG) is removed and the amine **3-IV** is acylated with an unsaturated acid **1-V** to give the final product **3-V** by methods that have been described in scheme 1. The oxo-group in **3-III** can be reduced to give **3-VII** employing reducing agents like, for example, lithium aluminium hydride. Other methods are described in, for example, Smith, M.B.; March, J.; March's Advanced Organic Chemistry, John Wiley & Sons, Hoboken; New Jersey, 2007, 1841-1842. The sequence of deprotection and acylation with an unsaturated acid gives the final product **3-IX. 3-VII** can also be obtained by reacting heteroarylaminocompound **3-I** with **3-VI** instead of **3-II**. **3-VI** contains a suitable leaving group X, like, for example, chloride or methanesulfonyl under conditions that are described in, for example, WO2006/60461 (example 303-304.4) or EP1574504 (example 2). Aminoacid derivatives **3-II** are commercially available and can be transformed by methods known to a person skilled in the art to compounds **3-VI**.

[0285] Intermediates of formula **3-IV** in which Y^1-Y^4 are C, substituted by R^{12}, R^{13} R^{14} and R^{15} = halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl or phe-

nyl, and wherein at least one of R^{12} and R^{13} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, B is N, A is N or a bond, n is 2 or 3, R^6 and R^7 = H, and R^4 and R^5 are defined as in formula (I) or (II) above, are new and a subject of this invention. In one preferred embodiment R^{12} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, in another preferred embodiment R^{13} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy.

Scheme 4:

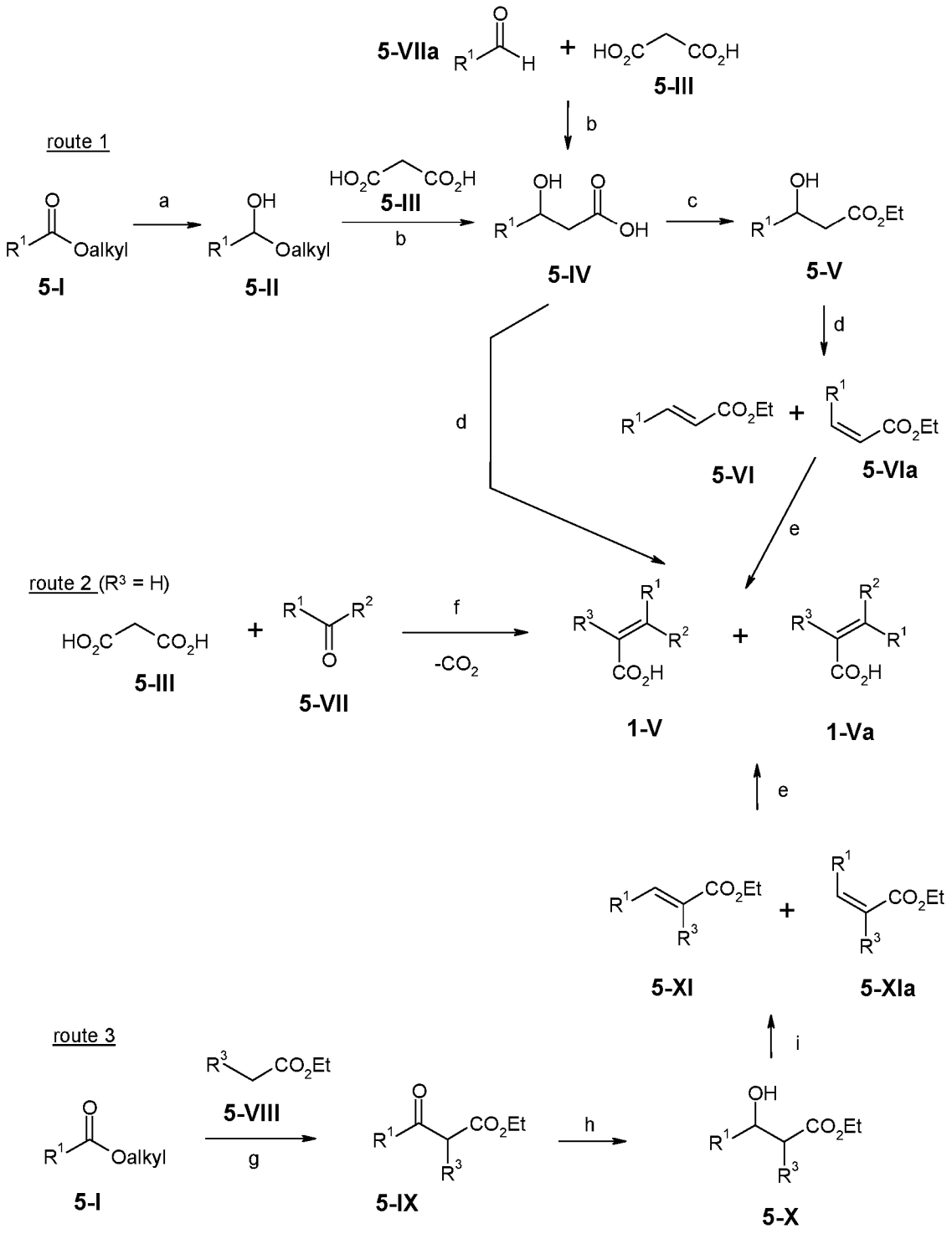


[0286] Exemplary conditions: a: Lawesson's reagent; b: HBTU, diisopropylethylamine , DMF, room temperature

[0287] A compound of general formula **4-III** can be synthesized as shown in scheme 4: The oxo-group in **3-III** can converted to a thioxo-group by methods known to a person skilled in the art, for example, the Laweson's reagent can be used. This and other methods is described in, for example, Smith, M.B.; March, J.; March's Advanced Organic Chemistry, John Wiley & Sons, Hoboken; New Jersey, 2007, 1277-1280. The sequence of deprotection and acylation with an unsaturated acid that has been described in scheme 1 gives the final product **4-III**. Alternativly, the conversion of the oxo- into the thioxo-group can be done after deprotection of **3-III** to **3-IV** to give the thioxo compound **4-II** which is then acylated to the final product **4-III.**

[0288] Intermediates of formula **4-II** in which Y^1-Y^4 is C, substituted by R^{12}, R^{13}, R^{14} and R^{15} = halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl or phenyl, and wherein at least one of $R^{12}$and R^{13} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, B is N, A is N or a bond, n is 2 or 3, R^6 and R^7 = H, and R^4 and R^5 are defined as in formula (I) or (II) above, are new and a subject of this invention. In one preferred embodiment R^{12} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, in another preferred embodiment R^{13} = C_1-C_6-alkoxy or C_1-C_6-haloalkoxy.

Scheme 5:



[0289] Exemplary conditions: a: sodium borohydride, methanol; b: pyridine, piperidine; c: ethanol, HCl; d: phosphorpentoxide; e: NaOH; f: pyridine, piperidine, reflux; g: $LiN(Si(CH_3)_3)_2$, THF; h: sodium borohydride, toluene; i: phosphorpentoxide

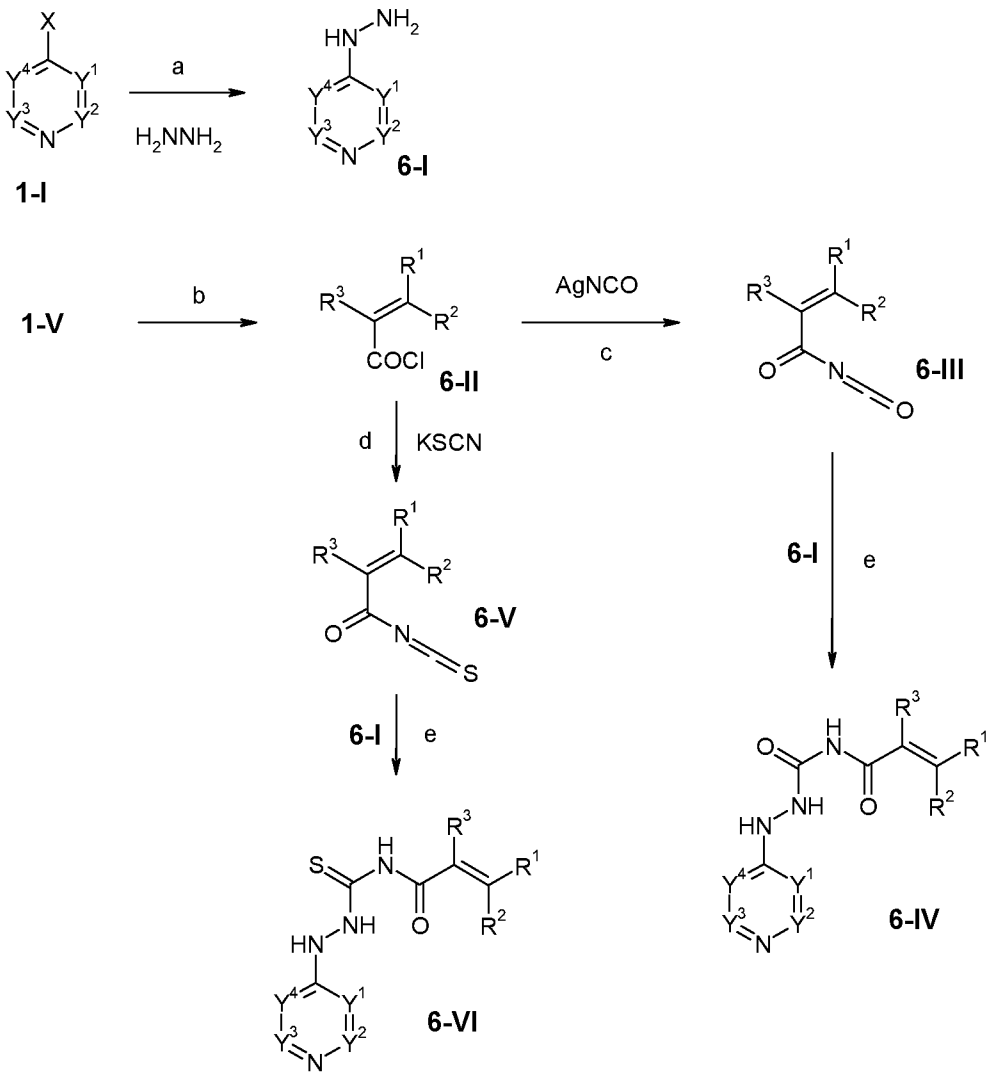
[0290] The unsaturated acids used for acylation (**1-V** in scheme 1) can be synthesized in several ways, many of which are described in: J. Falbe in volume E5, part1 of Methods of Organic Chemistry (Houben-Weyl), Carboxylic acids, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1985**.** The prefered route will be chosen by a person skilled in the

art according to the nature of the radicals R^1, R^2 and R^3. For example, in scheme 5, if R^2 is H and R^1 is alkyl preferably route 2 will be chosen. If R^2 is H and R^1 is alkyl substituted by halogen like F and/or Cl, route 1 or 3 will preferably be chosen. According to route 2 in scheme 5 malonic acid **5-III** is condensed with an aldehyde or ketone **5-VII** to yield directly the crotonic acid 1-V, which can be accompanied by the isomeric **1-Va.** Suitable reaction conditions include heating the reactants in a solvent, preferably pyridine with the addition of piperidine. According to route 1, a carboxylic ester **5-I** is reduced to the hemiacetal **5-II**, which is condensed with malonic acid in a manner analogous to route 1. Alternativly, the aldehyde **5-VIIa** can be condensed with malonic acid to give the hydroxyacid **5-IV.** The hydroxyacid **5-IV** might be isolated or used directly in a dehydration step to yield **I-V**. Preferably, the hydroxyacid is esterified to **5-V** which is dehydrated to **5-VI** and hydrolysed to the acid **1-V**. Methods for the dehydration of **5-IV** and **5-V** are described in, for example, M. Jagodzinska et al.; Tetrahedron 63 (2007), 2042-2046; P.F. Bevilaqua, J. Org. Chem. 94 (1984), 1430-1434 and include treatment of a hydroxyacid or -ester like **5-IV** or **5-V** with P_2O_5 at preferably elevated temperatures or treatment with diethylazodicarboxylate and triphenylphosphine.

[0291] According to route 3 an ester **5-I** is condensed with a CH-acidic ester **5-VIII** to give a beta-keto ester **5-IX** which is reduced to the hydroxyester **5-X.** Methods for the condensation of an ester with another CH-acidic ester are known to a person skilled in the art, as well as methods for the reduction of a keto group to a hydroxygroup and are described in, for example, M. Jagodzinska et al.; Tetrahedron 63 (2007), 2042-2046; T. Kitazume; J. Fluorine Chemistry 42 (1989), 17-29. **5-X** is then converted to the crotonic acid **1-V** in a manner analogous to the one described above for **5-V.**

[0292] In all of the desribed routes, **1-V** might be accompanied by the isomeric **1-Va.** Depending on the nature of the radicals R^1 and R^2 the isomers **1-V** and **1-Va** can be formed in varying proportions. For example if R^2 is H, the E-isomer **1-V** is predominantly formed. The isomeric **1-V** and **1-Va** can be separated by methods known to a person skilled in the art, e.g. by chromatography and can be used as pure isomers in subsequent reactions. Or **1-V** and **1-Va** can be used as a mixture in subsequent reactions and the resulting isomeric products can be separated in a later step. Unsaturated acids with R^1 = alkyl substituted by alkylamino or dialkylamino and R^2 = H and R^3 = H can also be obtained as described in, for example, WO2006/127203 or US2003/50222, respectively. Unsaturated acids with $R^1 = SF_5$ and R^2 = H and R^3 = H can also be obtained as described in, for example, V. K. Brel, Synthesis 2006, 339-343. Unsaturated acids with R^1 = alkylthio and alkylsulfonyl and R^2 = H and R^3 = H can also be obtained as described in, for example, J. T. Moon, Bioorg. Med. Chem. Letters 20 (2010) 52-55. Many unsaturated acids **1-V** used as starting materials are also commercially available by a large number of vendors as listed in, for example, the Symyx Available Chemicals Directory (ACD).

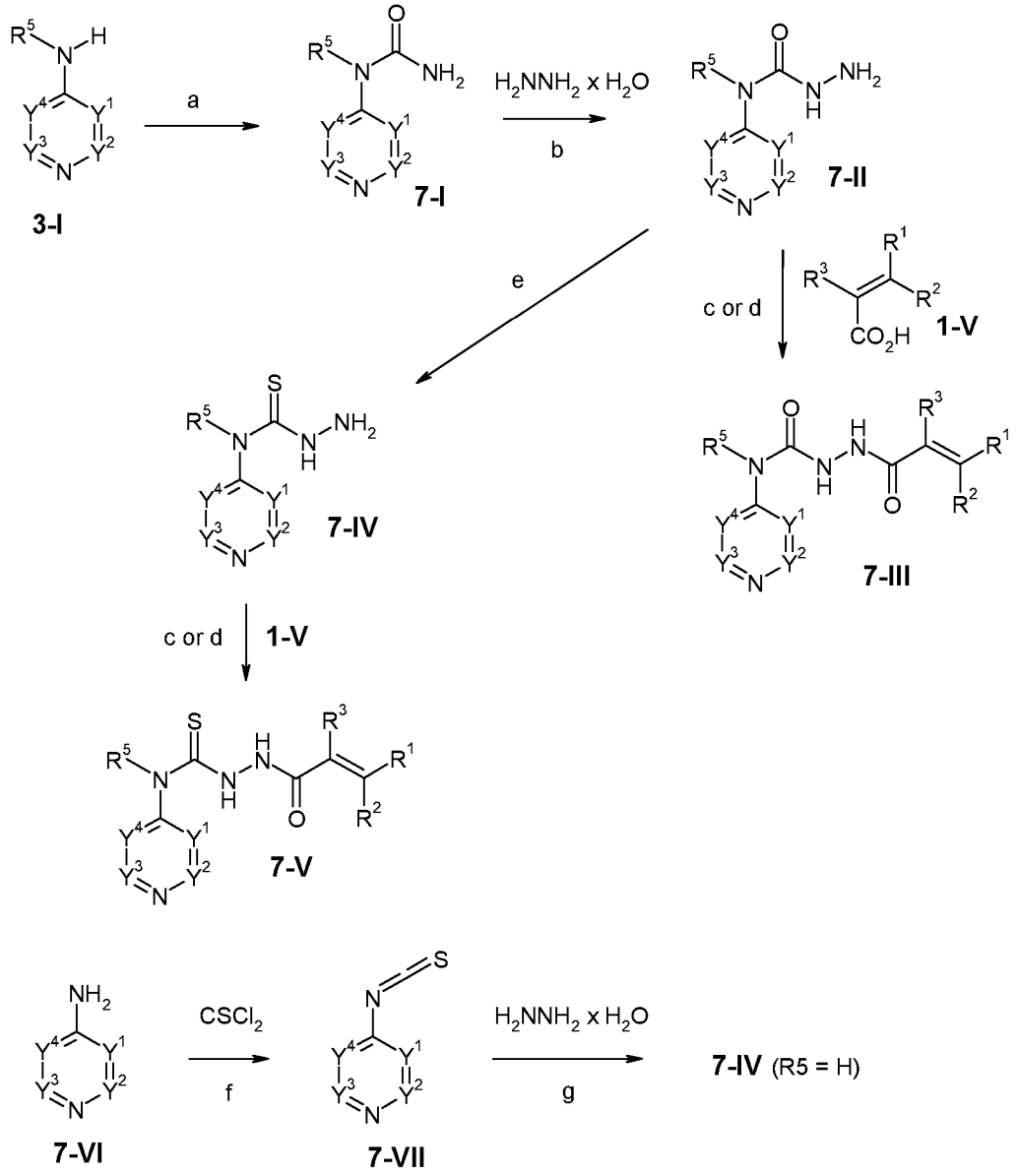
Scheme 6:



[0293] Exemplary conditions: a: hydrazine hydrate, 150°C; b: DCM, oxalyl chloride, DMF, room temperature; c: benzene, room temperature; d: acetonitrile, room temperature; e: DMF, K_2CO_3, room temperature

[0294] Compounds of the general formula **6-IV** can be synthesized as shown in scheme 6: A heteroaryl compound **1-I** containing a suitable leaving group X is reacted with hydrazine to give the hydrazino compound **6-I**. Suitable leaving groups comprise, for example, a halogen like chloro. The reaction is performed preferably at elevated temperatures. An unsaturated carboxylic acid 1-V is converted into its acid chloride **6-II** by methods known to a person skilled in the art, which is converted to the acyl isocyanate **6-III** by reaction with an isocyanate salt like, for example, silver isocyanate. **6-III** is then reacted with the hydrazino compound **6-I** to give the final product **6-IV**, for example by reaction in a solvent like DMF in the presence of a base like potassium carbonate. The thioxo analogue **6-VI** is synthesized analogously by employing the acyl isothiocyanate **6-V**, that is obtained from the carboxylic acid chloride **6-II** by reaction with an isothiocyanate salt like, for example, potassium isothiocyanate in a solvent like, for example, acetonitrile. Similar reactions are described in, for example, WO2004/48347; O. Tsuge, T. Hatta, R. Mizuguchi, Heterocycles 38, (1994), 235-241; G. Shaw, R. N. Warrener, J. Chem. Soc. (1958) 157-161; G. Shaw, R. N. Warrener, J. Chem. Soc. (1958) 153-156.

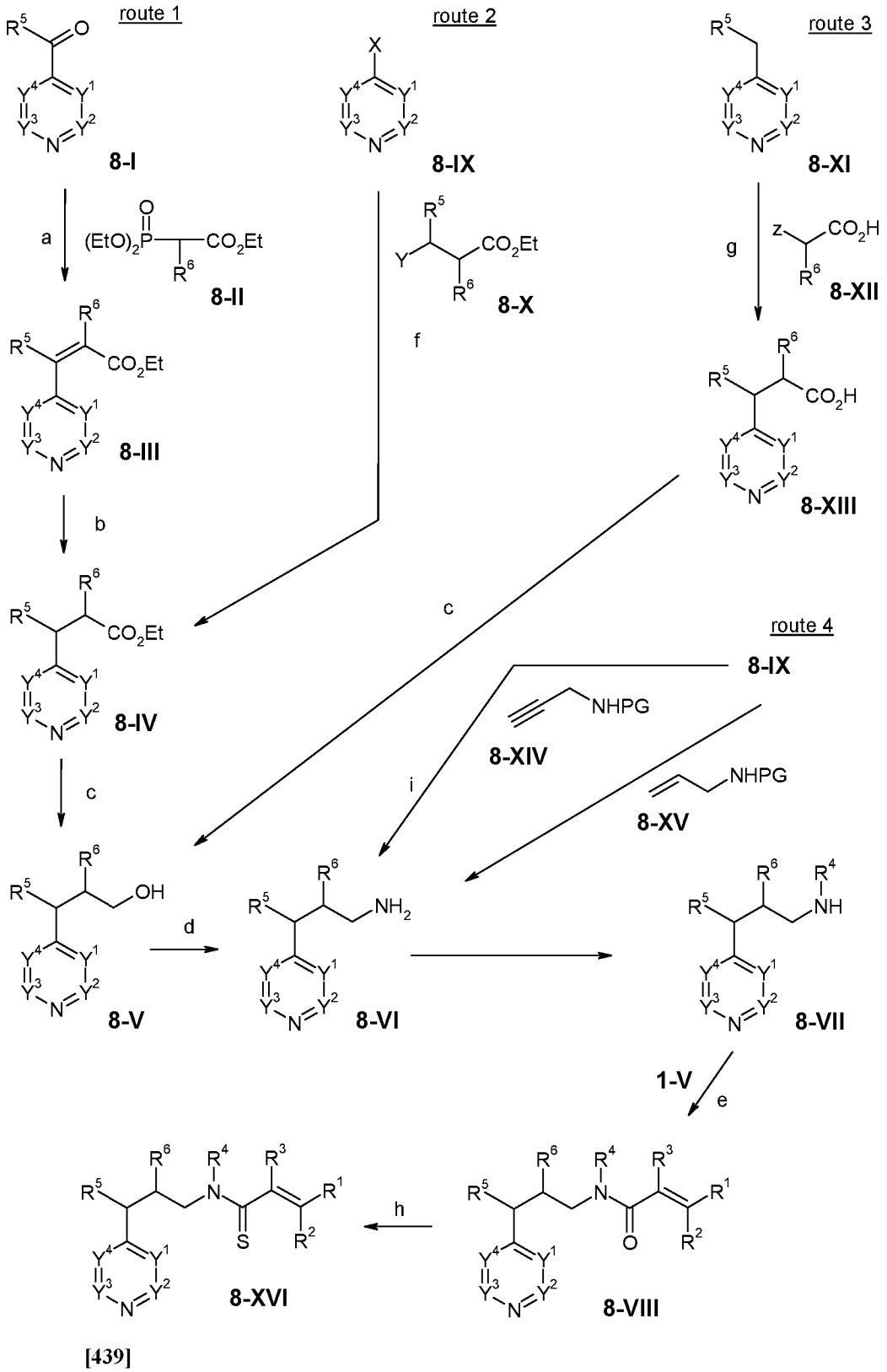
Scheme 7:



[0295] Exemplary conditions: a: sodium cyanate, acetic acid; b: water, ethanol, reflux; c: oxalyl chloride, DCM, DMF then DCM, triethylamine; d: HBTU, diisopropylethylamine , DMF, room temperature; e: Lawesson's reagent; f: benzene, triethylamine, reflux; g: THF.

[0296] A compound of general formula **7-III** can be synthesized as shown in scheme 7: a heteroarylamine **3-I** is converted to the corresponding urea **7-I** by treatment with sodium cyanate. Reaction with hydrazine according to US patent 5098462 yields the carbazine **7-II** which is acylated with an unsaturated acid **1-V** as described in scheme 1 to give the final product **7-III**. The thioxo-analogue **7-V** is obtained by converting the carbazine **7-II** to the thiocarbazine **7-IV** with, for example, Lawesson's reagent, followed by acylation with **1-V** as described above. The thiocarbazine **7-IV** can also be obtained by conversion of the heteroarylamine **7-VI** into the isothiocyanate **7-VII** by reaction with thiophosgen followed by addition of hydrazine.

Scheme 8:

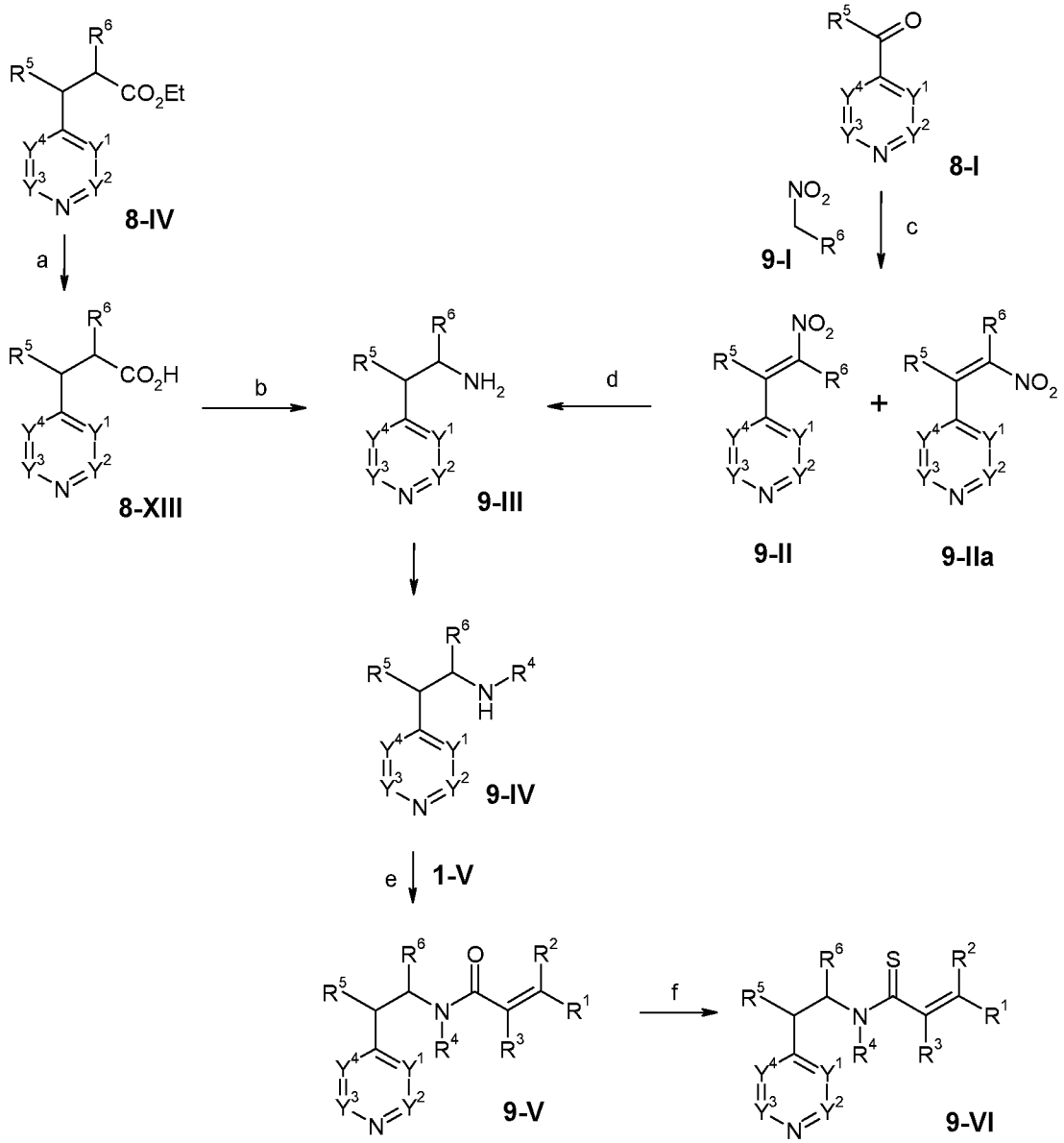


[439]

[0297] Exemplary conditions: a: THF, LiOH; b: hydrogen, ethanol, Pd/C; c: $LiAlH_4$; d: 1. phthalimide, PPh_3, $N_2(COOEt)_2$, THF, 2. N_2H_4, methanol; e: HBTU, diisopropylethylamine , DMF; f: Zn/Cu, $Pd(PPh_3)_2$, dimethylacetamide ; g: $NaNH_2$, $NH_{3(l)}$; h: Lawesson's reagent, THF, 130°C; i: $Pd(PPh_3)_2Cl_2$, 1,4-diazabicyclo[2,2,2]octane, THF.

[0298] A compound of general formula **8-VIII** can be synthesized as shown in scheme 8: in route 1 a heteroarylcarbonyl compound **8-I** is reacted with a phosphonic acid derivative **8-II** in a Horner-Wadsworth-Emmons reaction to form the unsaturated ester **8-III** which is reduced to the saturated ester **8-IV** by methods known to a person skilled in the art, e.g. hydrogenation with a suitable catalyst like, for example, palladium on charcoal. Reduction of the ester to the alcohol **8-V** by, for example, a hydride transfering reagent like lithium aluminium hydride is followed by transformation to the amine **8-VI**. The latter transformation can be achived by, for example, the known Gabriel synthesis via formation of an intermediate phthalimide. Substitution of the nitrogen in **8-VI** to give **8-VII** can be done by methods known to a person skilled in the art using, for example, alkylation agents like alkylhalogens or using reductive alkylation procedures as described in, for example, Smith, M.B.; March, J.; March's Advanced Organic Chemistry, John Wiley & Sons, Hoboken; New Jersey, 2007, 1288-1292. Acylation with the unsaturated acid **1-V** under conditions that have been described in scheme 1 gives the final product **8-VIII**. A person skilled in the art can choose an alternative route depending on the availability, for example commercial availability of starting materials. In route 2 a heteroaryl compound **8-IX** containing a suitable leaving group X like a halogen, preferably a iodine, is reacted with a zincorganic reagent that is synthesized, for example in situ, from the ester **8-X** containing a halogen atom Y, preferably an iodine, by methods known to a person skilled in the art, for example as described in Sakamoto, T., Synthesis, (1988), 485-486 to give the intermediate ester **8-IV.** In route 3 a heteroarylalkyl compound **8-IX** is reacted with a carboxylic acid **8-XII** containing a halogen atom z to give the substituted acid **8-XIII** as described in, for example, Adger, B. M., et. Al. J. Chem. Soc. Perkin Trans. / (1988), 2791-2796, that is reduced to the hydroxy intermediate **8-V** by methods known to a person skilled in the art. In route 4, a heteroaryl compound **8-IX** containing a suitable leaving group X like a halogen, preferably an iodine or bromine, is reacted with a protected amine **8-XIV** containing a terminal triple bond in a Sonogashira-type coupling. Reduction of the triple bond and removal of the protecting group yields the amine **8-VI**. Alternatively, **8-IV** can be obtained by coupling of the protected amine **8-XV** containing a terminal double bond with **8-IX** in a Heck-type reaction followed by reduction and deprotection. Conversion into the thiocarbonyl analogue **8-XVI** can be achieved by treatment with, for example, Lawesson's reagent under microwave heating. Other methods are described in, for example, Smith, M.B.; March, J.; March's Advanced Organic Chemistry, John Wiley & Sons, Hoboken; New Jersey, 2007, 1277-1280.

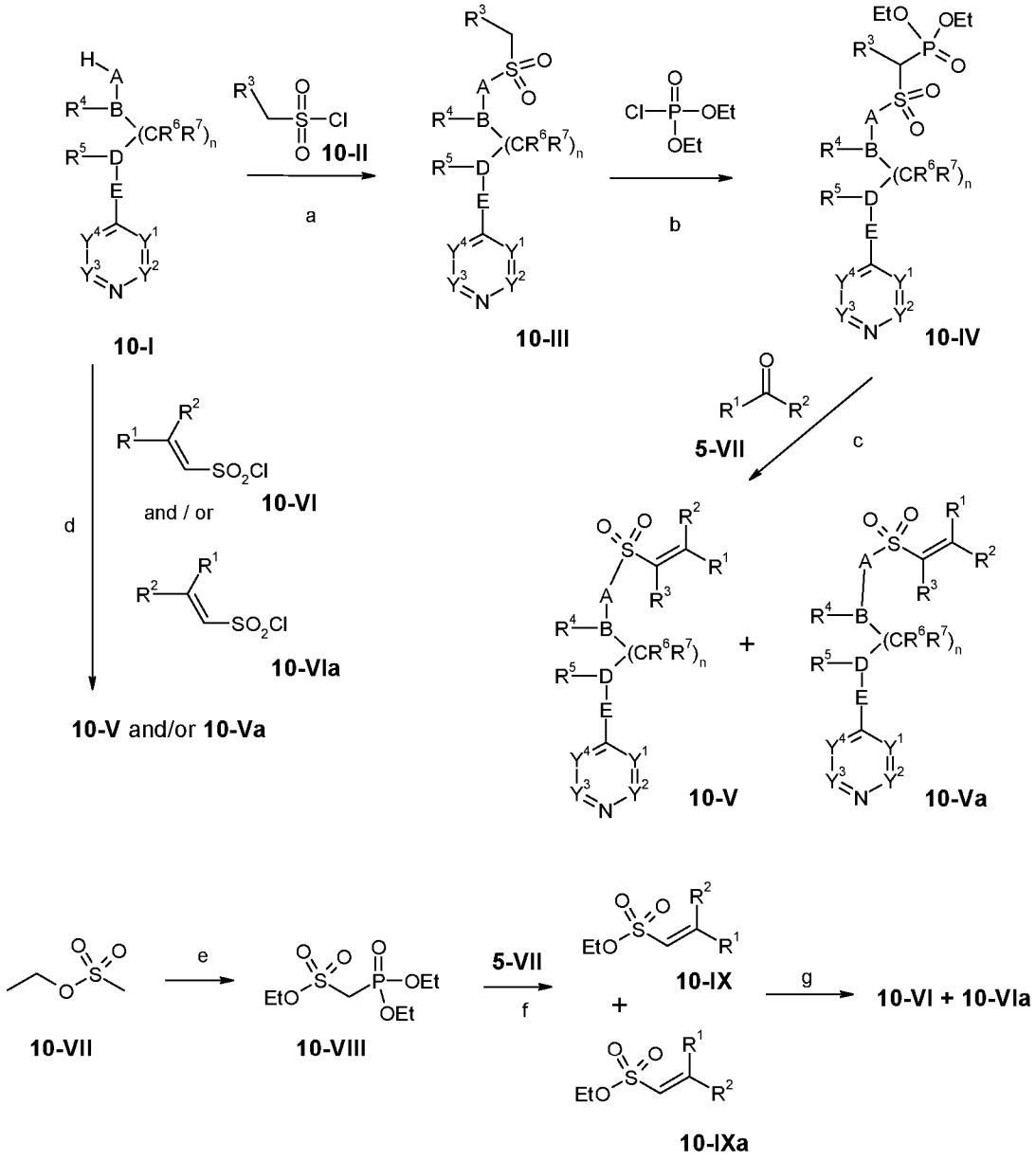
Scheme 9:



[0299] Exemplary conditions: a: NaOH, H_2O; b: NaN_3, H_2SO_4; c: 1. DCM, TEA 2. DCM, methanesulfonyl chloride, TEA; d: hydrogen, Raney nickel, methanol; e: HBTU, diisopropylethylamine , DMF; f: Lawesson's reagent, THF, 130°C.

[0300] Compounds of the general formula 9-V can be synthesized as shown in scheme 9: a heteroarylcarboxylic acid **8-XIII** that has been described in scheme 8 is transformed into the amine **9-III** with a Schmidt reaction as described in, for example, Claudi, F. et al. Eur. J. Med. Chem. 30(5), (1995), 415-421. **8-XIII** can also be obtained by hydrolysis of the ester 8-IV that has been described in scheme 8. Alternatively, a heteroarylcarbonyl compound **8-I** can be transformed to a mixture of **9-II** and the isomeric **9-IIa** as described in, for example, WO2008/125839 (example 36) followed by reduction to **9-III** as described in, for example, Monti, D. et al. Farmaco, 36(6), (1981), 412-418. The primary amine in **9-III** is then substituted as has been described in scheme 8 and acylation with a unsaturated acid as has been decribed in scheme 1 gives the final product **9-V.** Conversion into the thiocarbonyl analogue **9-VI** can be achieved by treatment with, for example, Lawesson's reagent under microwave heating.

Scheme 10:

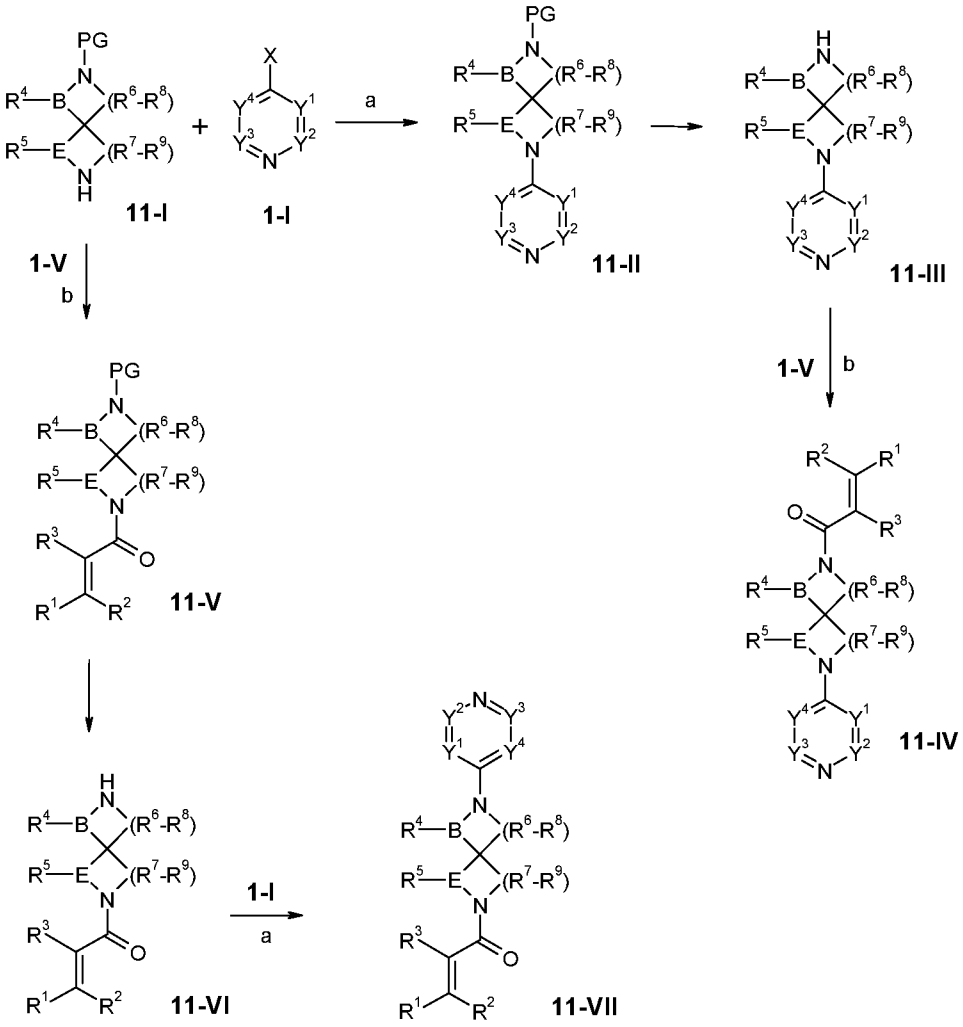


[0301] Exemplary conditions: a: DCM, TEA, 0°C; b: $LiN(Si(CH_3)_3)_2$, THF, -78°C; c: LiBr, DBU, THF, -10°C to room temperature; d: TEA, DCM, ; e: $(EtO)_2POCl$, n-butyllithium (n-BuLi), THF, -80°C; f: tetrabutylammonium iodide, acetone, reflux, then sulfuryl chloride, triphenylphosphine, DCM.

[0302] A compound of the general formula **10-V** can be synthesized as shown in scheme 10: A compound **10-I** which contains an NH-group is reacted with an alkylsulfonic acid chloride **10-II** in the presence of a suitable base like triethylamine in a solvent like dichloromethane. **10-I** can be synthesized, for example, according to schemes 1, 2, 3, 4, 8 or 9. The sulfonamide **10-III** is deprotonated with a strong base like lithium diisopropylamide, lithium hexamethyldisilazide or n-butyllithium at low temperature like -78°C and reacted with diethylchlorophosphate to give **10-IV. 10-IV** is then reacted with a carbonylcompound **5-VII** to give the final product **10-V**. The last step is carried out in the presence of lithium bromide and a strong base like 1,8-diaza-7-bicyclo[5.4.0]undecene (DBU). Similar reactions are described in, for example, Z. Wróbel, Tetrahedron 57 (2001), 7899-7907. Depending on the nature of the radicals R^1, R^2 and R^3 the isomeric final products **10-V** and **10-Va** can be formed in differing proportions. For example, if R^2 is H and R^3 is H, then the E-isomer **10-V** is formed predominantly. If a mixture of **10-V** and **10-Va** is formed, this can be separated by methods known to a person skilled in the art, e.g. by chromatography. Alternatively, the vinylsulfonyl chloride **10-VI** can be synthesized first starting from the methanesulfonate **10-VII** by deprotonation and reaction with diethylchlorophosphate, followed by deprotonation and reaction with a carbonylcompound **5-VII** leading to the unsaturated sulfonate **10-IX** which is converted

to **10-VI**. This sulfonyl chloride is then coupled to the amino compound **10-I** to give the final product **10-VI**.

Scheme 11:



[0303] Exemplary conditions: a: $Pd_2(dba)_3$, BINAP, potassium *tert*.butylat, TEA, toluene, b: HBTU, diisopropylethylamine , DMF

[0304] A spiro-compound that is formed when R^6 is joined together with R^8 to form a C_1-C_3 alkylene group and R^7 is joined together with R^9 to form a C_1-C_3 alkylene group can be synthesized as shown in scheme 11: A spirocyclic diamine **11-I** is coupled to a heteroarylcompound **1-I** to give **11-II**. **11-I** can be monoprotected by a suitable protecting group like the ones that have been described in scheme 1. The synthesis of compounds like **11-I** has been described in, for example, Burckhard, J., Carreira, E.M., Organic Lett. 10 (2008), 3525-3526 and Burckhard, J., Guerot, C., Knust, H., Rogers-Evans, M., Carreira, E.M., Organic Lett. 12 (2010), 1944-1947. Pd-catalysis can be used employing a Pd-containing molecule like palladium acetate or $Pd_2(dba)_3$, a phosphorus-containing ligand like BINAP, a base like caesium carbonate or sodium *tert*-butoxide in a solvent like an ether-containing solvent like diethylether, dioxane or tetrahydrofuran, or an inert solvent like toluene as described in, for example, Burckhard, J., Carreira, E.M., Organic Lett. 10 (2008), 3525-3526. Deprotection and acylation with an unsaturated acid **1-V** gives the final product **11-IV**. The sequence might be altered so that the spirocyclic diamine **11-I** is first acylated to give **11-V**. Deprotection and coupling with the heteroarylcompound **1-I** gives **11-IV**.

[0305] Heteroaryl compounds **1-I and 8-IX** can be synthesized by several methods known to those skilled in the art. Quinoline derivatives are described in, for example, R. Kreher (editor), volume E7a of Methods of Organic Chemistry (Houben-Weyl), Hetarenes II, part 1, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1991; pyridine derivatives are described in, for example, R. Kreher (editor), volume E7b of Methods of Organic Chemistry (Houben-Weyl), Hetarenes II, part 2, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1992; pyrimidines are described in, for example, E. Schaumann (editor), volume E9b of Methods of Organic Chemistry (Houben-Weyl), Hetarenes IV, part 2a,, 4th edition,

Georg Thieme Verlag, Stuttgart - New York, 1998; quinazoline derivatives are described in E. Schaumann (editor), in volume E9b of Methods of Organic Chemistry (Houben-Weyl), Hetarenes IV, part 2b,, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1997; pyridazines and cinnolines in, for example, E. Schaumann (editor), volume E9a of Methods of Organic Chemistry (Houben-Weyl), Hetarenes IV, part I,, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1997; pyridopyridines in The Chemistry of Heterocyclic Compounds, Volume 63, The Naphthyridines, D. J. Brown, P. Wipf, E. C. Taylor (Eds), John Wiley & Sons, New York, 2007; thienopyridines, furopyridines, thienopyrimidines, furopyrimidines, pyrrolopyridines, pyrazolopyrimidines, pyrazolopyridines, pyridopyridines and triazolopyrimidines are described in, for example, A. R. Katritzky, C. W. Rees, E. F. V. Scriven (Editors), volume 7 of Comprehensive Heterocyclic Chemistry II, Elsevier Science Ltd., Oxford - New York, 1996. The synthesis of furopyridines is also described in, for example, S. Shiotani, K. Tanaguchi, J. Heterocyclic Chem., 33, (1996), 1051-1056; S. Shiotani, K. Tanaguchi, J. Heterocyclic Chem., 34, (1997), 925-929. 2-3-Dihydrofuropyridines are described in, for example, F. Suzenet, M. Khouili, S. Lazar, G. Guillaument, Synlett, (2009), 92-96. 2,3-Dihydro-1,4-dioxinopyridines are described in, for example, B. Joseph, A. Benarab, G. Guillaument, Heterocycles 38, (1994), 1355-1360. Many heteroaryl compounds **1-I** used materials are also commercially available by a large number of vendors as listed in, for example, the Symyx Available Chemicals Directory (ACD).

[0306] Amines **1-II**, **1-VII**, **2-I**, **3-I**, **7-VI**, amino acid derivatives **3-II**, used as starting materials are commercially available by a large number of vendors as well as carboxylic esters **5-I** and **5-VIII**, aldehydes **5-VIIa**, ketones **8-I**, halocarboxylic esters **8-X**, halocarboxylic acids **8-XII**, phosphonic acid derivatives **8-II** and carbonyl compounds **5-VII** as listed in, for example, the Symyx Available Chemicals Directory (ACD).). In addition, carboxylic esters can be obtained by methods known to a person skilled in the art and described in, for example, J. Falbe (editor), volume E5 of Methods of Organic Chemistry (Houben-Weyl), Carboxylic acids and Derivatives, part I,, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1985. Likewise, aldehydes can be obtained by methods described in, for example, J. Falbe (editor), volume E3 of Methods of Organic Chemistry (Houben-Weyl), Aldehydes, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1983 and ketones as described in, for example, volume VII, part 2 a-c of Methods of Organic Chemistry (Houben-Weyl), Ketones I-III, 4th edition, Georg Thieme Verlag, Stuttgart - New York, 1973-1977.

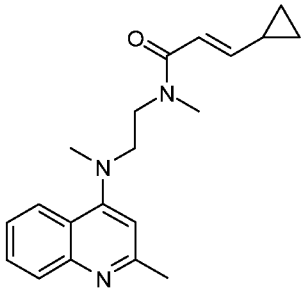
B. Synthesis Examples

[0307] The following examples are for illustrative purposes only and are not intended to limit the scope of the invention. The compounds were named using Symyx®draw version 3.1.Net software (Symyx Technologies, Inc.).

[0308] The methods described in the examples can be easily adapted by a person skilled in the art to make other compounds, and intermediates thereof. For instance, a person skilled in the art could replace in the examples the exemplified starting compounds by other compounds of the formulae **1-I**, **1-II**, **1-V, 1-VII**, **I-IX**, **2-I**, **3-I, 3-II**, **3-VI**, **5-I**, **5-VII**, **5-VIII**, **5-XI**, **7-VI**, **8-I**, **8-II**, **8-IX, 8-X, 8-XI**, **8-XII**, **10-I**, **10-II**, **10-V** (e.g. commercially available compounds), perform routine adaptions of the reaction conditions, if any, and use them for the synthesis of further compounds according to this invention.

Example 1: Synthesis of (*E*)-3-cyclopropyl-N-methyl-N-[2-[methyl-(2-methyl-4-quinolyl)amino]ethyl]prop-2-enamide (A-197)

[0309]



Step A: N,N'-Dimethyl-N-(2-methyl-4-quinolyl)ethane-1,2-diamine

[0310] 4-Chloroquinaldine (1.5 g, 5 mmol) was mixed with N,N'-dimethylethylenediamine (2.45 ml, 25 mmol) and 1-methoxy-2-propanol (8 ml) and stirred at 110°C overnight. The mixture was purified by column chromatography (prepacked silica column, gradient of heptane / ethyl acetate each containing 1% triethylamine). 0.4 g were obtained (1.75

mmol; 35%). MS (APCI) m/z = 230.0 $[M+H]^+$.

Step B: (*E*)-3-Cyclopropylprop-2-enoic acid

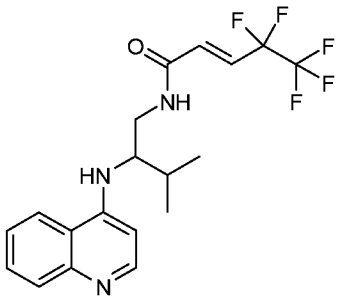
[0311] Malonic acid (18.9 g, 180 mmol), cyclopropanecarbaldehyde (4.5 g, 60 mmol) and piperidine (0.7 ml) were mixed with pyridine (37 ml) and stirred under reflux for 2 hours, stirring was continued overnight at room temperature. The mixture was poured into 2M hydrochloric acid (200 ml), the phases were seperated and the aqueous phase was extracted with dichloromethane (60 ml). The organic phases were combined, the solvent was removed under reduced pressure and the residue was purified by column chromatography (pre-packed silica column, gradient of petrolether / ethyl acetate). 6.2 g of an off-white crystalline solid was obtained (51.6 mmol, 86%). MS (APCI) m/z = 112.9 $[M+H]^+$.

Step C: (*E*)-3-Cyclopropyl-N-methyl-N-[2-[methyl-(2-methyl-4-quinolyl)amino]ethyl]prop-2-enamide

[0312] (*E*)-3-Cyclopropylprop-2-enoic acid (22 mg, 0.2 mmol) and HBTU (76 mg, 0.2 mmol) were dissolved in a 1:1 mixture of anhydrous THF and anhydrous DMF (2 ml). After 5 minutes N,N'-dimethyl-N-(2-methyl-4-quinolyl)ethane-1,2-diamine (52 mg, 0.23 mmol) and triethylamine (62 µl, 0.45 mmol) were added and the mixture was stirred at room temperature for 2 hours. The mixture was diluted with ethyl acetate, washed with water, saturated sodium bicarbonate solution, brine and dried over magnesium sulfate. The solvent was removed under reduced pressure and purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 28.3 mg (0.087 mmol, 43.5 %).

Example 2: Synthesis of (*E*)-4,4,5,5,5-pentafluoro-N-[3-methyl-2-(4-quinolylamino)butyl]pent-2-enamide (B-4)

[0313]



Step A: 1-Ethoxy-2,2,3,3,3-pentafluoro-propan-1-ol

[0314] Ethyl 2,2,3,3,3-pentafluoropropionate (10.99 grams, 57.2 mmol) was dissolved in anhydrous methanol (57 ml) and cooled under argon to -60°C. Sodium borohydride (2.16 grams, 57.2 mmol) was added in four portions. After the addition was complete, stirring was continued for one hour and the temperature was held below -45°C. The mixture was cooled to -60°C and 1M hydrochloric acid (172ml) was added dropwise so that the temperature remained below -45°C. The mixture was slowly warmed to room temperature and extracted with diethylether (3x100 ml). The combined organic phases were washed with water (two times), dried over magnesium sulfate, the solvent was removed under reduced pressure. 9.76 g (50.3 mmol, 88%) were obtained and used directly in the next step.

Step B: 6,6,7,7,7-Pentafluoro-3-hydroxy- pentanoic acid

[0315] 1-Ethoxy-2,2,3,3,3-pentafluoro-propan-1-ol (9.76 g, 50.3 mmol) was mixed with malonic acid (15.73 g, 0.15 mole), piperidine (0.611 ml) and pyridine (30 ml) and heated at 120°C until gas evolution ceased (4 hours). The solvent was removed under reduced pressure, the residue treated with 1 M hydrochloric acid and extracted with diethylether (3x). The combined organic phases were washed with water (2x), dried over magnesium sulfate, the solvent was removed under reduced pressure. 9.81 g (47.2 mmol, 94%) were obtained and used directly in the next step.

Step C: Ethyl 4,4,5,5,5-pentafluoro-3-hydroxy-pentanoate

[0316] 6,6,7,7,7-Pentafluoro-3-hydroxy- (9.81 g, 47.2 mmol) was dissolved in anhydrous ethanol (47 ml), concentrated sulfuric acid was added (0.534 ml) and the mixture was heated under reflux. A solution of hydrochloric acid in anhydrous methanol was added (1M, 8 ml) and heating was continued for 3 hours. The solvent was removed under reduced pressure

and 11.9 g were obtained which were used directly in the next step.

Step D: Ethyl (*E*)-4,4,5,5,5-pentafluoropent-2-enoate

[0317] Ethyl 4,4,5,5,5-pentafluoro-3-hydroxy-pentanoate (11.9 g from step C) was placed in a 25 ml round-bottom flask and phosphorpentoxid was added in small portions until the educt was almost completely absorbed. The temperature was raised slowly to 140°C until a brown sirup was obtained. The flask was connected to a distilling apparatus and the product isolated by distillation at reduced pressure (50 mbar, 50°C). 5.5 g (25.2 mmol, 50% over 2 steps) were obtained.

Step E: (*E*)-4,4,5,5,5-Pentafluoropent-2-enoic acid

[0318] Ethyl (*E*)-4,4,5,5,5-pentafluoropent-2-enoate (5.5 g, 25.2 mmol) was suspended in 10% NaOH (14.5 ml) and heated at reflux until a homogenous solution was obtained (40 min). After cooling to room temperature the mixture was washed with diethylether (2x) and acidified under ice-cooling with concentrated sulfuric acid. The mixture was extracted with diethylether (3x), the combined organic phases were washed with water, dried over magnesium sulfate and the solvent removed under reduced pressure. 2.64 g (13.9 mmol, 55%) were obtained. MS (ES) M/z = 189.0 $[M-H]^-$.

Step F: 3-Methyl-2-(4-quinolylamino)butanamide

[0319] 4-Chloroquinoline (0.82 g, 5 mmol), valinamide (0.64 g, 5.5 mmol) and diisopropylamine (1.9 ml, 11 mmol) were mixed with 1-methoxy-2-propanol (8 ml) and heated with stirring at reflux for 48 hours. The solvent was removed under reduced pressure, the residue was partitioned between water and ethyl acetate, the phases were separated, the aqueous phase was washed 3 times with ethyl acetate and basified with 50% NaOH. A precipitate formed that was filtered off and dried in air to give 0.2 g of a solid (0.78 mmol, 14%). MS (APCI) M/z = 243.6 $[M+H]^+$.

Step G: 3-Methyl-N2-(4-quinolyl)butane-1,2-diamine

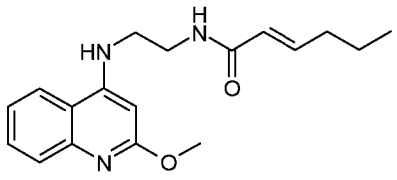
[0320] 3-Methyl-2-(4-quinolylamino)butanamide (460 mg, 1.9 mmol) was dissolved in anhydrous THF (30 ml) under argon, the mixture was cooled to 0°C and a 1M solution of borane in anhydrous THF (8 ml, 8 mmol) was added with stirring. Stirring was continued for 1 hour at 0°C, the cooling bath was removed and the mixture was allowed to warm to room temperature overnight with stirring. The mixture was quenched with 1 M NaOH and extracted with ethyl acetate. The organic phase was evaporated to dryness under reduced pressure and the residue was purified by column chromatography (pre-packed silica column, gradient of ethyl acetate / methanol containing 1% ammonia). 220 mg was obtained (0.96 mmol, 51%). MS (APCI) m/z = 229.8 $[M+H]^+$.

Step H: (*E*)-4,4,5,5,5-Pentafluoro-N-[3-methyl-2-(4-quinolylamino)butyl]pent-2-enamide

[0321] (*E*)-4,4,5,5,5-Pentafluoropent-2-enoic acid (29 mg, 0.15 mmol) was dissolved in anhydrous DMF (1 ml), HBTU (60 mg, 0.15 mmol) and diisopropylamine (26µl, 0.15 mmol) were added and the mixture was stirred at room temperature for 15 minutes. 3-Methyl-N2-(4-quinolyl)butane-1,2-diamine (34.4 mg, 0.15 mmol) dissolved in 1 ml anhydrous DMF together with diisopropylethylamine (26µl, 0.15 mmol) was added and the resulting mixture was stirred at room temperature for 3 hours. The mixture was evaporated to dryness under reduced pressure and the resulting residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 7.3 mg (0.018 mmol, 12 %).

Example 3: Synthesis of (*E*)-N-[2-[(2-methoxy-4-quinolyl)amino]ethyl]hex-2-enamide (A-177)

[0322]



Step A: 4-Chloro-2-methoxy-quinoline

[0323] To a solution of (2.5 g, 12,6 mmol) 2,4-dichloro-quinoline in anhydrous toluene (20 ml) was added a suspension

of solid sodium methoxide (2.5 g, 46.3 mmol) in anhydrous toluene (20 ml). The mixture was stirred under reflux for 16 hours and then allowed to cool to room temperature. The solid that had formed was filtered off and washed with 50 ml toluene. The filtrate was evaporated to dryness under reduced pressure to yield a red solid (2.1 g, 10.8 mmol, 86%). MS (ES) m/z = 193.1 $[M+H]^+$.

Step B: N-(2-Methoxy-4-quinolyl)ethane-1,2-diamine

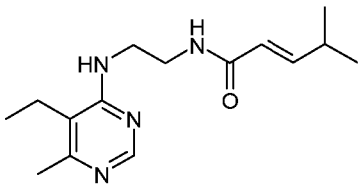
[0324] 4-Chloro-2-methoxy-quinoline (484 mg, 2.5 mmol) and 1,2-diaminoethan (751 mg, 12.5 mmol) were mixed with 1-methoxy-2-propanol and stirred at 110°C for 24 hours. The mixture was evaporated to dryness and the residue was purified by column chromatography (pre-packed silica column, gradient of ethyl acetate / methanol each containing 1% triethylamine). 0.324 g were obtained (1.49 mmol; 60%). MS (APCI) m/z = 218.0 $[M+H]^+$.

Step C: (*E*)-N-[2-[(2-Methoxy-4-quinolyl)amino]ethyl]hex-2-enamide

[0325] N-(2-Methoxy-4-quinolyl)ethane-1,2-diamine (21.7 mg, 0.1 mmol) was dissolved in anhydrous dichloromethane (1 ml) together with triethylamine (17.4 µl, 0.125 mmol). (*E*)-hex-2-enoyl chloride (16.6 mg, 0.125 mmol) was added and the mixture was shaken for 10 minutes, diluted with dichloromethane and washed with 10% sodium bicarbonate solution (2 times), water and evaporated to dryness under reduced pressure. The resulting residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 3.4 mg (0.0109 mmol, 11 %).

Example 4: Synthesis of (*E*)-N-[2-[(5-ethyl-6-methyl-pyrimidin-4-yl)amino]ethyl]-4-methyl-pent-2-enamide (A-20)

[0326]



Step A: N-(5-Ethyl-6-methyl-pyrimidin-4-yl)ethane-1,2-diamine hydrochloride

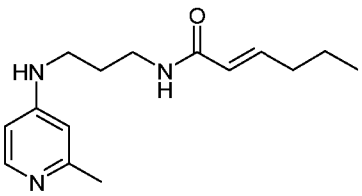
[0327] 4-Chloro-5-ethyl-6-methylpyrimidin (570 mg, 4 mmol) was mixed with 1,2-diaminoethane (2 ml, 30 mmol) and stirred at 150 °C in a closed vessel under microwave heating. The mixture was evaporated to dryness under reduced pressure to yield 1.255 g of a solid. MS (APCI) m/z = 181.1 $[M+H]^+$.

Step B: (*E*)-N-[2-[(5-Ethyl-6-methyl-pyrimidin-4-yl)amino]ethyl]-4-methyl-pent-2-enamide

[0328] (*E*)-4-Methylpent-2-enoic acid (46 mg, 0.4 mmol), HBTU (152 mg, 0.4 mmol) and triethylamine (82 µl, 0.6 mmol) were dissolved in a 1:1 mixture of anhydrous DMF and anhydrous acetonitrile (2 ml), after 20 minutes N-(5-ethyl-6-methyl-pyrimidin-4-yl)ethane-1,2-diamine hydrochloride (40 mg, 0.185 mmol) was added. The mixture was stirred at room temperature for 2 hours and left to stand at room temperature overnight. The reaction mixture was diluted with ethyl acetate, washed with water, saturated sodium bicarbonate solution and brine, dried over magnesium sulfate and evaporated to dryness under reduced pressure. The residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 9 mg (0.033 mmol, 18 %).

Example 5: Synthesis of (*E*)-N-[3-[(2-methyl-4-pyridyl)amino]propyl]hex-2-enamide (A-89)

[0329]



Step A: N-(2-Methyl-4-pyridyl)propane-1,3-diamine hydrochloride

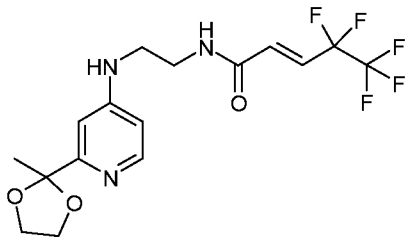
[0330] 4-Chloro-2-picoline (441μl, 4 mmol) was mixed with 1,3-diaminopropane (1.67 ml, 20 mmol) and stirred in a closed vessel at 180°C under microwave heating for one hour. The solvent was removed under reduced pressure, toluene was added to the residue and the mixture was evaporated to dryness under reduced pressure to yield 1.076 of a solid. MS (APCI) m/z = 165.8 $[M+H]^+$.

Step B: (*E*)-N-[3-[(2-Methyl-4-pyridyl)amino]propyl]hex-2-enamide

[0331] (*E*)-4-Hex-2-enoic acid (23 mg, 0.2 mmol) and HBTU (76 mg, 0.2 mmol) were dissolved in a 1:1 mixture of anhydrous DMF and anhydrous acetonitrile (2 ml), after 5 minutes triethylamine (82 μl, 0.6 mmol) and N-(2-Methyl-4-pyridyl)propane-1,3-diamine hydrochloride (40 mg, 0.2 mmol) was added. To the mixture basic aluminium oxide was added, stirring was continued for one hour, the mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 20.2 mg (0.077 mmol, 39 %).

Example 6: Synthesis of (*E*)-4,4,5,5,5-pentafluoro-N-[2-[[2-(2-methyl-1,3-dioxolan-2-yl)-4-pyridyl]amino]ethyl]pent-2-enamide (A-133)

[0332]



Step A: 4-Chloro-2-(2-methyl-1,3-dioxolan-2-yl)pyridine

[0333] 1-(4-Chloro-2-pyridyl)ethanone (440 mg, 2.83 mmol) and ethyleneglycol (480 mg, 3 mmol) were mixed with toluene (10 ml), a catalytic amount of p-toluenesulfonic acid was added and the mixture was heated at reflux overnight. The mixture was evaporated to dryness to yield 523 mg of a solid (2.6 mmol, 93%). MS (APCI) m/z = 200.0 $[M+H]^+$.

Step B: N-[2-(2-Methyl-1,3-dioxolan-2-yl)-4-pyridyl]ethane-1,2-diamine

[0334] 4-Chloro-2-(2-methyl-1,3-dioxolan-2-yl)pyridine (500 mg, 2.5 mmol) was mixed with 1,2-diaminoethane (1.09 ml, 26.2 mmol) and stirred in a closed vessel at 180°C with microwave heating for 30 minutes in two batches. The mixture was evaporated to dryness, the solid residue was washed with acetone. The washing solution was evaporated to dryness and this solid residue was washed with acetonitrile. The solid residues were combined and dried under reduced pressure to yield 531 mg of a solid (2.38 mmol, 95%). MS (APCI) m/z = 224.1 $[M+H]^+$.

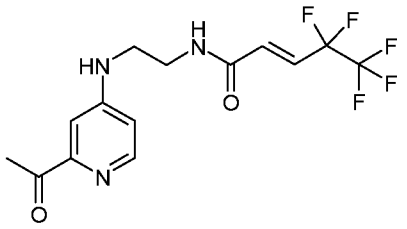
Step C: (*E*)-4,4,5,5,5-Pentafluoro-N-[2-[[2-(2-methyl-1,3-dioxolan-2-yl)-4-pyridyl]amino]-ethyl]pent-2-enamide

[0335] (*E*)-4,4,5,5,5-Pentafluoropent-2-enoic acid (133 mg, 0.7 mmol) and HBTU (265 mg, 0.7 mmol) were dissolved in a 2:1 mixture of anhydrous DMF and anhydrous THF (3 ml) and stirred at room temperature for 15 minutes. N-[2-(2-Methyl-1,3-dioxolan-2-yl)-4-pyridyl]ethane-1,2-diamine (100 mg, 0.45 mmol) was added and stirring was continued for 3 hours. The reaction mixture was diluted with ethyl acetate, washed with water, saturated sodium bicarbonate solution

and brine, dried over magnesium sulfate and evaporated to dryness under reduced pressure. The residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 47 mg (0.12 mmol, 26 %).

Example 7: Synthesis of (*E*)-N-[2-[(2-acetyl-4-pyridyl)amino]ethyl]-4,4,5,5,5-pentafluoro-pent-2-enamide (A-134)

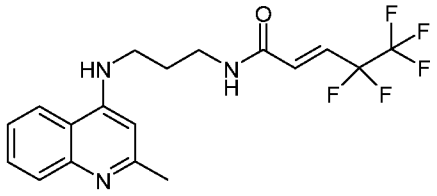
[0336]



[0337] (*E*)-4,4,5,5,5-Pentafluoro-N-[2-[[2-(2-methyl-1,3-dioxolan-2-yl)-4-pyridyl]amino]ethyl]pent-2-enamide (35 mg, 0.09 mmol) was dissolved in aceton (1 ml), 4M hydrochloric acid (0.5 ml) was added and the mixture was stirred in a closed vessel at 100°C for 15 minutes with microwave heating. The mixture was dilutted with water, extracted with ethyl acetate and the organic phase was washed with brine, dried over magnesium sulfate and evaporated to dryness. The resulting residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 2.5 mg (0.0071 mmol, 7.9%).

Example 8: Synthesis of (*E*)-4,4,5,5,5-pentafluoro-N-[3-[(2-methyl-4-quinolyl)amino]propyl]pent-2-enamide (A-217)

[0338]



Step A: *tert*-Butyl N-[2-[(2-methyl-4-quinolyl)amino]propyl]carbamate

[0339] Palladium(II)acetate (126 mg, 0.56 mmol), caesium carbonate (2.6 g, 8 mmol) and BINAP (498 mg, 0.8 mmol) were suspended in anhydrous dioxane under an athmosphere of argon and sonicated for 40 minutes. To this mixture was added 4-chloroquinaldine (711 mg, 4 mmol) and *tert*-butyl N-(3-aminopropyl)carbamate (697 mg, 4 mmol) and the mixture was stirred at 110°C overnight. After cooling to room temperature, the mixture was diluted with ethyl acetate and filtered, the filtrate was evaporated to dryness, the resulting residue was dissolved in dichloromethane and filtered through a column packed with basic alumina. The product was eluted with ethyl acetate, the solution evaporated to dryness and 771 mg (2.44 mmol, 61 %) were obtained. MS (APCI) m/z = 315.8 $[M+H]^+$.

Step B: N-(2-Methyl-4-quinolyl)propane-1,3-diamine hydrochloride

[0340] *tert*-Butyl N-[2-[(2-methyl-4-quinolyl)amino]propyl]carbamate (771 mg, 2.44 mmol) was dissolved in dichloromethane (20 ml), trifluoroacetic acid (1.5 ml) was added and the mixture was stirred at room temperature for 3 hours. The mixture is evaporated to dryness under reduced pressure, the residue dissolved in dioxane and evaporated again. The residue is again dissolved in dioxane and a 4M solution of HCl in dioxane is added to precipitate the hydrochloride salt of the product which is filtered off and dried under reduced pressure. MS (APCI) m/z = 216.1 $[M+H]^+$.

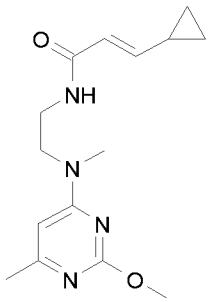
Step C: (*E*)-4,4,5,5,5-Pentafluoro-N-[3-[(2-methyl-4-quinolyl)amino]propyl]pent-2-enamide

[0341] (*E*)-4,4,5,5,5-Pentafluoropent-2-enoic acid (38 mg, 0.2 mmol) and HBTU (76 mg, 0.2 mmol) were dissolved in a 1:1 mixture of anhydrous DMF and anhydrous acetonitrile (2 ml), after 5 minutes triethylamine (82 µl, 0.6 mmol) and N-(2-methyl-4-quinolyl)propane-1,3-diamine hydrochloride (48 mg, 0.24 mmol) was added and stirring was continued

for 3 hours. To the mixture basic aluminium oxide was added, stirring was continued for one hour, the mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 28.4 mg (0.076 mmol, 38 %).

Example 9: Synthesis of (*E*)-3-cyclopropyl-N-[2-[(2-methoxy-6-methyl-pyrimidin-4-yl)-methyl-amino]ethyl]prop-2-enamide (A-77)

[0342]



Step A: 4-Chloro-2-methoxy-6-methyl-pyrimidine

[0343] To anhydrous methanol (10 ml) was added sodium (230 mg, 10 mmol) and the mixture was stirred under an argon athmosphere until a clear solution had formed. This solution was added dropwise over two hours with stirring to a solution of 2,4-dichloro-6-methylpyrimidine (1.79 g, 11 mmol) in anhydrous methanol (10 ml) under cooling so that the temperature remained below 10°C. Stirring was continued for 30 minutes, then water was added (2 ml), the mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by column chromatography (pre-packed silica column, gradient of heptane / ethyl acetate). 750 mg was obtained (4.75 mmol, 47%). MS (APCI) m/z = 159.2 $[M+H]^+$.

Step B: N-(2-Methoxy-6-methyl-pyrimidin-4-yl)-N-methyl-ethane-1,2-diamine

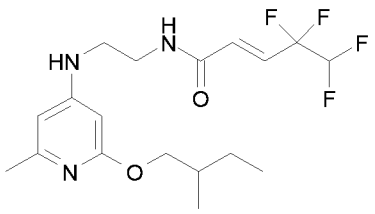
[0344] 4-Chloro-2-methoxy-6-methyl-pyrimidine (320 mg, 2 mmol) was mixed with N-Boc-N'-methyl-2,3-diaminoethan (464 mg, 2.2. mmol), diisopropylethylamine (285 mg, 2.2 mmol) and dipropyleneglycolmomomethylether (4 ml) and stirred overnight at 120 °C. The mixture was evaporated to dryness. The residue was dissolved in a 1:1 mixture of dichloromethane and trifluoroacetic acid and stirred at room temperature for 3 hours. The volatiles were removed under reduced pressure, the residue taken up in dichloromethane and evaporated again. Dissolving in dichloromethane and evaporation was repeated two times. The residue was dissolved in water, basified with 5N NaOH and extracted with ethyl acetate. Evaporation of the organic phase yielded 450 mg of light brown, viscous oil (quantitative). MS (APCI) m/z = 197.1 $[M+H]^+$.

Step C: (*E*)-3-Cyclopropyl-N-[2-[(2-methoxy-6-methyl-pyrimidin-4-yl)-methylamino]ethyl]prop-2-enamide

[0345] (*E*)-3-Cyclopropylprop-2-enoic acid (11.2 mg, 0.1 mmol) and diisopropylethylamine (17.4 µl, 1 mmol) were dissolved in anhydrous DMF (0.5 ml), HBTU (39 mg, 0.1 mmol) was added and the mixture was stirred for 15 minutes at room temperature. N-(2-methoxy-6-methyl-pyrimidin-4-yl)-N-methyl-ethane-1,2-diamine (19.6 mg, 0.1 mmol) and diisopropylethylamine (17.4 µl, 0.1 mmol), dissolved in anhydrous DMF (0.5 ml) were added and the mixture was stirred at room temperature overnight. The mixture was purified directly by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 13.7 mg (0.047 mmol, 47.2 %).

Example 10: Synthesis of (*E*)-4,4,5,5-tetrafluoro-N-[2-[[2-methyl-6-(2-methylbutoxy)-4-pyridyl]amino]ethyl]pent-2-enamide (A-323)

[0346]



Step A: 2-Chloro-6-methyl-pyridine 1-oxide

[0347] 2-Chloro-6-methylpyridine (12.76 g, 0.1 mol) was dissolved together with m-chloroperbenzoic acid (17.56 g, 0.15 mol) in DCM (100 ml) and stirred at 40°C for 90 minutes. The heating bath was removed and stirring was continued overnight at room temperature. The reaction mixture was quenched with saturated sodium thiosulfate solution and the pH was adjusted to 8 with 1 M NaOH. The phases were separated, the aqueous phase extracted with DCM and the combined organic phases were dried over magnesium sulfate. The solvent was removed under reduced pressure and unreacted 2-chloro-6-methylpyridine was removed by destillation (2 mbar, 65°C). 2-Chloro-6-methylpyridine 1-oxide was obtained as residue (6.0 g of a yellow oil, 0.042 mol, 42%). MS(ESI) m/z = 144.0 $[M+1]^+$.

Step B: 2-Chloro-4-nitro-6-methyl-pyridine 1-oxide

[0348] 2-Chloro-6-methyl-pyridine 1-oxide (5.0 g, 0.035 mol) was dissolved in concentrated sulfuric acid (20 ml) at 0°C. An ice-cooled mixture of concentrated nitric acid (12 ml) in concentrated sulfuric acid (20 ml) was added dropwise with stirring at 0°C. The cooling bath was removed, stirring was continued for 3 hours at 90°C. The mixture was poured into a mixture of icewater and ethyl acetate and the resulting precipitate was removed by filtration. The phases of the filtrate were separated, the aqueous phase was extracted several times with ethyl acetate, basified with NaOH and extracted again with ethyl acetate. The combined organic phases were dried over magnesium sulfate and the solvent removed under reduced pressure. The residue was combined with the filtered residue above to yield 6.21 g of a yellow solid (0.033 mol, 94%). MS(ESI) m/z = 189.0 $[M+1]^+$.

Step C: 2-Chloro-4-nitro-6-methyl-pyridine

[0349] 2-Chloro-4-nitro-6-methyl-pyridine 1-oxide (6.2 g, 0.033 mol) was dissolved in chloroform (100ml), phosphorus trichloride was added (22.6 g, 0.165 mol) and the mixture was heated under reflux for 2 days. The mixture was cooled to room temperature, poured into icewater and the mixture was neutralized with solid potassium carbonate. The phases were separated, the aqueous phase was extracted three times with chloroform, the combined organic phases were dried over magnesium sulfate. The solvent was removed under reduced pressure after which 5.326 g of a brown oil was obtained (0.031 mol, 94%) which was used directly in the next step.

Step D: N-(2-Chloro-6-methyl-4-pyridyl)ethane-1,2-diamine

[0350] 2-Chloro-4-nitro-6-methyl-pyridine (5.29 g, 0.031 mol) was dissolved in ethanol (100 ml) and added dropwise with stirring to a solution of ethylenediamine (18.4 g, 0.31 mol) in ethanol (200 ml). The mixture was stirred at 60°C for 2 days. The solvent was removed under reduced pressure and excess of ethylenediamine was removed by repeated azeotropic evaporation with toluene under reduced pressure. The raw product was dissolved in chloroform, extracted three times with 1 M HCl, the combined aqueous extracts were basified with NaOH and extracted with DCM and ethyl acetate. The combined organic extracts were dried over magnesium sulfate, the solvent was removed under reduced pressure to yield 3.92 g of a solid residue (0.021 mol, 68%). MS(APCI) m/z = 186.0 $[M+1]^+$.

Step E: N-[2-Methyl-6-(2-methylbutoxy)-4-pyridyl]ethane-1,2-diamine

[0351] N-(2-Chloro-6-methyl-4-pyridyl)ethane-1,2-diamine (0.205 g, 1.2 mmol) was combined with the sodium salt of 2-methylbutan-1-ol (0.66 g, 6 mmol, that had been obtained by treating 2-methylbutan-1-ol with sodium hydride dispersion in THF), diphenylether (2.2 g) and DMSO (0.75 ml). The mixture was heated at 160°C for 16 hours and purified by column chromatography (silica, ethyl acetate / methanol, 1% concentrated NH_3) to yield 200 mg of a brown oil (0.84 mmol, 70%). MS(APCI) m/z = 237.9 $[M+1]^+$.

Step F: Ethyl 4,4,5,5-tetrafluoro-3-oxo-pentanoate

[0352] Lithium hexamethyldisilazide (250 ml of a 1M solution in THF, 0.25 mol) was cooled in an argon athmosphere to -78 °C and ethyl acetate (23 ml, 0.26 mol) was added dropwise with stirring. Stirring was continued for one hour at -78°C, then methyl 2,2,3,3-tetrafluoropropionate (22g, 0.137 mol) was added dropwise with stirring. Stirring was continued for three hours at -78°C, then a saturated solution of ammonium chloride (175 ml) was added dropwise. The mixture was allowed to reach room temperature overnight. The mixture was acidified with 1 M HCl, the phases were separated. The aqueous phase was extracted with ethyl acetate, the combined organic phases were washed two times with 1 M HCl, brine, dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was purified by vacuum distillation to yield 25.7 g (0.119 mmol, 87%) of a colourless liquid that was used directly in the next step.

Step G: Ethyl 4,4,5,5-tetrafluoro-3-hydroxy-pentanoate

[0353] Ethyl 4,4,5,5-tetrafluoro-3-oxo-pentanoate (25.7 g, 0.119 mol) was dissolved in toluene (260 ml) and cooled to 0°C. Sodium borohydride (5.4 g, 0.143 mol) was added portionwise, and the mixture was allowed to reach room temperature overnight with stirring. The mixture was then cooled to 0°C and acidified with 1 M HCl. The phases were separated, the aqueous phase was extracted two times with ethyl acetate, the combined organic phases were dried over magnesium sulfate and the solvent was reduced under reduced pressure. The residue was dissolved in a minimum amount of methanol and evaporated to dryness under reduced pressure to yield 22.9 g (0.105 mol, 88%) that were used directly in the next step.

Step H: Ethyl (*E*)-4,4,5,5-tetrafluoropent-2-enoate

[0354] Ethyl 4,4,5,5-tetrafluoro-3-hydroxy-pentanoate (22.9 g, 0.105 mol) was mixed with phosphorus pentoxide (7.5 g, 0.053mol) and the resulting mixture was stirred at 80°C for two hours. The product was isolated by vacuum distillation (53 mbar, 92°C) to yield 15.9 g of a liquid (0.08 mol, 76%) that was used directly in the next step.

Step I: (*E*)-4,4,5,5-tetrafluoropent-2-enoic acid

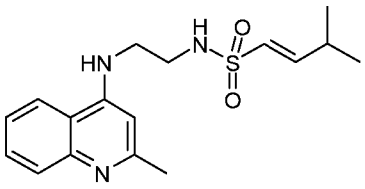
[0355] Ethyl (*E*)-4,4,5,5-tetrafluoropent-2-enoate (15.9 g, 0.08 mol) was dissolved in ethanol (30 ml), 4M NaOH was added (15 ml) and the mixture was stirred at room temperature overnight. The mixture was diluted with water, washed with ethylacetate, acidified with 1 M HCl and extracted with ethyl acetate. The organic extract was dried over magnesium sulfate, the solvent was removed under reduced pressure. 12.8 g of a colourless oil was obtained (0.074 mmol, 93%). MS(ESI, negative detection) m/z = 170.9 $[M-1]^-$.

Step J: (*E*)-4,4,5,5-tetrafluoro-N-[2-[[2-methyl-6-(2-methylbutoxy)-4-pyridyl]amino]ethyl]-pent-2-enamide

[0356] (*E*)-4,4,5,5-tetrafluoropent-2-enoic acid (21 mg, 0.12 mmol) was dissolved in DCM (1 ml), oxalyl chloride was added (10µl, 0.12 mmol) followed by a drop of DMF. The mixture was stirred for 10 minutes at room temperature. N-[2-methyl-6-(2-methylbutoxy)-4-pyridyl]-ethane-1,2-diamine (18 mg, 0.1 mmol) was dissolved in DMF (0.5 ml), the mixtures were combined, TEA (42µl, 0.3 mmol) was added and the resulting mixture was stirred at room temperature for 1 hour. The mixture was diluted with ethyl acetate, washed with water and saturated sodium bicarbonate solution, dried over magnesium sulfate, the solvent was removed under reduced pressure. The residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 13 mg of a white solid (0.039 mmol, 39 %).

Example 11: Synthesis of (*E*)-3-methyl-N-[2-[(2-methyl-4-quinolyl)amino]ethyl]but-1-ene-1-sulfonamide (A-447)

[0357]



Step A: Ethyl diethoxyphosphorylmethanesulfonate

[0358] A solution of ethyl methanesulfonate (4.14 mL, 40.2 mmol) in anhydrous tetrahydrofuran (100 ml) was cooled to -78°C under a nitrogen atmosphere. N-Butyllithium (20 ml, 50.0 mmol) was added slowly in 7 minutes after which stirring was continued for 15 minutes. Diethyl phosphorochloridate (4.36 mL, 30.2 mmol) was added, the reaction mixture was stirred for 2.5 h, the cooling bath was removed and the mixture was allowed to reach room temperature. The reaction mixture was quenched with aqueous saturated ammonium chloride (150 ml) and the resulting mixture was extracted with EtOAc (2x 100 ml). The combined extracts were dried over sodium sulfate and concentrated under reduced pressure to yield 9.20 g of a yellow oil. The oil was purified over silicagel (600 g) using a gradient of ethyl acetate (0-100%) in heptane to yield 1.75 g of the product (6.7 mol, 17%).

Step B: Ethyl (*E*)-3-methylbut-1-ene-1-sulfonate

[0359] Mineral oil was removed from sodium hydride (84.4 mg, 2.110 mmol) with heptane (2x4 ml) under a nitrogen atmosphere after which anhydrous tetrahydrofuran (10 ml) was added. To this suspension was added dropwise a solution of ethyl (diethoxyphosphoryl)methanesulfonate (500 mg, 1.921 mmol) in anhydrous tetrahydrofuran (10 ml) upon which hydrogen gas evolved from the mixture. After 5 minutes a clear slightly yellow solution was obtained. Isobutyraldehyde (200 μl, 2.191 mmol) was added and the resulting mixture was stirred at room temperature over night. The reaction mixture was quenched with a mixture of brine (50 ml) and aqueous saturated ammonium chloride solution (150 ml). The aqeuous mixture was extracted with dichloromethane (3x70 ml), the combined organic layers were dried over sodium sulfate and concentrated under reduced pressure to yield 550 mg of a slightly yellow oil that was used directly in the next step.

Step C: Tetrabutylammonium (*E*)-3-methylbut-1-ene-1-sulfonate

[0360] A solution of (*E*)-ethyl 3-methylbut-1-ene-1-sulfonate (550 mg of step B) and tetrabutylammonium iodide (1128 mg, 3.05 mmol) in acetone (40 ml) was refluxed over night after which volatiles were removed under reduced pressure. 1.26 g of a white solid was obtained and used as such in the next reaction step.

Step D: (*E*)-3-Methylbut-1-ene-1-sulfonyl chloride

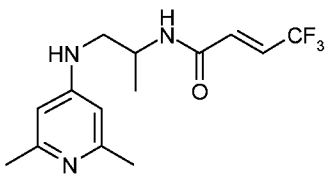
[0361] To a solution of triphenylphosphine (1.055 g, 4.02 mmol) in dichloromethane (50 ml) under a nitrogen atmosphere was added at 0°C sulfuryl dichloride (0.359 ml, 4.42 mmol). The mixture was stirred at 0°C for 15 minutes after which a solution of tetrabutylammonium (*E*)-3-methylbut-1-ene-1-sulfonate (1.25 g of Step C) in dichloromethane (10 ml) was added dropwise. The reaction mixture was stirred at room temperature for 5 h after which the mixture was concentrated under reduced pressure. The residue was taken up in diethylether and filtered over a glass filter to remove triphenylphosphinoxide. The filtrate was concentrated under reduced pressure to yield 102 mg of a brown oil which was usecd directly in the next step.

Step E: (*E*)-3-methyl-N-[2-[(2-methyl-4-quinolyl)amino]ethyl]but-1-ene-1-sulfonamide

[0362] To a solution of N1-(2-methylquinolin-4-yl)ethane-1,2-diamine (161 mg, 0.800 mmol) and triethylamine (0.350 ml, 2.51 mmol) in acetonitrile (5 ml) was added a solution of (*E*)-3-methylbut-1-ene-1-sulfonyl chloride (102 mg of step D) in dichloromethane (1 ml). The mixture was stirred 30 minutes at room temperture, concentrated under reduced pressure and the residue was purified by column chromatography over aluminum oxide using a gradient of methanol (2-10%) in dichloromethane to yield 83 mg of an off-white foam (0.25 mmol; 13% over 4 steps).

Example 12: Synthesis of (*E*)-N-[2-[(2,6-dimethyl-4-pyridyl)amino]propyl]-4,4,4-trifluoro-but-2-enamide (B-13)

[0363]



Step A: *tert*-Butyl N-[2-[(2,6-dimethyl-4-pyridyl)amino]propyl]carbamate

[0364] A mixture of 4-Chloro-2,6-dimethylpyridine (131 mg, 0.925 mmol), *tert*-butyl 2-aminopropylcarbamate hydrochloride (151 mg, 0.717 mmol), cesium carbonate (750 mg, 2.302 mmol), and anhydrous 1,4-dioxane (3 ml) was treated with tris(dibenzylideneacetone)dipalladium(0) (39 mg, 0.043 mmol) and 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (74 mg, 0.128 mmol) under an athmosphere of argon. The mixture was heated at 110 °C for 8 hours, allowed to reach room temperature and filtered. The filter residue was washed with DCM, the combined filtrates were evaporated. The residue was purified by column chromatography using a gradient of methanol (1-10%) in dichloromethane to yield 241 mg of a yellow oil. MS(ESI) m/z = 280.2.

Step B: N2-(2,6-Dimethyl-4-pyridyl)propane-1,2-diamine hydrochloride

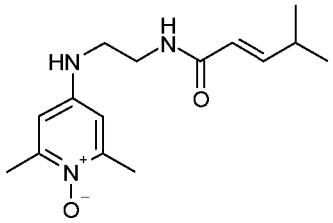
[0365] To *tert*-butyl 2-(2,6-dimethylpyridin-4-ylamino)propylcarbamate (147 mg, 0.526 mmol) dissolved in 1,4-dioxane (1 ml) a 4N solution of HCl in dioxane (2 ml, 8.00 mmol) was added. Within a few minutes a precipitate started to form. The solvent was removed in a stream of nitrogen, to the residue was added diethylether and the mixture was allowed to stand at room temperature overnight. The solvent was filtered off, the residue was dried under reduced pressure to yield 135 mg of an off-white solid MS(ESI) m/z = 180.0.

Step C: (*E*)-N-[2-[(2,6-Dimethyl-4-pyridyl)amino]propyl]-4,4,4-trifluoro-but-2-enamide

[0366] (*E*)-4,4,4-Trifluorobut-2-enoic acid (15.4 mg, 0.11 mmol) was dissolved in DCM (0.75 ml containing one drop of dimethyl formamide), oxalyl chloride was added (14 mg, 0.11 mmol) and the solution was stirred at room temperature for 15 minutes. This solution was added to a solution of N2-(2,6-dimethyl-4-pyridyl)propane-1,2-diamine (21.6 mg, 0.1 mmol) and diisopropylethylamine (44μl, 0.25 mmol) dissolved in dimethylformamide (1 ml) and the resulting mixture was stirred at room temperature overnight. The volatiles were removed under reduced pressure and the residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 10.7 mg (0.035 mmol, 35 %).

Example 13: Synthesis of (*E*)-N-[2-[(2,6-dimethyl-1-oxo-4-pyridyl)amino]ethyl]-4-methyl-pent-2-enamide (Aa-4)

[0367]



Step A: 4-Bromo-2,6-dimethyl-pyridine 1-oxide

[0368] 4-Bromo-2,6-dimethylpyridine (0.5 g, 2.69 mmol) was dissolved in DCM (10 ml), cooled to 0°C and combined with a solution of m-chloroperbenzoic acid in DCM (75%, 0.928 g, 4.03 mmol in 5 ml). The resulting mixture was stirred at 0°C for 15 minutes and for 5 hours at room temperature. The mixture was washed with saturated sodium bicarbonate solution, the phases were separated with a phase separator, the organic phase was evaporated under reduced pressure. The residue was purified by column chromatography (silica, gradient of 0.5 to 10% methanol in DCM). 475 of a yellow solid was obtained (2.35 mmol, 88%). MS(ESI) m/z = 204.0 $[M+1]^+$.

Step B: *tert*-Butyl N-[2-[(2,6-dimethyl-1-oxo-4-pyridyl)amino]ethyl]carbamate

[0369] 4-Bromo-2,6-dimethyl-pyridine 1-oxide (475 mg, 2.35 mmol), *tert*-butyl N-(2-aminoethyl)carbamate (452 mg, 2.82 mmol), cesium carbonate (1.68 g, 5.17 mmol) and BINAP (racemic, 73.2 mg, 0.118 mmol) were mixed with anhydrous dioxane (10ml) under an argon athmosphere. Tris(dibenzylideneacetone)dipalladium(0) was added (108 mg, 0.118 mmol) and the mixture was stirred at 100°C overnight. The mixture was diluted with dioxane, filtered through Celite, the filter residue was washed three times with dioxane, the combined filtrates were evaporated under reducd pressure. The residue was purified by column chromatography (silica, gradient of DCM to DCM containing 10% 7N ammonia in methanol) to yield 482 mg (1.71 mmol, 73%). MS(ESI) m/z = 282.2 $[M+1]^+$.

Step C: N-(2,6-Dimethyl-1-oxo-4-pyridyl)ethane-1,2-diamine hydrochloride

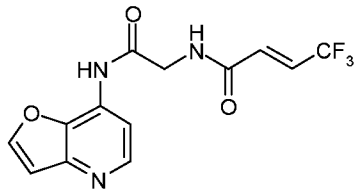
[0370] *tert*-Butyl N-[2-[(2,6-dimethyl-1-oxo-4-pyridyl)amino]ethyl]carbamate (482 mg, 1.71 mmol) was dissolved in DCM (50 ml) and a 4N solution of HCl in dioxane was added (2.15 ml, 8.6 mmol). The mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and 397 mg of a beige solid was obtained that was used directly in the next step. MS(ESI) m/z = 182.2 $[M+1]^+$.

Step D: (*E*)-N-[2-[(2,6-Dimethyl-1-oxo-4-pyridyl)amino]ethyl]-4-methyl-pent-2-enamide

[0371] (*E*)-4-Methylpent-2-enoic acid (118 mg, 1.034 mmol), HATU (327 mg, 0.861 mg) and N, N-diisopropylethylamine (0.236 ml, 1.378 mmol) were mixed with DCM (2 ml) and stirred at room temperature for 30 minutes. The resulting solution was added with stirring to a suspension of N-(2,6-dimethyl-1-oxo-4-pyridyl)ethane-1,2-diamine hydrochloride (125 mg, 0.574 mmol) and N, N-diisopropylethylamine (0.098 ml, 0.574 mmol) in DCM (2 ml). The resulting mixture was stirrred overnight at room temperature. The solvent was removed in a stream of nitrogen and the residue was purified by column chromatography (silica, gradient of 2.5% of 7N ammonia in methanol in DCM to 10% of 7N ammonia in methanol in DCM) to yield 53.1 mg of a yellow solid (0.191 mmol, 33%).

Example 14: Synthesis of (*E*)-4,4,4-trifluoro-N-[2-(furo[3,2-b]pyridin-7-ylamino)-2-oxoethyl]but-2-enamide (B-44)

[0372]



Step A: *tert*-Butyl N-[2-(furo[3,2-b]pyridin-7-ylamino)-2-oxo-ethyl]carbamate

[0373] To a solution of 2-(*tert*-butoxycarbonylamino)acetic acid (660 mg, 3.77 mmol) in acetonitrile (20 ml) was added HBTU (1.491 g, 3.93 mmol) and the resulting solution was stirred 40 minutes at room temperature. Then triethylamine (0.785 ml, 5.63 mmol) was added and the mixture was stirred another five minutes at room temperature. Next furo[2,3-b]pyridin-4-amine (253 mg, 1.886 mmol) was added and the reaction mixture was stirred at 60°C over night. The acetonitrile was removed under reduced pressure and the residue was redissolved in dichloromethane (50 ml). The solution in dichloromethane was washed with aqueous 1N NaOH (40 ml). The aqueous phase was extracted with dichloromethane (2x15 ml), the combined organic phases were dried over sodium sulfate and concentrated under reduced pressure to yield 1.03 g of a slightly brown oil. The crude product was purified by column chormatography (silicagel using a gradient of 2 to 6 % MeOH in DCM to yield 350 mg of a white foam (1.2 mmol, 64%). MS(ESI) m/z = 292.2 $[M+1]^+$.

Step B: 2-Amino-N-furo[3,2-b]pyridin-7-yl-acetamide hydrochloride

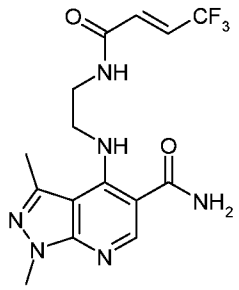
[0374] *Tert*-Butyl 2-(furo[2,3-b]pyridin-4-ylamino)-2-oxoethylcarbamate (350 mg, 1.2 mmol) was placed in ethanol (96%) (3.0 ml) and hydrogen chloride in dioxane (5.0 ml, 20.00 mmol) was added after which the resulting mixture was stirred at room temperature over night. The solids were filtered off, washed subsequently with EtOH and diethylether and dried in a stream of air. 230 mg of a white powder was obtained (1.01 mmol, 84%). MS(ESI) m/z = 191.9 $[M+1]^+$.

Step C: (*E*)-4,4,4-Trifluoro-N-[2-(furo[3,2-b]pyridin-7-ylamino)-2-oxo-ethyl]but-2-enamide

[0375] (*E*)-4,4,4-Trifluorobut-2-enoic acid (15.4 mg, 0.11 mmol) was dissolved in DCM (0.75 ml containing one drop of dimethyl formamide), oxalyl chloride was added (14 mg, 0.11 mmol) and the solution was stirred at room temperature for 15 minutes. This solution was added to a solution of 2-amino-N-furo[3,2-b]pyridin-7-yl-acetamide hydrochloride (25.3 mg, 0.11 mmol) and diisopropylethylamine (44μl, 0.25 mmol) dissolved in dimethylformamide (1 ml) and the resulting mixture was stirred at room temperature overnight. The volatiles were removed under reduced pressure and the residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 6.9 mg (0.022 mmol, 20 %).

Example 15: Synthesis of 1,3-dimethyl-4-[2-[[(*E*)-4,4,4-trifluorobut-2-enoyl]amino]-ethylamino]pyrazolo-[3,4-b]-pyridine-5-carboxamide (A-381)

[0376]



Step A: Ethyl 4-[2-(*tert*-butoxycarbonylamino)ethylamino]-1,3-dimethyl-pyrazolo[3,4-b]pyridine-5-carboxylate

[0377] To a mixture of ethyl 4-chloro-1,3-dimethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate (500 mg, 1.971 mmol) and potassium carbonate (817 mg, 5.91 mmol) in acetonitrile (15 ml) was slowly added *tert*-butyl N-(2-aminoethyl)carbamate (1.248 ml, 7.88 mmol) via a syringe. The reaction mixture was stirred at room temperature for 3 hours. The solids were filtered off over a glassfilter and washed with a 1:1 mixture of EtOH and DCM. The combined filtrates were concentrated under reduced pressure to give a white semisolid, which was purified by column chromatography (silicagel using a gradient of ethanol (0-5%) in DCM) to yield 658 mg of a white solid (1.743 mmol, 88%). MS(ESI) m/z = 378.2 $[M+1]^+$.

Step B: 4-[2-(*tert*-Butoxycarbonylamino)ethylamino]-1,3-dimethyl-pyrazolo[3,4-b]pyridine-5-carboxylic acid

[0378] To a solution of ethyl 4-[2-(*tert*-butoxycarbonylamino)ethylamino]-1,3-dimethyl-pyrazolo[3,4-b]pyridine-5-carboxylate (303 mg, 0.803 mmol) in methanol (30 ml) was added sodium hydroxide (4.02 g, 101 mmol) in water (10 ml) and the resulting mixture was heated at reflux for 1.5 hours. The mixture was allowed to cool to ~50°C after which ammonium chloride (6.07 g, 113 mmol) was added. The mixture was stirred at reflux for 15 minutes after which the solids were filtered off. The solids were washed with ethanol (150 ml) and the combined filtrates were concentrated under reduced pressure to yield 2.32 g of a white solid that was purified by filtration over a pad of silicagel in a glassfilter using 10% (1% AcOH in MeOH) in DCM. The filtrate was concentrated under reduced pressure to yield 240 mg (0.687 mmol, 86%). MS(ESI) m/z = 350.2 $[M+1]^+$.

Step C: *tert*-Butyl N-[2-[[5-[(4-methoxyphenyl)methylcarbamoyl]-1,3-dimethyl-pyrazolo[3,4-b]pyridin-4-yl]amino]ethyl]carbamate

[0379] To a solution of 4-[2-(*tert*-butoxycarbonylamino)ethylamino]-1,3-dimethyl-pyrazolo[3,4-b]pyridine-5-carboxylic acid (96.1 mg, 0.275 mmol) in N,N-dimethylformamide (2.5 ml) was subsequently added N1-((ethylimino)methylene)-N3,N3-dimethylpropane-1,3-diamine hydrochloride (91.8 mg, 0.479 mmol), 3-hydroxytriazolo[4,5-b]pyridine (39.7 mg, 0.292 mmol) and triethylamine (0.115 ml, 0.825 mmol). The reaction mixture was stirred for five minutes after which (4-methoxyphenyl)methanamine (0.072 ml, 0.550 mmol) was added. The reaction mixture was stirred at room temperature over night. The reaction mixture was partitioned between water (40 ml) and EtOAc (50 ml). The organic layer was separated and the aqueous phase was further extracted with EtOAc (3x40 ml) and dichloromethane (1x50 ml). The combined organic layers were dried over sodium sulfate and concentrated under reduced pressure to yield 360 mg of a yellow liquid which was purified by column chromatography (silicagel using a gradient of MeOH (1-7%) in dichloromethane) to give 43 mg of a colorless sticky oil (0.092 mmol, 33%) MS(ESI) m/z = 469.3 $[M+1]^+$.

Step D: 4-(2-Aminoethylamino)-1,3-dimethyl-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoromethanesulfonate

[0380] To a solution of *tert*-Butyl N-[2-[[5-[(4-methoxyphenyl)methylcarbamoyl]-1,3-dimethyl-pyrazolo[3,4-b]pyridin-4-yl]amino]ethyl]carbamate (43 mg, 0.092 mmol) in dichloromethane (2.0 ml) was added trifluoromethanesulfonic acid (2.0 mL, 22.60 mmol) and the resulting orange-red mixture was stirred at room temperature over night. The reaction mixture was diluted with dichloromethane (40 ml) and diethylether (100 ml) subsequently upon which a white precipitate was formed. The mixture was stirred for 15 minutes after which the white solids were filtered off, washed with diethylether and dried in a stream of air. 43 mg of an off-white solid was obtained and used directly in the next step.. MS(ESI) m/z

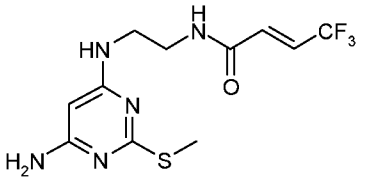
= 249.2.

Step E: 1,3-Dimethyl-4-[2-[[(*E*)-4,4,4-trifluorobut-2-enoyl]amino]ethylamino]pyrazolo-[3,4-b]-pyridine-5-carboxamide

[0381] (*E*)-4,4,4-Trifluorobut-2-enoic acid (21 mg, 0.15 mmol) was dissolved in DCM (2 ml containing one drop of dimethyl formamide), oxalyl chloride was added (19 mg, 0.15 mmol) and the solution was stirred at room temperature for 15 minutes. This solution was added to a solution of 4-(2-aminoethylamino)-1,3-dimethyl-pyrazolo[3,4-b]pyridine-5-carboxamide trifluoromethanesulfonate (40 mg, 0.1 mmol) and diisopropylethylamine (60μl, 0.35 mmol) dissolved in dimethylformamide (1 ml) and the resulting mixture was stirred at room temperature overnight. The volatiles were removed under reduced pressure and the residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 2.1 mg (0.005 mmol, 5.7 %).

Example 16: Synthesis of (*E*)-N-[2-[(6-amino-2-methylsulfanyl-pyrimidin-4-yl)amino]-ethyl]-4,4,4-trifluoro-but-2-enamide (A-374)

[0382]



Step A: *tert*-Butyl N-[2-[(6-amino-2-methylsulfanyl-pyrimidin-4-yl)amino]ethyl]carbamate

[0383] 6-Chloro-2-methylsulfanyl-pyrimidin-4-amine (176 mg, 1 mmol) was dissolved together with *tert*-butyl N-(2-aminoethyl)carbamate (200 mg, 1.25 mmol) and triethylamine (174 μl, 1.25 mmol) in THF (2 ml). The mixture was stirred at 180°C under microwave heating for 8 hours. The mixture was diluted with ethyl acetate and the resulting solution was washed with a solution of sodium bicarbonate (5%) and brine, dried over magnesium sulfate, the volatiles were removed under reduced pressure. The residue dissolved in DCM and purified by filtration over silica to yield 105 mg (0.35 mmol, 35%) MS(ESI) m/z = 300.2 $[M+1]^+$.

Step B: N6-(2-Aminoethyl)-2-methylsulfanyl-pyrimidine-4,6-diamine trifluoromethanesulfonate

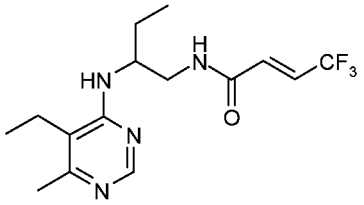
[0384] *Tert*-Butyl N-[2-[(6-amino-2-methylsulfanyl-pyrimidin-4-yl)amino]ethyl]carbamate (105 mg, 0.35 mmol) was dissolved in a mixture of DCM (20 ml) and trifluoromethanesulfonic acid (5ml) and stirred at room temperature for 2 hours. The volatiles were removed under reduced pressure, the residue was taken up in THF and evaporated again to yield 182 mg of a residue that was used directly in the next step.

Step C: (*E*)-N-[2-[(6-Amino-2-methylsulfanyl-pyrimidin-4-yl)amino]ethyl]-4,4,4-trifluoro-but-2-enamide

[0385] (*E*)-4,4,4-Trifluorobut-2-enoic acid (21 mg, 0.15 mmol) was dissolved in DCM (1 ml containing one drop of DMF), oxalyl chloride was added (13 μl, 0.15 mmol) and the solution was stirred at room temperature for 15 minutes. This solution was added to a solution of N6-(2-Aminoethyl)-2-methylsulfanyl-pyrimidine-4,6-diamine trifluoromethanesulfonate (20 mg, 0.057 mmol) and diisopropylethylamine (51μl, 0.3 mmol) dissolved in dimethylformamide (1 ml) and the resulting mixture was stirred at room temperature for 2 hours. The mixture was diluted with ethyl acetate, washed with water and saturated sodium bicarbonate solution, dried over magnesium sulfate, the solvent was removed under reduced pressure. The residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 3.3 mg of a white solid (0.001 mmol, 18 %).

Example 17: Synthesis of (*E*)-N-[2-[(5-ethyl-6-methyl-pyrimidin-4-yl)amino]butyl]-4,4,4-trifluoro-but-2-enamide (A-347)

[0386]



Step A: N2-(5-Ethyl-6-methyl-pyrimidin-4-yl)-N1,N2-bis[(4-methoxyphenyl)methyl]butane-1,2-diamine

[0387] N1,N1-Bis(4-methoxybenzyl)butane-1,2-diamine dihydrochloride (552 mg, 1.375 mmol), 4-chloro-5-ethyl-6-methylpyrimidine (331 mg, 2.113 mmol) and N,N-diisopropylethylamine (824 µl, 4.81 mmol) were mixed with acetonitrile (1.5 ml) and heated in a closed vial at 150°C in an argon athmosphere for two days. The mixture was concentrated under reduced pressure and purified by column chromatography (silica, gradient from DCM to DCM containing 5% methanol) to yield 353 mg of a yellow oil (0.787 mmol, 57%). MS (ESI) m/z = 449.2 $[M+1]^+$.

Step B: N2-(5-Ethyl-6-methyl-pyrimidin-4-yl)butane-1,2-diamine

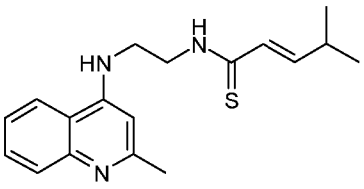
[0388] N2-(5-Ethyl-6-methyl-pyrimidin-4-yl)-N1,N2-bis[(4-methoxyphenyl)methyl]butane-1,2-diamine (353 mg, 0.787 mmol) was dissolved in acetic acid (2 ml), the vial was flushed with argon, palladium (10% on activated carbon, 109 mg, 0.102 mmol) was added, and the mixture was stirred in an athmosphere of hydrogen at room temperature overnight. The mixture was filtered, the filter residue was washed with acetic acid, the combined filtrates were concentrated under reduced pressure to yield 472 mg of a brown oil. The residue was dissolved in DCM, washed with a saturated solution of sodium bicarbonate, the combined aqueous solutions were extracted three times with DCM. The organic phases were combined and concentrated under reduced pressure, the residue was purified by column chromatography (silica, gradient from DCM to a 9 to 1 mixture of DCM and 7N NH_3 in methanol) to yield 94.6 mg of a yellow oil. The oil was dissolved in a mixture of diethylether and DCM, 1M HCl in diethylether was added until the product precipitated. The precipitate was isolated by decantation, washed with diethylether and dried in stream of nitrogen and under reduced pressure to give 127 mg of a white solid (0.498 mmol, 63%). MS(ESI) m/z = 209.2 $[M+1]^+$.

Step C: (*E*)-N-[2-[(5-Ethyl-6-methyl-pyrimidin-4-yl)amino]butyl]-4,4,4-trifluoro-but-2-enamide

[0389] (*E*)-4,4,4-Trifluorobut-2-enoic acid (15 mg, 0.11 mmol) was dissolved in DCM (1 ml containing one drop of dimethyl formamide), oxalyl chloride was added (9.5 µl, 0.11 mmol) and the solution was stirred at room temperature for 15 minutes. This solution was added to a solution of N2-(5-Ethyl-6-methyl-pyrimidin-4-yl)butane-1,2-diamine (24.5 mg, 0.1 mmol) and diisopropylethylamine (44 µl, 0.25 mmol) dissolved in DMF (1 ml) and the resulting mixture was stirred at room temperature overnight. The volatiles were removed under reduced pressure and the residue was purified by preparative HPLC (gradient of water containing 0.1% NH_3 and acetonitrile) to yield 12.7 mg (0.038 mmol, 38 %).

Example 18: Synthesis of (*E*)-4-methyl-N-[2-[(2-methyl-4-quinolyl)amino]ethyl]pent-2-enethioamide (A-449)

[0390]



Step A: (*E*)-N-[2-[(2-Methyl-4-quinolyl)amino]ethyl]but-2-enamide

[0391] (*E*)-4-Methylpent-2-enoic acid (190 mg, 1.3 mmol) was mixed together with HBTU (470 mg, 1.3 mmol) and N-(2-methyl-4-quinolyl)ethane-1,2-diamine (250 mg, 1.2 mmol) in acetonitrile (5 ml). Triethylamine (1 mll) was added with stirring at 0°C over 15 minutes and the resulting mixture was stirred at room temperature overnight. The volatiles were removed under reduced pressure, the residue was dissolved in DCM and washed with a saturated solution of sodium bicarbonate. The combined aqueous solutions were extracted three times with DCM. The organic layers were

combined, dried over sodium sulfate, the solvent was removed under reduced pressure to give 245 mg of a yellow solid (0.82 mmol, 66%). MS(APCI) m/z = 298.2 $[M+1]^+$.

Step B: (*E*)-4-Methyl-N-[2-[(2-methyl-4-quinolyl)amino]ethyl]pent-2-enethioamide

[0392] (*E*)-4-Methyl-N-[2-[(2-methyl-4-quinolyl)amino]ethyl]pent-2-enamide (50 mg, 0.15 mmol) was dissolved in dioxane (2 ml), Lawesson's reagent (75 mg, 0.18 mmol) was added in one portion and the resulting mixture was stirred at 130°C under microwave heating for 0.5 hrs. The volatiles were removed under reduced pressure and the residue was purified by preparative HPLC (gradient of water containing 0.1% ammonia and acetonitrile) to yield 15 mg (0.047 mmol, 28,5 %).

C. Analytics: HPLC Methods

Method 1

HPLC-MS system:

[0393] Agilent LC/MSD Trap 1100 series composed of:

Binary pump G 1312A included degasser G1379A, well plate sampler G1367A, column oven G1316A, diode array detector G1315B, and mass detector G2445D with APCI-source.

Chromatographic system:

[0394]

Column:	Waters Xbridge C-18 , 4.6*50 mm, . 2.5 µ
Oven:	40°C
Injection:	2.0 µl

Eluents:

Solvent A:	water / ammonia : 99.9 / 0.1 vol. / vol.
Solvent B:	acetonitrile / ammonia : 99.9 / 0.1 vol. / vol.
Flow:	1.0 ml / min

Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	95	5
5	0	100
7	0	100

Run time: 10 min (equilibration included)

Detection methods:

UV at 254 nm, 210 nm
APCI/MS (100-1500 m/z), positive ions

Comment: Samples diluted in a 1 to 1 mixture of solvents A and B prior to analysis

Method 2

HPLC-MS system:

[0395] Agilent LC/MSD Trap 1100 series composed of:

Binary pump G 1312A included degasser G1379A, well plate sampler G1367A, column oven G1316A, diode array detector G1315B, and mass detector G2445D with APCI-source.

Chromatographic system:

[0396]

Column: Waters Xbridge C-18 , 4.6*50 mm,. 2.5 µ
Oven: 40°C
Injection: 2.0 µl

Eluents:

Solvent A: water / ammonia : 99.9 / 0.1 vol. / vol.
Solvent B: acetonitrile / ammonia : 99.9 / 0.1 vol. / vol.
Flow: 1.0 ml / min

Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	90	10
4	0	100
5	0	100

Run time: 7 min (equilibration included)

Detection methods:

UV at 254 nm, 210 nm
APCI/MS (80-1000 m/z), positive ions

Comment: Samples diluted in a 1 to 1 mixture of solvents A and B prior to analysis

Method 3

HPLC-MS system:

[0397] Agilent HPLC/MSD 1100 series composed of:

Binary pump G 1312A included degasser G1379A, well plate sampler G1367A, column oven G1316A, diode array detector G1315B, mass detector G1946D SL with ESI-source and evaporative light scattering detector Sedex 75.

Chromatographic system:

[0398]

Column: Chromolith FastGradient RP-18e from Merck, 2*50mm
Oven: 30°C
Injection: 1.0 µl

Eluents:
Solvent A: water / formic acid : 99.9 / 0.1 vol. / vol.
Solvent B: acetonitrile / formic acid : 99.9 / 0.1 vol. / vol.
Flow: 1.2 ml / min

Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	98	2
0.2	98	2
2.2	2	98
2.7	2	98

Run time: 3.5 min (equilibration included)

Detection methods:

UV at 210 nm and 254 nm
ESI/MS (100-1000 m/z), positive ions
ELSD (Sedex 75)

Comment: Samples diluted in a 1 to 1 mixture of solvents A and B prior to analysis

Method 4

HPLC-MS system:

[0399] Agilent HPLC/MSD 1100 series composed of:

Binary pump G 1312A included degasser G1379A, well plate sampler G1367A, column oven G1316A, diode array detector G1315B, mass detector G1946D SL with ESI-source and evaporative light scattering detector Sedex 75.

Chromatographic system:

[0400]

Column: Chromolith FastGradient RP-18e from Merck, 2*50mm
Oven: 30°C
Injection: 1.0 µl

Eluents:
Solvent A: water / formic acid : 99.9 / 0.1 vol. / vol.
Solvent B: acetonitrile / formic acid : 99.9 / 0.1 vol. / vol.
Flow: 1.2 ml / min

Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	90	10
2	0	100
2.7	0	100

Run time: 3.5 min (equilibration included)

Detection methods:

UV at 210 nm and 254 nm
ESI/MS (105-1000 m/z), positive ions
ELSD (Sedex 75)

Comment: Samples diluted in a 1 to 1 mixture of solvents A and B prior to analysis

Method 5

HPLC-MS system:

[0401] Agilent LC/MSD Trap 1100 series composed of:

Binary pump G 1312A included degasser G1379A, well plate sampler G1367A, column oven G1316A, diode array detector G1315B, and mass detector G2445D with APCI-source.

Chromatographic system:

[0402]

Column: Waters Sunfire C-18 , 4.6*50 mm,. 3.5 µ
Oven: 40 °C
Injection: 2.0 µl

Eluents:

Solvent A: water / formic acid : 99.9 / 0.1 vol. / vol.
Solvent B: acetonitrile / formic acid : 99.9 / 0.1 vol. / vol.
Flow: 1.0 ml / min

Gradient:

Time [min]	Solvent A [%]	Solvent B [%]
0.0	90	10
4	0	100
5	0	100

Run time: 7.5 min (equilibration included)

Detection methods:

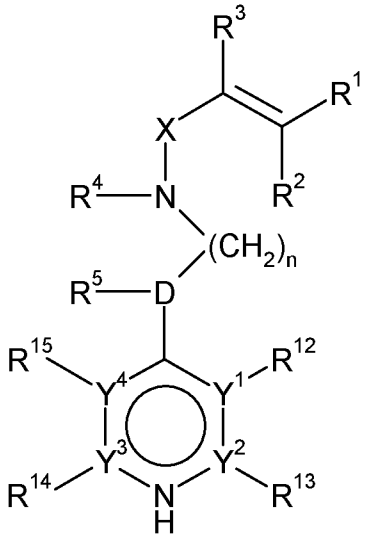
UV at 254 nm, 210 nm
APCI/MS (80-1000 m/z), positive ions

Comment: Samples diluted in a 1 to 1 mixture of solvents A and B prior to analysis

D. Specific Compounds

[0403] Table A below provides for each of the exemplified compounds of the formula (A') the structure, the calculated molecular weight (MW) (gram/mol), the observed MS signal (m/z), the HPLC retention time (Rt) in minutes, and the number of the HPLC-method as described in paragraph C above ("Analytics: HPLC-Methods") used for analysis. From compound A-451 until the end of Table A the methods by which the compounds are synthesized are identified by referring to the synthetic steps described in the synthesis examples of paragraph B above ("Synthesis Examples"). If a compound contains a chiral center, mentioning of such compound is indicating the racemate.

[0404] In Table A - in case of a) a ring formation between Y^1 and Y^2 by the substituents R^{12} and R^{13} or b) a ring formation between Y^3 and Y^4 by the substituents R^{14} and R^{15} - in the columns for R^{12} and R^{13} or in the columns for R^{14} and R^{15}, as the case may, be the symbols Y1, Y2, Y3 and Y4 indicate the ring atoms Y^1, Y^2, Y^3 and Y^4 in formula (A') to which the group joining them is bound.



Formula (A')

Table A :

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-1	CF_3	H	H	CO	N	C	C	C	-	CH_3	CH_2CH_3	H	2	H	H	N	2	3.09	303.2	302.3
A-2	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	CH_2CH_3	H	2	H	H	N	2	3.13	335.2	334.3
A-3	C_2F_5	H	H	CO	N	C	C	C	-	CH_3	CH_2CH_3	H	2	H	H	N	2	3.43	353.2	352.3
A-4	$(CF_2)_2CF_3$	H	H	CO	N	C	C	C	-	CH_3	CH_2CH_3	H	2	H	H	N	2	3.69	403.2	402.3
A-5	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	4	1.29	401.9	401.3
A-6	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	4	1.23	387.9	387.3
A-7	CF_3	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	3	1.34	303.0	302.3
A-8	CF_2CHF_2	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	3	1.36	335.0	334.3
A-9	C_2F_5	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	3	1.48	353.0	352.3
A-10	$CF(CF_3)_2$	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	3	1.58	402.9	402.3
A-11	CF_3	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	3.89	289.1	288.3
A-12	CF_2CHF_2	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	2.95	321.2	320.3
A-13	C_2F_5	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	3.25	339.2	338.3
A-14	$CF(CF_3)_2$	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	3.52	389.2	388.3
A-15	CH_2CH_3	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	2.66	249.2	248.3
A-16	$CH(CH_3)_2$	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	2.90	263.2	262.4
A-17	$CH(CH_3)CH_2CH_3$	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	3.13	277.2	276.4
A-18	cyclopropyl	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	2.69	261.2	260.3
A-19	$(CH_2)_2CH_3$	H	H	CO	N	C	C	C	-	H	CH_3	CH_3	2	H	H	N	2	2.93	263.2	262.4
A-20	$CH(CH_3)_2$	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	2.98	277.2	276.4
A-21	$CH(CH_3)CH_2CH_3$	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	3.21	291.2	290.4
A-22	$(CH_2)_2CH_3$	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	3.01	277.2	276.4
A-23	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.59	275.9	275.4
A-24	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.41	261.9	261.4
A-25	CF_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.41	288.2	287.3
A-26	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.49	320.2	319.3
A-27	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.90	338.2	337.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-28	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	4.37	388.2	387.3
A-29	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.09	248.2	247.3
A-30	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.39	262.2	261.4
A-31	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.73	276.3	275.4
A-32	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.09	260.2	259.4
A-33	CF_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.58	302.2	301.3
A-34	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.69	334.2	333.3
A-35	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	4.21	352.2	351.3
A-36	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	4.69	402.1	401.3
A-37	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.29	262.2	261.4
A-38	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.68	276.2	275.4
A-39	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	4.04	290.3	289.4
A-40	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.35	274.2	273.4
A-41	CF_2CH_3	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	2.98	299.2	298.3
A-42	CHF_2	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	2.79	285.2	284.3
A-43	CH_2OCH_3	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	2.53	279.2	278.4
A-44	CF_3	H	CH_3	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	3.26	317.2	316.3
A-45	CF_3	CH_3	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	3.28	317.2	316.3
A-46	CF_2CH_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.40	284.2	283.3
A-47	CF_2CH_3	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	H	N	2	3.32	284.2	283.3
A-48	CHF_2	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	2.90	270.1	269.3
A-49	CHF_2	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	H	N	2	2.95	270.2	269.3
A-50	CHF_2	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	3	H	H	N	2	3.12	284.2	283.3
A-51	CH_2OCH_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	2.63	264.2	263.3
A-52	CH_2OCH_3	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	H	N	2	2.72	264.2	263.3
A-53	CH_2OCH_3	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	3	H	H	N	2	2.84	278.2	277.4
A-54	CF_3	H	CH_3	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.57	302.2	301.3
A-55	CF_3	H	CH_3	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	H	N	2	3.58	302.2	301.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-56	CF_3	CH_3	H	CO	C	C	C	C	H	H	CH_3	CH_3	3	H	H	N	2	3.79	316.2	315.3
A-57	CF_3	CH_3	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	3.63	302.2	301.3
A-58	CF_3	CH_3	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	H	N	2	3.62	302.2	301.3
A-59	CF_3	CH_3	H	CO	C	C	C	C	H	H	CH_3	CH_3	3	H	H	N	2	3.85	316.2	315.3
A-60	CF_3	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	H	N	2	3.39	305.1	304.3
A-61	CF_3	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	CH_3	N	2	3.82	319.2	318.3
A-62	CF_3	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.62	319.2	318.3
A-63	CF_3	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	CH_3	N	2	4.05	333.2	332.3
A-64	CF_2CHF_2	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	H	N	2	3.43	337.2	336.3
A-65	CF_2CHF_2	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	CH_3	N	2	3.82	351.2	350.3
A-66	CF_2CHF_2	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.65	351.2	350.3
A-67	CF_2CHF_2	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	CH_3	N	2	4.03	365.2	364.3
A-68	CF_2CF_3	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	H	N	2	3.72	355.2	354.3
A-69	CF_2CF_3	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	CH_3	N	2	4.12	369.2	368.3
A-70	CF_2CF_3	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.92	369.2	368.3
A-71	CF_2CF_3	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	CH_3	N	2	4.32	383.2	382.3
A-72	CF_2CH_3	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	H	N	2	3.29	301.2	300.3
A-73	CF_2CH_3	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	CH_3	N	2	3.69	315.2	314.3
A-74	CF_2CH_3	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.51	315.2	314.3
A-75	CF_2CH_3	H	H	CO	N	C	C	C	-	OCH_2CH_3	CH_3	H	2	H	CH_3	N	2	3.92	329.2	328.4
A-76	cyclopropyl	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	H	N	2	3.19	277.2	276.3
A-77	cyclopropyl	H	H	CO	N	C	C	C	-	OCH_3	CH_3	H	2	H	CH_3	N	2	3.60	291.2	290.4
A-78	CF_3	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	CH_3	N	2	3.43	318.2	317.3
A-79	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	CH_3	N	2	3.47	350.2	349.3
A-80	CF_2CF_3	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	CH_3	N	2	3.77	368.2	367.3
A-81	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	CH_3	N	2	3.30	314.2	313.3
A-82	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	4	1.24	387.9	387.3
A-83	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	4	1.30	401.9	401.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-84	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	4	1.26	387.9	387.3
A-85	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	4	1.16	373.9	373.3
A-86	CF_3	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	3	1.28	274.0	273.3
A-87	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	3	1.30	306.0	305.3
A-88	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	3	1.44	323.9	323.3
A-89	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.29	261.9	261.4
A-90	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.65	275.9	275.4
A-91	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.49	275.9	275.4
A-92	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	3.78	373.7	373.3
A-93	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	2.77	233.9	233.3
A-94	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	3.06	247.9	247.3
A-95	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	3.35	261.9	261.4
A-96	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	2.79	245.9	245.3
A-97	CF_3	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.26	288.2	287.3
A-98	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.31	320.2	319.3
A-99	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.66	338.2	337.3
A-100	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	4.02	388.2	387.3
A-101	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.93	248.2	247.3
A-102	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.24	262.2	261.4
A-103	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.55	276.2	275.4
A-104	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	H	H	3	H	H	N	2	3.02	260.2	259.4
A-105	CF_3	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.37	288.2	287.3
A-106	CF_2CHF_2	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.43	320.2	319.3
A-107	C_2F_5	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.82	338.1	337.3
A-108	$CF(CF_3)_2$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	4.21	388.2	387.3
A-109	CH_2CH_3	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.14	248.2	247.3
A-110	$CH(CH_3)_2$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.45	262.2	261.4
A-111	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.82	276.2	275.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-112	cyclopropyl	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.16	260.2	259.4
A-113	CF_3	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.60	302.2	301.3
A-114	CF_2CHF_2	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.64	334.2	333.3
A-115	C_2F_5	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	4.04	352.2	351.3
A-116	$CF(CF_3)_2$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	4.47	402.2	401.3
A-117	CH_2CH_3	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.29	262.2	261.4
A-118	$CH(CH_3)_2$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.62	276.2	275.4
A-119	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.97	290.3	289.4
A-120	cyclopropyl	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	3	H	H	N	2	3.34	274.2	273.4
A-121	CF_3	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.46	302.2	301.3
A-122	CF_2CHF_2	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.51	334.3	333.3
A-123	C_2F_5	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.86	352.2	351.3
A-124	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	4.14	402.2	401.3
A-125	CH_2CH_3	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.22	262.2	261.4
A-126	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.49	276.2	275.4
A-127	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.76	290.3	289.4
A-128	cyclopropyl	H	H	CO	C	C	C	C	H	$CH(CH_3)_2$	H	H	2	H	H	N	2	3.24	274.2	273.4
A-129	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	3.13	247.9	247.3
A-130	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	CH_3	CH_3	H	H	2	H	H	N	2	3.52	261.9	261.4
A-131	CF_3	H	H	CO	C	C	C	C	H	2-methyl-1,3-dioxolan-2-yl	H	H	2	H	H	N	2	2.95	346.2	345.3
A-132	CF_2CHF_2	H	H	CO	C	C	C	C	H	2-methyl-1,3-dioxolan-2-yl	H	H	2	H	H	N	2	2.99	378.2	377.3
A-133	C_2F_5	H	H	CO	C	C	C	C	H	2-methyl-1,3-dioxolan-2-yl	H	H	2	H	H	N	2	3.30	396.2	395.3
A-134	C_2F_5	H	H	CO	C	C	C	C	H	$COCH_3$	H	H	2	H	H	N	2	3.37	352.2	351.3
A-135	CF_2CHF_2	H	H	CO	C	C	C	C	H	$COCH_3$	H	H	2	H	H	N	2	3.05	334.2	333.3
A-136	CF_3	H	H	CO	C	C	C	C	H	$COCH_3$	H	H	2	H	H	N	2	2.98	302.1	301.3
A-137	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.30	277.9	277.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-138	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.30	304.2	303.3
A-139	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.34	336.2	335.3
A-140	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.64	354.2	353.3
A-141	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.89	404.2	403.3
A-142	CH_2CH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.04	264.2	263.3
A-143	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.29	278.2	277.4
A-144	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.52	292.3	291.4
A-145	cyclopropyl	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.06	276.2	275.3
A-146	CF_2CH_3	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	2.97	270.1	269.3
A-147	CHF_2	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	2.64	256.1	255.3
A-148	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.16	300.2	299.3
A-149	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	2.96	286.2	285.3
A-150	CH_2OCH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	2.67	280.2	279.3
A-151	CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	CH_3	N	2	3.64	333.2	332.3
A-152	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	H	N	2	3.31	351.2	350.3
A-153	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	CH_3	N	2	3.65	365.2	364.3
A-154	CF_2CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	H	N	2	3.61	369.2	368.3
A-155	CF_2CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	CH_3	N	2	3.96	383.2	382.3
A-156	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	H	N	2	3.15	315.2	314.3
A-157	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	CH_3	N	2	3.49	329.2	328.4
A-158	CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	CH_3	N	2	3.36	319.2	318.3
A-159	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	H	N	2	3.08	337.2	336.3
A-160	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	CH_3	N	2	3.40	351.2	350.3
A-161	CF_2CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	H	N	2	3.39	355.2	354.3
A-162	CF_2CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	CH_3	N	2	3.72	369.2	368.3
A-163	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	H	N	2	2.90	301.2	300.3
A-164	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	CH_3	N	2	3.22	315.0	314.3
A-165	cyclopropyl	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	CH_3	N	2	3.10	291.2	290.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-166	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	4	1.36	409.9	409.3
A-167	$(CF_2)_2CF_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	4	1.40	423.9	423.3
A-168	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.47	284.2	283.4
A-169	CH_2CH_3	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.40	270.2	269.3
A-170	CF_3	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.45	310.1	309.3
A-171	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.48	326.2	325.5
A-172	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.38	312.2	311.4
A-173	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.50	326.1	325.5
A-174	CF_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.44	352.2	351.4
A-175	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.67	314.2	313.4
A-176	CH_2CH_3	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.61	300.2	299.4
A-177	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.67	314.2	313.4
A-178	CF_3	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.63	340.1	339.3
A-179	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.49	284.2	283.4
A-180	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.42	312.2	311.4
A-181	CH_2CH_3	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.39	298.2	297.4
A-182	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.44	312.2	311.4
A-183	CF_3	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	3	1.38	338.2	337.3
A-184	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.52	298.2	297.4
A-185	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.45	284.2	283.4
A-186	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.52	298.2	297.4
A-187	CF_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.46	324.1	323.3
A-188	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.77	372.2	371.3
A-189	C_2F_5	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	4.06	390.2	389.3
A-190	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	4.27	440.2	439.3
A-191	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.99	328.3	327.4
A-192	cyclopropyl	H	H	CO	C	C	C	C	H	OCH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.56	312.2	311.4
A-193	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.63	384.2	383.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-194	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.93	402.2	401.4
A-195	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	4.18	452.2	451.4
A-196	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.88	340.3	339.5
A-197	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.43	324.3	323.4
A-198	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.32	342.2	341.3
A-199	C_2F_5	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.62	360.2	359.3
A-200	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.87	410.2	409.3
A-201	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.56	298.2	297.4
A-202	cyclopropyl	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.09	282.2	281.4
A-203	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.52	370.2	369.4
A-204	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	4.05	438.2	437.4
A-205	C_2F_5	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.81	388.2	387.4
A-206	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.76	326.3	325.5
A-207	cyclopropyl	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-CH=CH-Y4		2	CH3	CH_3	N	2	3.32	310.2	309.4
A-208	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.68	311.9	311.4
A-209	$(CH_2)_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.74	325.9	325.5
A-210	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.47	355.8	355.3
A-211	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.79	373.8	373.3
A-212	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	4.06	423.7	423.3
A-213	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.74	311.9	311.4
A-214	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.26	295.9	295.4
A-215	CF_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.56	337.8	337.3
A-216	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.61	369.8	369.4
A-217	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.95	387.8	387.4
A-218	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	4.20	437.7	437.4
A-219	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.36	297.9	297.4
A-220	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.63	311.9	311.4
A-221	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.90	325.9	325.5

No	R1	R2	R3	X	Y1	Y2	Y3	Y4	R12	R13	R14	R15	n	R4	R5	D	HPLC	Rt	m/z	MW
A-222	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		3	H	H	N	2	3.37	309.9	309.4
A-223	CF_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.70	351.8	351.4
A-224	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.71	383.8	383.4
A-225	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	4.03	401.8	401.4
A-226	$CF(CF_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	4.33	451.7	451.4
A-227	CH_2CH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.44	311.9	311.4
A-228	$CH(CH_3)_2$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.69	325.9	325.5
A-229	$CH(CH_3)CH_2CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.96	339.9	339.5
A-230	cyclopropyl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		4	H	H	N	2	3.47	323.9	323.4
A-231	CF_2CH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.36	320.2	319.4
A-232	CHF_2	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.10	306.2	305.3
A-233	CH_2OCH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	2.86	300.2	299.4
A-234	CF_3	H	CH_3	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.60	338.2	337.3
A-235	CF_3	CH_3	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.65	338.2	337.3
A-236	$CH(CH_3)_2$	H	H	CO	N	C	C	C	-	H	Y3-S-CH=CH-Y4		2	CH_3	H	N	1	3.59	304.9	304.4
A-237	$(CH_2)_2CH_3$	H	H	CO	N	C	C	C	-	H	Y3-S-CH=CH-Y4		2	CH_3	H	N	1	3.63	304.9	304.4
A-238	CH_2CH_3	H	H	CO	N	C	C	C	-	H	Y3-S-CH=CH-Y4		2	CH_3	H	N	1	3.32	290.9	290.4
A-239	CF_3	H	H	CO	N	C	C	C	-	H	N-pyrrolidinyl	H	2	H	H	N	2	3.11	329.8	329.3
A-240	CF_3	H	H	CO	N	C	C	C	-	H	N-piperidinyl	H	2	H	H	N	2	3.44	343.8	343.4
A-241	CF_3	H	H	CO	N	C	C	C	-	H	N-morpholinyl	H	2	H	H	N	2	2.84	345.8	345.3
A-242	CF_3	H	H	CO	N	C	C	C	-	H	CH_3	$(CH_2)_2CH_3$	2	H	H	N	2	3.31	316.8	316.3
A-243	CF_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	CH_3	N	2	3.31	301.8	301.3
A-244	CF_3	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	H	N	2	3.00	302.8	302.3
A-245	CF_3	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	CH_3	N	2	3.31	316.8	316.3
A-246	CF_3	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	CH_3	N	2	3.65	330.8	330.4
A-247	C_2F_5	H	H	CO	N	C	C	C	-	CH_3	CH_3	H	2	H	CH_3	N	2	3.38	352.8	352.3
A-248	C_2F_5	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-S-Y4		2	H	CH_3	N	2	3.57	379.7	379.4
A-249	C_2F_5	H	H	CO	N	C	C	C	-	H	N-piperidinyl	H	2	H	H	N	2	3.76	393.7	393.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-250	C_2F_5	H	H	CO	N	C	C	C	-	H	N-morpholinyl	H	2	H	H	N	2	3.22	395.7	395.3
A-251	C_2F_5	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-S-Y4		2	H	H	N	2	3.45	365.7	365.3
A-252	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	CH_3	N	2	3.64	351.8	351.3
A-253	C_2F_5	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	CH_3	N	2	3.62	351.8	351.3
A-254	CF_3	H	H	CO	N	C	C	C	-	CH_3	OCH_2CH_3	H	2	H	H	N	2	3.26	318.8	318.3
A-255	C_2F_5	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	H	N	2	3.38	352.8	352.3
A-256	cyclopropyl	H	H	CO	N	C	C	C	-	CH_3	OCH_3	H	2	H	H	N	2	2.73	276.8	276.3
A-257	C_2F_5	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.70	366.8	366.3
A-258	C_2F_5	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	CH_3	N	2	3.66	366.8	366.3
A-259	C_2F_5	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	CH_3	N	2	3.97	380.8	380.4
A-260	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_3	CH_3	H	2	H	CH_3	N	2	2.87	298.8	298.3
A-261	CF_2CH_3	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-S-Y4		2	H	CH_3	N	2	3.10	325.8	325.4
A-262	CF_2CH_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	CH_3	N	2	3.26	297.8	297.3
A-263	CF_2CH_3	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	CH_3	N	2	3.17	297.8	297.3
A-264	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	CH_3	N	2	3.17	312.8	312.4
A-265	CF_2CH_3	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	CH_3	N	2	3.50	326.8	326.4
A-266	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	CH_3	H	2	H	CH_3	N	2	3.05	334.8	334.3
A-267	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-S-Y4		2	H	CH_3	N	2	3.27	361.7	361.4
A-268	CF_2CHF_2	H	H	CO	N	C	C	C	-	H	N-morpholinyl	H	2	H	H	N	2	2.91	377.7	377.3
A-269	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_3	CH_3	H	2	H	H	N	2	2.82	320.8	320.3
A-270	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	Y3-CH=CH-S-Y4		2	H	H	N	2	3.15	347.7	347.3
A-271	CF_2CHF_2	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	CH_3	N	2	3.63	333.8	333.3
A-272	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	CH_3	CH_3	2	H	CH_3	N	2	3.31	333.8	333.3
A-273	CF_2CHF_2	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.39	348.8	348.3
A-274	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	CH_3	N	2	3.34	348.8	348.3
A-275	CF_2CHF_2	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	CH_3	N	2	3.66	362.8	362.4
A-276	$(CH_2)_2CCH$	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	H	H	N	2	2.85	286.8	286.4
A-277	$(CO)CH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	2.71	298.2	297.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-278	$(CO)OC_2H_5$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.27	328.2	327.4
A-279	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_3	N	2	4.43	381.7	381.3
A-280	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$CO_2C_2H_5$	N	2	4.08	426.2	425.4
A-281	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$COCH_3$	N	2	3.69	396.1	395.3
A-282	C_2F_5	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	3.44	340.2	339.3
A-283	C_2F_5	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	H	$COCH_3$	N	2	3.23	380.2	379.3
A-284	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_3	N	2	3.80	368.2	367.3
A-285	C_2F_5	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	2	H	H	N	2	4.07	382.2	381.3
A-286	C_2F_5	H	H	CO	C	C	C	C	H	$O(CH_2)_2CH_3$	H	H	2	H	H	N	2	3.85	368.2	367.3
A-287	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	CH_3	H	N	2	3.67	367.7	367.3
A-288	C_2F_5	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	3.59	353.7	353.3
A-289	C_2F_5	H	H	CO	C	C	C	C	H	OCH_2-cyclopropyl	CH_3	H	2	H	H	N	2	4.08	394.2	393.4
A-290	C_2F_5	H	H	CO	C	C	C	C	H	$OCH_2CH(CH_3)C_2H_5$	CH_3	H	2	H	H	N	2	4.44	410.2	409.4
A-291	C_2F_5	H	H	CO	C	C	C	C	H	$(CO)NHCH_3$	H	H	2	H	H	N	2	3.24	367.1	366.3
A-292	C_2F_5	H	H	CO	C	C	C	C	H	CN	CH_3	H	2	H	H	N	2	3.52	349.1	348.3
A-293	C_2F_5	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	H	H	2	H	H	N	2	3.83	368.2	367.3
A-294	C_2F_5	H	H	CO	N	C	C	C	-	$(CH_2)_3CH_3$	CH_3	H	2	H	H	N	2	3.81	381.2	380.4
A-295	C_2F_5	H	H	CO	N	C	C	C	-	$(CH_2)_2CH_3$	CH_3	H	2	H	H	N	2	4.05	367.2	366.3
A-296	C_2F_5	H	H	CO	C	C	C	C	H	$OCHF_2$	H	H	2	H	H	N	2	3.89	376.1	375.2
A-297	C_2F_5	H	H	CO	C	C	C	C	H	CO_2CH_3	H	H	2	H	H	N	2	3.23	368.1	367.3
A-298	C_2F_5	H	H	CO	C	C	C	C	H	Cl	CH_3	H	2	H	H	N	2	3.59	358.1	357.7
A-299	C_2F_5	H	H	CO	C	C	C	C	H	H	Y3-N(CH_3)-CH=CH-Y4		2	H	H	N	2	3.42	363.1	362.3
A-300	C_2F_5	H	H	CO	C	C	C	C	$CONH_2$	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	2	3.82	450.1	449.4
A-301	C_2F_5	H	H	CO	C	C	C	C	H	$CONH_2$	H	H	2	H	H	N	2	3.11	353.1	352.3
A-302	C_2F_5	H	H	CO	N	C	C	C	-	H	Y3-N=CH-NH-Y4		2	H	H	N	2	2.43	351.1	350.2
A-303	C_2F_5	H	H	CO	C	C	C	C	$CONH_2$	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	2	2.97	421.1	420.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-304	C_2F_5	H	H	CO	C	C	C	C	CO_2H	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	4	3.08	422.1	421.3
A-305	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.39	314.2	313.3
A-306	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$CO_2C_2H_5$	N	2	3.64	372.2	371.4
A-307	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	2.93	286.1	285.3
A-308	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_3	N	2	3.34	314.2	313.3
A-309	CF_2CH_3	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	3.09	299.8	299.3
A-310	CF_2CH_3	H	H	CO	C	C	C	C	H	CN	CH_3	H	2	H	H	N	2	3.02	294.7	294.3
A-311	CF_2CH_3	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	H	N	2	2.90	299.2	298.3
A-312	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.55	350.2	349.3
A-313	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$CO_2C_2H_5$	N	2	3.79	408.2	407.4
A-314	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	3.12	322.2	321.3
A-315	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_3	N	2	3.50	350.2	349.3
A-316	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_2CH_3	N	2	4.12	363.7	363.4
A-317	CF_2CHF_2	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	H	H	2	H	H	N	2	3.55	350.2	349.3
A-318	CF_2CHF_2	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.77	364.2	363.4
A-319	CF_2CHF_2	H	H	CO	C	C	C	C	H	$O(CH_2)_2CH_3$	H	H	2	H	H	N	2	3.57	350.2	349.3
A-320	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	CH_3	H	N	2	3.38	349.7	349.3
A-321	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	3.28	335.7	335.3
A-322	CF_2CHF_2	H	H	CO	C	C	C	C	H	OCH_2-cyclopropyl	CH_3	H	2	H	H	N	2	3.80	376.2	375.4
A-323	CF_2CHF_2	H	H	CO	C	C	C	C	H	$OCH_2CH(CH_3)C_2H_5$	CH_3	H	2	H	H	N	2	4.19	392.2	391.4
A-324	CF_2CHF_2	H	H	CO	C	C	C	C	H	$(CO)NHCH_3$	H	H	2	H	H	N	2	2.94	349.2	348.3
A-325	CF_2CHF_2	H	H	CO	C	C	C	C	H	CN	CH_3	H	2	H	H	N	2	3.21	331.1	330.3
A-326	CF_2CHF_2	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	H	N	2	3.08	335.2	334.3
A-327	CF_2CHF_2	H	H	CO	N	C	C	C	-	$(CH_2)_3CH_3$	CH_3	H	2	H	H	N	2	3.52	363.2	362.4
A-328	CF_2CHF_2	H	H	CO	N	C	C	C	-	$(CH_2)_2CH_3$	CH_3	H	2	H	H	N	2	3.69	349.2	348.3
A-329	CF_2CHF_2	H	H	CO	C	C	C	C	H	$OCHF_2$	H	H	2	H	H	N	2	3.63	358.1	357.3
A-330	CF_2CHF_2	H	H	CO	C	C	C	C	H	CO_2CH_3	H	H	2	H	H	N	2	2.93	350.1	349.3
A-331	CF_2CHF_2	H	H	CO	C	C	C	C	H	Cl	CH_3	H	2	H	H	N	2	3.30	340.1	339.7

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-332	CF_2CHF_2	H	H	CO	C	C	C	C	H	$CONH_2$	H	H	2	H	H	N	2	2.79	335.1	334.3
A-333	CF_2Cl	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.42	320.1	319.7
A-334	CF_2Cl	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	H	N	2	3.10	319.1	318.8
A-335	CF_2Cl	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.43	333.2	332.8
A-336	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.52	318.2	317.3
A-337	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$COCH_3$	N	2	3.31	345.32	345.3
A-338	CF_3	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	3.06	290.1	289.3
A-339	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_3	N	2	3.47	318.2	317.3
A-340	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$CO_2C_2H_5$	N	2	3.80	376.2	375.3
A-341	CF_3	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	H	H	2	H	H	N	2	3.53	318.2	317.3
A-342	CF_3	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.76	332.2	331.3
A-343	CF_3	H	H	CO	C	C	C	C	H	$O(CH_2)_2CH_3$	H	H	2	H	H	N	2	3.55	318.2	317.3
A-344	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_2CH_3	N	2	4.14	331.7	331.3
A-345	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	CH_3	H	N	2	3.32	317.8	317.3
A-346	CF_3	H	H	CO	C	C	C	C	H	CH_3	CH_3	H	2	CH_3	H	N	2	3.77	301.8	301.3
A-347	CF_3	H	H	CO	N	C	C	C	-	H	CH_3	CH_2CH_3	2	CH_3	H	N	2	3.05	316.8	316.3
A-348	CF_3	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	3.23	303.7	303.3
A-349	CF_3	H	H	CO	C	C	C	C	H	OCH_2-cyclopropyl	CH_3	H	2	H	H	N	2	3.79	344.2	343.3
A-350	CF_3	H	H	CO	C	C	C	C	H	$OCH_2CH(CH_3)C_2H_5$	CH_3	H	2	H	H	N	2	4.20	360.2	359.4
A-351	CF_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	CH_3	H	N	2	3.50	338.2	337.3
A-352	CF_3	H	H	CO	C	C	C	C	H	$(CO)NHCH_3$	H	H	2	H	H	N	2	2.86	317.2	316.3
A-353	CF_3	H	H	CO	C	C	C	C	$CO_2C_2H_5$	SCH_3	Y3-CH=CH-CCl=CH-Y4		2	H	H	N	2	4.71	462.2	461.9
A-354	CF_3	H	H	CO	C	C	C	C	H	CH_3	Y3-N=CH-CH=CH-Y4		2	H	H	N	2	2.90	325.2	324.3
A-355	CF_3	H	H	CO	C	C	C	C	CO_2CH_3	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	2	3.32	386.2	385.3
A-356	CF_3	H	H	CO	N	C	C	C	-	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	2	2.86	329.1	328.3
A-357	CF_3	H	H	CO	N	C	C	C	-	H	Y3-CH=CH-S-Y4		2	H	H	N	2	2.93	317.1	316.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-358	CF_3	H	H	CO	C	C	C	C	H	CN	CH_3	H	2	H	H	N	2	3.15	299.1	298.3
A-359	CF_3	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.37	317.2	316.3
A-360	CF_3	H	H	CO	N	C	C	C	-	$(CH_2)_3CH_3$	CH_3	H	2	H	H	N	2	3.49	331.2	330.4
A-361	CF_3	H	H	CO	N	C	C	C	-	$(CH_2)_2CH_3$	CH_3	H	2	H	H	N	2	3.68	317.2	316.3
A-362	CF_3	H	H	CO	N	C	C	C	-	$N(CH_3)_2$	CH_3	CH_3	2	H	H	N	2	4.14	332.2	331.3
A-363	CF_3	H	H	CO	N	C	C	C	-	N-pyrrolidinyl	CH_3	H	2	H	H	N	2	4.02	344.2	343.4
A-364	CF_3	H	H	CO	C	C	C	C	H	$OCHF_2$	H	H	2	H	H	N	2	3.86	326.1	325.2
A-365	CF_3	H	H	CO	C	C	C	C	H	CF_3	H	H	2	H	H	N	2	3.67	328.1	327.2
A-366	CF_3	H	H	CO	N	C	C	C	-	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.12	311.1	310.3
A-367	CF_3	H	H	CO	C	C	C	C	Cl	H	Y3-CH=C(OCH_3)-CH=CH-Y4		2	H	H	N	2	3.68	374.1	373.8
A-368	CF_3	H	H	CO	C	C	C	C	NO_2	H	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.48	355.1	354.3
A-369	CF_3	H	H	CO	C	C	C	C	H	H	Y3-CH=C(CF_3)-CH=CH-Y4		2	H	H	N	2	3.82	378.1	377.3
A-370	CF_3	H	H	CO	C	C	C	C	H	Cl	CH_3	H	2	H	H	N	2	3.26	308.1	307.7
A-371	CF_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	3	H	H	N	2	3.40	318.1	317.3
A-372	CF_3	H	H	CO	C	C	C	C	H	OCH_3	H	H	3	H	H	N	2	3.18	304.1	303.3
A-373	CF_3	H	H	CO	C	C	C	C	CH_3	H	H	H	2	H	H	N	2	3.20	274.1	273.3
A-374	CF_3	H	H	CO	N	C	C	C	-	SCH_3	NH_2	H	2	H	H	N	2	3.06	322.1	321.3
A-375	CF_3	H	H	CO	N	C	C	C	-	H	Y3-O-CH=CH-Y4		2	H	H	N	2	2.94	301.1	300.2
A-376	CF_3	H	H	CO	C	C	C	C	CF_3	H	H	H	2	H	H	N	2	3.32	328.1	327.2
A-377	CF_3	H	H	CO	C	C	C	C	H	CO_2CH_3	H	H	2	H	H	N	2	2.86	318.1	317.3
A-378	CF_3	H	H	CO	C	C	C	N	H	CH_3	Y3=N-CH=N-Y4		2	H	H	N	2	2.67	315.1	314.3
A-379	CF_3	H	H	CO	C	C	C	C	$CONH_2$	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	2	2.69	371.1	370.3
A-380	CF_3	H	H	CO	C	C	C	C	H	H	Y3-N(CH_3)-CH=CH-Y4		2	H	H	N	2	3.08	313.1	312.3
A-381	CF_3	H	H	CO	C	C	C	C	$CO_2C_2H_5$	H	Y3-N(CH_3)-N=C(CH_3)-Y4		2	H	H	N	2	3.54	400.1	399.4
A-382	CF_3	H	H	CO	C	C	C	C	H	H	Y3-O-$(CH_2)_2$-O-Y4		2	H	H	N	2	2.92	318.1	317.3
A-383	CF_3	H	H	CO	C	C	C	C	H	$N(CH_3)_2$	H	H	2	H	H	N	2	3.32	303.1	302.3
A-384	CF_3	H	H	CO	C	C	C	C	H	$S(CH_3)$	H	H	2	H	H	N	2	3.19	306.1	305.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-385	CF_3	H	H	CO	C	C	C	C	H	$CONH_2$	H	H	2	H	H	N	2	2.77	303.1	302.3
A-386	CF_3	H	H	CS	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	3	1.57	320.1	319.3
A-387	CF_3	H	H	CO	C	C	C	C	H	H	Y3-CH=C(OCF_3)-CH=CH-Y4		2	H	H	N	2	3.79	394	393.3
A-388	CF_3	H	H	CO	C	N	C	C	H	-	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	2.97	311.1	310.3
A-389	$CH(CH_3)_2$	H	H	CO	N	C	C	C	-	H	Y3-O-CH=CH-Y4		2	H	H	N	2	2.95	275.2	274.3
A-390	$CH(CH_3)_2$	H	H	CO	C	C	C	N	H	CH_3	Y3=N-CH=N-Y4		2	H	H	N	2	2.69	289.2	288.4
A-391	CH_2Cl	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	2.91	283.7	283.8
A-392	$CH_2N(CH_3)_2$	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$CO_2C_2H_5$	N	2	3.22	365.3	364.4
A-393	CH_3	CH_3	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.42	283.8	283.4
A-394	$CHCHCH_3$	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.62	296.2	295.4
A-395	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	CH_3	H	2	H	H	N	2	3.21	300.2	299.3
A-396	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$CO_2C_2H_5$	N	2	3.48	358.2	357.4
A-397	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	$COCH_3$	N	2	2.99	328.2	327.3
A-398	CHF_2	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	2.70	272.1	271.3
A-399	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	CH_3	N	2	3.16	300.2	299.3
A-400	CHF_2	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	H	H	2	H	H	N	2	3.21	300.2	299.3
A-401	CHF_2	H	H	CO	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.45	314.2	313.3
A-402	CHF_2	H	H	CO	C	C	C	C	H	$O(CH_2)_2CH_3$	H	H	2	H	H	N	2	3.25	300.2	299.3
A-403	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	CH_3	H	N	2	3.04	299.8	299.3
A-404	CHF_2	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	2.89	285.8	285.3
A-405	CHF_2	H	H	CO	C	C	C	C	H	$(CO)NHCH_3$	H	H	2	H	H	N	2	2.55	299.1	298.3
A-406	CHF_2	H	H	CO	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	2	H	H	N	2	3.04	299.2	298.3
A-407	CHF_2	H	H	CO	C	C	C	C	H	CN	CH_3	H	2	H	H	N	2	2.81	280.7	280.3
A-408	CHF_2	H	H	CO	N	C	C	C	-	CH_2CH_3	CH_3	H	2	H	H	N	2	2.70	285.2	284.3
A-409	CHF_2	H	H	CO	N	C	C	C	-	$(CH_2)_3CH_3$	CH_3	H	2	H	H	N	2	3.20	313.2	312.4
A-410	CHF_2	H	H	CO	N	C	C	C	-	$(CH_2)_2CH_3$	CH_3	H	2	H	H	N	2	3.32	299.2	298.3
A-411	CHF_2	H	H	CO	C	C	C	C	H	$OCHF_2$	H	H	2	H	H	N	2	3.32	308.1	307.2
A-412	CHF_2	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	3	H	H	N	2	3.09	300.2	299.3

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-413	CHF_2	H	H	CO	C	C	C	C	H	OCH_3	H	H	3	H	H	N	2	2.86	286.1	285.3
A-414	CHF_2	H	H	CO	C	C	C	N	H	CH_3	Y3=N-CH=N-Y4		2	H	H	N	2	2.37	296.7	296.3
A-415	CHF_2	H	H	CO	C	C	C	C	H	H	Y3-O-$(CH_2)_2$-O-Y4		2	H	H	N	2	2.58	300.1	299.3
A-416	CHF_2	H	H	CO	C	C	C	C	H	$N(CH_3)_2$	H	H	2	H	H	N	2	2.90	285.1	284.3
A-417	CHF_2	H	H	CO	C	C	C	C	H	$S(CH_3)$	H	H	2	H	H	N	2	2.89	288.1	287.3
A-418	CHF_2	H	H	CO	C	C	C	C	H	$CONH_2$	H	H	2	H	H	N	2	2.38	285.1	284.3
A-419	Cl	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	2.88	269.8	269.7
A-420	Cl	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	2.69	256.1	255.7
A-421	Cl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.28	290.1	289.8
A-422	furan-2-yl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.41	322.2	321.4
A-423	H	Cl	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	2.44	256.0	255.7
A-424	H	$N(CH_3)_2$	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	2.49	265.1	264.3
A-425	H	Cl	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.01	290.1	289.8
A-426	$CH_2N(CH_3)_2$	H	H	CO	C	C	C	C	H	OCH_3	CH_3	H	2	H	H	N	2	2.60	293.2	292.4
A-427	OC_2H_5	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.28	300.2	299.4
A-428	phenyl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.83	332.2	331.4
A-429	SCH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.24	302.1	301.4
A-430	thiophen-2-yl	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.69	338.2	337.4
A-431	CF_3	H	H	CO	C	C	C	C	H	SC2H5	H	H	2	H	H	N	2	3.43	320.1	319.3
A-432	CF_3	H	H	CO	C	C	C	C	H	H	H	H	1	H	H	C	2	2.87	245.1	244.2
A-433	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	H	H	1	H	H	C	2	2.95	277.1	276.2
A-434	C_2F_5	H	H	CO	C	C	C	C	H	H	H	H	1	H	H	C	2	3.29	295.1	294.2
A-435	CF_3	H	H	CO	C	C	C	C	H	H	H	H	2	H	H	C	2	3.05	259.1	258.2
A-436	CF_2CHF_2	H	H	CO	C	C	C	C	H	H	H	H	2	H	H	C	2	3.11	291.1	290.3
A-437	C_2F_5	H	H	CO	C	C	C	C	H	H	H	H	2	H	H	C	2	3.44	309.1	308.2
A-438	$CH(CH_3)_2$	H	H	SO_2	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.38	314.2	313.4
A-439	$CH(CH_3)_2$	H	H	SO_2	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	3.23	300.2	299.4
A-440	SCH_3	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	5	1.65	282.1	281.4

No	R^1	R^2	R^3	X	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	n	R^4	R^5	D	HPLC	Rt	m/z	MW
A-441	SF_5	H	H	CO	C	C	C	C	H	CH_3	H	H	2	H	H	N	2	3.52	332.0	331.3
A-442	SF_5	H	H	CO	C	C	C	C	H	OCH_2CH_3	H	H	2	H	H	N	2	3.51	362.0	361.3
A-443	SO_2CH_3	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	2.82	334.1	333.4
A-444	SCH_3	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	2.71	268.1	267.4
A-445	SF_5	H	H	CO	C	C	C	C	H	OCH_3	H	H	2	H	H	N	2	3.33	348.0	347.3
A-446	SF_5	H	H	CO	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.82	382.1	381.4
A-447	$CH(CH_3)_2$	H	H	SO_2	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	2	3.63	334.3	333.5
A-448	CF_3	H	H	CO	N	C	C	N	-	OCH_3	CH_2CH_3	-	2	H	H	N	2	3.14	320.1	319.3
A-449	$CH(CH_3)_2$	H	H	CS	C	C	C	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		2	H	H	N	3	1.62	314.1	313.5
A-450	$CH(CH_3)_2$	H	H	SO_2	C	C	C	C	H	CH_3	CH_3	H	2	H	H	N	2	4.38	298.2	297.4

Table A continued (X=CO, n = 2, D = N):

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-451	CH_2OCH_3	H	H	C	C	C	C	H	CH_3	H	H	H	H	4A; 2H
A-452	CH_2OCH_3	H	H	C	C	C	C	H	CH_3	CH_3	H	H	H	4A; 2H
A-453	CH_2OCH_3	H	H	C	C	C	C	CH_3	CH_3	H	H	H	H	4A; 2H
A-454	CH_2OCH_3	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	4A; 2H
A-455	CH_2OCH_3	H	H	N	C	C	C	-	CH_3	CH_3	H	H	H	4A; 2H
A-456	CH_2OCH_3	H	H	N	C	C	C	-	CH_2CH_3	CH_3	H	H	H	4A; 2H
A-457	CH_2OCH_3	H	H	C	C	C	C	H	OCH_3	H	H	H	H	9A; 4A; 2H
A-458	CH_2OCH_3	H	H	C	C	C	C	H	OCH_2CH_3	H	H	H	H	9A; 4A; 2H
A-459	CH_2OCH_3	H	H	C	C	C	C	H	OCH_3	CH_3	H	H	H	9A; 4A; 2H
A-460	CH_2OCH_3	H	H	N	C	C	C	-	H	CH_3	CH_2CH_3	H	H	4A; 2H
A-461	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	CH_3	H	H	H	H	4A; 2H
A-462	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	CH_3	CH_3	H	H	H	4A; 2H
A-463	$CH_2N(CH_3)_2$	H	H	C	C	C	C	CH_3	CH_3	H	H	H	H	4A; 2H
A-464	$CH_zN(CH_3)_2$	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	4A; 2H
A-465	$CH_2N(CH_3)_2$	H	H	N	C	C	C	-	CH_3	CH_3	H	H	H	4A; 2H
A-466	$CH_2N(CH_3)_2$	H	H	N	C	C	C	-	CH_2CH_3	CH_3	H	H	H	4A; 2H
A-467	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_3	H	H	H	H	9A; 4A; 2H
A-468	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_2CH_3	H	H	H	H	9A; 4A; 2H
A-469	$CH_2N(CH_3)_2$	H	H	N	C	C	C	-	H	CH_3	CH_2CH_3	H	H	4A; 2H
A-470	$N(CH_3)_2$	H	H	C	C	C	C	H	CH_3	H	H	H	H	4A; 2H
A-471	$N(CH_3)_2$	H	H	C	C	C	C	H	CH_3	CH_3	H	H	H	4A; 2H
A-472	$N(CH_3)_2$	H	H	C	C	C	C	CH_3	CH_3	H	H	H	H	4A; 2H
A-473	$N(CH_3)_2$	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	4A; 2H
A-474	$N(CH_3)_2$	H	H	N	C	C	C	-	CH_3	CH_3	H	H	H	4A; 2H
A-475	$N(CH_3)_2$	H	H	N	C	C	C	-	CH_2CH_3	CH_3	H	H	H	4A; 2H

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-476	$N(CH_3)_2$	H	H	C	C	C	C	H	OCH_3	H	H	H	H	9A; 4A; 2H
A-477	$N(CH_3)_2$	H	H	C	C	C	C	H	OCH_2CH_3	H	H	H	H	9A; 4A; 2H
A-478	$N(CH_3)_2$	H	H	N	C	C	C	-	H	CH_3	CH_2CH_3	H	H	4A; 2H
A-479	CH_2NHCH_3	H	H	C	C	C	C	H	CH_3	H	H	H	H	4A; 2H
A-480	CH_2NHCH_3	H	H	C	C	C	C	H	CH_3	CH_3	H	H	H	4A; 2H
A-481	CH_2NHCH_3	H	H	C	C	C	C	CH_3	CH_3	H	H	H	H	4A; 2H
A-482	CH_2NHCH_3	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	4A; 2H
A-483	CH_2NHCH_3	H	H	N	C	C	C	-	CH_3	CH_3	H	H	H	4A; 2H
A-484	CH_2NHCH_3	H	H	N	C	C	C	-	CH_2CH_3	CH_3	H	H	H	4A; 2H
A-485	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_3	H	H	H	H	9A; 4A; 2H
A-486	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_2CH_3	H	H	H	H	9A; 4A; 2H
A-487	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_3	CH_3	H	H	H	9A; 4A; 2H
A-488	CH_2NHCH_3	H	H	N	C	C	C	-	H	CH_3	CH_2CH_3	H	H	4A; 2H
A-489	CH_2OCH_3	H	H	C	C	C	C	H	$COCH_3$	H	H	H	H	6A-C; 7
A-490	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$COCH_3$	H	H	H	H	6A-C; 7
A-491	CH_2NHCH_3	H	H	C	C	C	C	H	$COCH_3$	H	H	H	H	6A-C; 7
A-492	CF_3	H	H	C	C	C	C	OCH_3	CH_3	H	H	H	H	2A-E; 4A; 2H
A-493	CHF_2	H	H	C	C	C	C	H	$COCH_3$	H	H	H	H	2A-E; 6A-C; 7
A-494	CHF_2	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	2A-E; 4A; 2H
A-495	CF_2CH_3	H	H	C	C	C	C	H	$COCH_3$	H	H	H	H	2A-E; 6A-C; 7
A-496	CF_2CH_3	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	2A-E; 4A; 2H
A-497	CF_2CF_3	H	H	C	C	C	C	H	OCH_2CH_3	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-498	CH_2OCH_2	H	H	C	C	C	C	H	OCH_2CH_3	CH_3	H	H	H	9A; 4A; 2H
A-499	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_2CH_3	CH_3	H	H	H	9A; 4A; 2H
A-500	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_2CH_3	CH_3	H	H	H	9A; 4A; 2H

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-501	CF_2CH_3	H	H	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-502	CH_2OCH_2	H	H	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	H	H	9A; 4A; 2H
A-503	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	H	H	9A; 4A; 2H
A-504	CH_2NHCH_3	H	H	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	H	H	9A; 4A; 2H
A-505	CF_3	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-506	CHF_2	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-507	CF_2CH_3	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-508	CF_2CHF_2	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-509	CF_2CF_3	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-510	CH_2OCH_2	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2H
A-511	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2H
A-512	CH_2NHCH_3	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	9A; 4A; 2H
A-513	CF_2CH_3	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2A-E; 2H
A-514	CH_2OCH_2	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-515	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-516	CH_2NHCH_3	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-517	CF_2CH_3	H	H	C	C	C	C	H	$OCH(CH_3)_2$	H	H	H	H	9A; 4A; 2A-E; 2H
A-518	CH_2OCH_2	H	H	C	C	C	C	H	$OCH(CH_3)_2$	H	H	H	H	9A; 4A; 2H
A-519	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$OCH(CH_3)_2$	H	H	H	H	9A; 4A; 2H
A-520	CH_2NHCH_3	H	H	C	C	C	C	H	$OCH(CH_3)_2$	H	H	H	H	9A; 4A; 2H
A-521	CF_3	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-522	CHF_2	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-523	CF_2CH_3	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-524	CF_2CHF_2	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-525	CF_2CF_3	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-526	CH_2OCH_2	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2H
A-527	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2H
A-528	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	9A; 4A; 2H
A-529	CF_3	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-530	CHF_2	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-531	CF_2CH_3	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-532	CF_2CHF_2	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-533	CF_2CF_3	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2A-E; 2H
A-534	CH_2OCH_2	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2H
A-535	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2H
A-536	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	9A; 4A; 2H
A-537	CF_3	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-538	CHF_2	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-539	CF_2CH_3	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-540	CF_2CHF_2	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-541	CF_2CF_3	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-542	CH_2OCH_2	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2H
A-543	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2H
A-544	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)z$	H	H	H	9A; 4A; 2H
A-545	CF_3	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-546	CHF_2	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-547	CF_2CH_3	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-548	CF_2CHF_2	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)z$	H	H	H	9A; 4A; 2A-E; 2H
A-549	CF_2CF_3	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2A-E; 2H
A-550	CH_2OCH_2	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2H

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-551	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2H
A-552	CH_2NHCH_3	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	9A; 4A; 2H
A-553	CF_3	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2A-E; 2H
A-554	CHF_2	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2A-E; 2H
A-555	CF_2CH_3	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2A-E; 2H
A-556	CF_2CHF_2	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2A-E; 2H
A-557	CF_2CF_3	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2A-E; 2H
A-558	CH_2OCH_2	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2H
A-559	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2H
A-560	CH_2NHCH_3	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2H
A-561	CF_3	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2A-E; 2H
A-562	CHF_2	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2A-E; 2H
A-563	CF_2CH_3	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2A-E; 2H
A-564	CF_2CHF_2	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2A-E; 2H
A-565	CF_2CF_3	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2A-E; 2H
A-566	CH_2OCH_2	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-567	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-568	CH_2NHCH_3	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-569	CF_3	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	2A-E; 6A-C; 7
A-570	CHF_2	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	2A-E; 6A-C; 7
A-571	CF_2CH_3	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	2A-E; 6A-C; 7
A-572	CF_2CHF_2	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	2A-E; 6A-C; 7
A-573	CF_2CF_3	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	2A-E; 6A-C; 7
A-574	CH_2OCH_2	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	6A-C; 7
A-575	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	6A-C; 7

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-576	CH_2NHCH_3	H	H	C	C	C	C	H	$COCH_3$	CH_3	H	H	H	6A-C; 7
A-577	CF_3	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	2A-E; 6A-C; 7
A-578	CHF_2	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	2A-E; 6A-C; 7
A-579	CF_2CH_3	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	2A-E; 6A-C; 7
A-580	CF_2CHF_2	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	2A-E; 6A-C; 7
A-581	CF_2CF_3	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	2A-E; 6A-C; 7
A-582	CH_2OCH_2	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	6A-C; 7
A-583	$CH_2N(CH_3)_2$	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	6A-C; 7
A-584	CH_2NHCH_3	H	H	C	C	C	C	H	$COCH_2CH_3$	H	H	H	H	6A-C; 7
A-585	CF_3	H	H	C	C	C	C	H	H	Y3-CH=CH-S-Y4		H	H	2A-E; 3B, 4B
A-586	CF_3	H	H	C	C	C	C	H	H	Y3-CH=CH-CH=N-Y4		H	H	2A-E; 3B, 4B
A-587	CF_3	H	H	C	C	C	N	H	CH_3	Y3=CH-CH=N-Y4		H	H	2A-E; 4A, B
A-588	CF_3	H	H	C	C	C	C	H	H	Y3-N(CH_3)-N=C(CH_3)-Y4		H	H	2A-E; 3B, 4B
A-589	CF_3	H	H	C	N	C	C	H	-	H	H	H	H	2A-E; 3B, 4B
A-590	CF_3	H	H	C	C	C	C	H	H	Y3-CH=CH-O-Y4		H	H	2A-E; 3B, 4B
A-591	CF_3	H	H	C	C	C	C	H	H	Y3-O-CH=CH-Y4		H	H	2A-E; 3B, 4B
A-592	CF_3	H	H	C	C	C	C	H	H	Y3-O-CH_2-CH_2-Y4		H	H	2A-E;8A-C
A-593	CF_2CF_3	H	H	C	C	C	C	CH_3	OCH_3	H	H	H	H	3A-B; 10F-I; 16C
A-594	CF_2CF_3	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-595	CF_2CF_3	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-596	CF_2CF_3	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-597	CF_2CF_3	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-598	CF_2CF_3	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-599	CF_2CF_3	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-600	CF_2CF_3	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-601	CF_2CF_3	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-602	CF_2CF_3	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-603	CF_2CF_3	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-604	CF_2CH_3	H	H	C	C	C	C	CH_3	OCH_3	H	H	H	H	3A-B; 10F-I; 16C
A-605	CF_2CH_3	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-606	CF_2CH_3	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-607	CF_2CH_3	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-608	CF_2CH_3	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-609	CF_2CH_3	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-610	CF_2CH_3	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-611	CF_2CH_3	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-612	CF_2CH_3	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-613	CF_2CH_3	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-614	CF_2CH_3	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-615	CF_2CHF_2	H	H	C	C		C	CH_3	OCH_3	H	H	H	H	3A-B; 10F-I; 16C
A-616	CF_2CHF_2	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-617	CF_2CHF_2	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-618	CF_2CHF_2	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-619	CF_2CHF_2	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-620	CF_2CHF_2	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-621	CF_2CHF_2	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-622	CF_2CHF_2	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-623	CF_2CHF_2	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-624	CF_2CHF_2	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-625	CF_2CHF_2	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-626	CF_2Cl	H	H	C	C	C	C	H	$CH(CH_3)_2$	H	H	H	H	10F-I; 4A; 2H
A-627	CF_2Cl	H	H	C	C	C	C	H	$CH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-628	CF_2Cl	H	H	C	C	C	C	H	CH_2CH_3	H	H	H	H	9A; 4A; 2H
A-629	CF_2Cl	H	H	C	C	C	C	H	CH_3	CH_3	H	H	H	4A; 2H
A-630	CF_2Cl	H	H	C	C	C	C	H	$COCH_3$	H	H	H	H	10F-I; 6A-C; 7
A-631	CF_2Cl	H	H	C	C	C	C	H	$OCH(CH_3)_2$	CH_3	H	H	H	10A-E; 2H
A-632	CF_2Cl	H	H	C	C	C	C	H	$OCH(CH_3)_2$	H	H	H	H	9A; 4A; 2H
A-633	CF_2Cl	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	CH_3	H	H	H	10A-E; 2H
A-634	CF_2Cl	H	H	C	C	C	C	H	$OCH_2CH_2CH_3$	H	H	H	H	9A; 4A; 2H
A-635	CF_2Cl	H	H	C	C	C	C	H	OCH_2CH_3	$CH(CH_3)_2$	H	H	H	10A-E; 2H
A-636	CF_2Cl	H	H	C	C	C	C	H	OCH_2CH_3	CH_2CH_3	H	H	H	10A-E; 2H
A-637	CF_2Cl	H	H	C	C	C	C	H	OCH_3	$CH(CH_3)_2$	H	H	H	10A-E; 2H
A-638	CF_2Cl	H	H	C	C	C	C	H	OCH_3	H	H	H	H	10A-I; 2H
A-639	CF_2Cl	H	H	C	C	C	C	H	OCH_2CH_3	CH_3	H	H	H	10A-I; 16C
A-640	CF_2Cl	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-641	CF_2Cl	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-642	CF_2Cl	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-643	CF_2Cl	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	10A-I; 16C
A-644	CF_2Cl	H	H	C	C	C	C	H	OCH_3	CH_3	H	H	H	10A-I; 16C
A-645	CF_2Cl	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-646	CF_2Cl	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-647	CF_2Cl	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-648	CF_2Cl	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-649	CF_2Cl	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-650	CF_2Cl	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J

(continued)

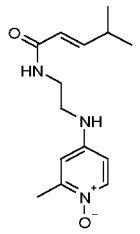
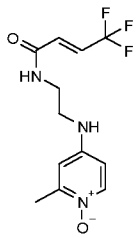
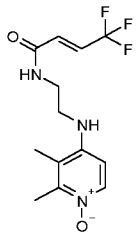
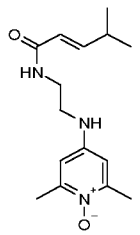
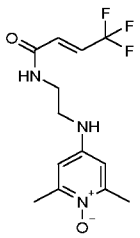
No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-651	CF_2Cl	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-652	CF_3	H	H	C	C	C	C	CH_3	OCH_3	H	H	H	H	3A-B; 10F-I; 16C
A-653	CF_3	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-654	CF_3	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-655	CF_3	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-656	CF_3	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-657	CF_3	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-658	CF_3	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-659	CF_3	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-660	CF_3	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-661	CH_2OCH_2	H	H	C	C	C	C	CH_3	OCH_3	H	H	H	H	3A-B; 10F-I; 16C
A-662	CH_2OCH_2	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-663	CH_2OCH_2	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-664	CH_2OCH_2	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-665	CH_2OCH_2	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-666	CH_2OCH_2	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-667	CH_2OCH_2	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-668	CH_2OCH_2	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-669	CH_2OCH_2	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-670	CH_2OCH_2	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-671	CH_2OCH_2	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-672	CHF_2	H	H	C	C	C	C	CH_3	OCH_3	H	H	H	H	3A-B; 10F-I; 16C
A-673	CHF_2	H	H	C	C	C	C	CH_3	OCH_2CH_3	H	H	H	H	3A-B; 10F-I; 16C
A-674	CHF_2	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C
A-675	CHF_2	H	H	C	C	C	C	H	OCH_2CH_3	H	CH_3	H	H	3A-B; 10F-I; 16C

(continued)

No	R^1	R^2	R^3	Y^1	Y^2	Y^3	Y^4	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	Synth. Methods
A-676	CHF_2	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-677	CHF_2	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-678	CHF_2	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-679	CHF_2	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-680	CHF_2	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-681	CHF_2	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-682	CHF_2	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-683	SF_5	H	H	C	C	C	C	H	OCH_3	CH_3	H	H	H	10A-I; 16C
A-684	SF_5	H	H	C	C	C	C	H	OCH_2CH_3	CH_3	H	H	H	10A-I; 16C
A-685	SF_5	H	H	C	C	C	C	H	OCH_2-cyclopropyl	H	H	H	H	10A-I; 16C
A-686	SF_5	H	H	C	C	C	C	H	OCH_3	CH_2CH_3	H	H	H	10A-I; 16C
A-687	SF_5	H	H	C	C	C	C	H	SCH_3	H	H	H	H	10A-J
A-688	SF_5	H	H	C	C	C	C	H	SCH_2CH_3	H	H	H	H	10A-J
A-689	SF_5	H	H	C	C	C	C	H	$S(CH_2)_2CH_3$	H	H	H	H	10A-J
A-690	SF_5	H	H	C	C	C	C	H	$SCH(CH_3)_2$	H	H	H	H	10A-J
A-691	SF_5	H	H	C	C	C	C	H	SCH_3	CH_3	H	H	H	10A-J
A-692	SF_5	H	H	C	C	C	C	H	SCH_2CH_3	CH_3	H	H	H	10A-J
A-693	SF_5	H	H	N	C	C	C	-	$CH(CH_3)_2$	CH_3	H	H	H	10F-I; 4A; 2H
A-694	SF_5	H	H	N	C	C	C	-	CH_2CH_3	CH_3	H	H	H	10F-I; 4A; 2H
A-695	SF_5	H	H	N	C	C	C	-	CH_3	CH_3	H	H	H	10F-I; 4A; 2H
A-696	SF_5	H	H	N	C	C	C	-	H	CH_3	CH_2CH_3	H	H	10F-I; 4A; 2H
A-697	SF_5	H	H	C	C	C	C	H	OCH_3	H	CH_3	H	H	3A-B; 10F-I; 16C

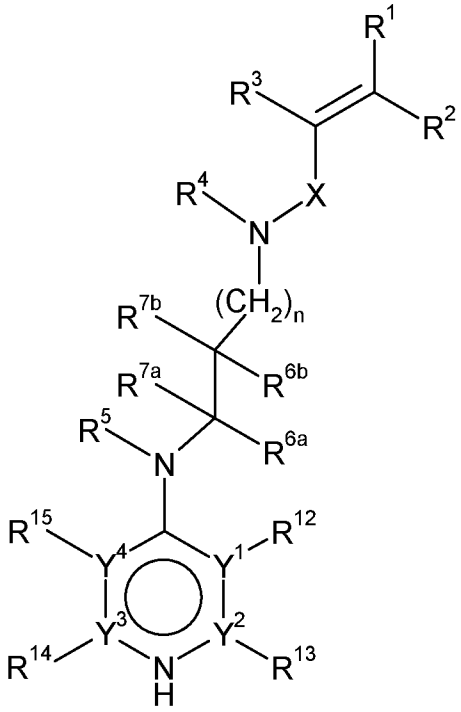
[0405] Further examples of specific compounds of the present invention include each of the compounds of table A above wherein X = SO_2 instead of CO and each of the compounds of table A wherein X = CS instead of CO if not already contained in table A and wherein n is equal to 2 or wherein n is equal to 3.

[0406] Further examples of specific compounds of the present invention include each of the compounds in table A and analogues wherein X = SO_2 or wherein X = CS and wherein n is equal to 2 or wherein n is equal to 3 in form of its pyridine-N-oxide such as the N-oxides shown in the table below:

No	Structure	HPLC	Rt	m/z	MW
Aa-1		2	2.48	264.2	263.3
Aa-2		2	2.40	290.1	289.3
Aa-3		2	2.62	304.2	303.3
Aa-4		2	2.53	278.2	277.4
Aa-5		2	2.57	304.2	303.3

[0407] Table B below provides for each of the exemplified compounds of the formula (B) the structure, the calculated molecular weight (MW) (gram/mol), the observed MS signal (m/z), the HPLC retention time (Rt) in minutes, and the number of the HPLC-method as described in paragraph C above ("Analytics: HPLC-Methods") used for analysis. From compound B-51 until the end of the table the methods by which the compounds are synthesized are identified by referring to the synthetic steps described in the synthesis examples of paragraph B above ("Synthesis Examples"). If a compound contains one or more chiral centers, the mentioning of such compound is indicating the racemate.

[0408] In Table B - in case of a) a ring formation between Y^1 and Y^2 by the substituents R^{12} and R^{13} or b) a ring formation between Y^3 and Y^4 by the substituents R^{14} and R^{15} - in the columns for R^{12} and R^{13} or in the columns for R^{14} and R^{15}, as the case may be, the symbols Y1, Y2, Y3 and Y4 indicate the ring atoms Y^1, Y^2, Y^3 and Y^4 in formula (B) to which the group joining them is bound.



Formula (B)

Table B (X=CO; R^2 = H; R^3 = H; Y^2, Y^3, Y^4 = C)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^{6a}	R^{7a}	R^4	R^{6b}	R^{7b}	R^5	n	HPLC	Rt	m/z	MW
B-1	CF_3	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	0	2	3.91	302.2	301.3
B-2	CF_3	C	H	H	Y3-CH=CH-CH=CH-Y4		$CH(CH_3)_2$	H	H	H	H	H	0	2	3.77	352.3	351.4
B-3	CF_2CHF_2	C	H	H	Y3-CH=CH-CH=CH-Y4		$CH(CH_3)_2$	H	H	H	H	H	0	2	3.79	384.3	383.4
B-4	C_2F_5	C	H	H	Y3-CH=CH-CH=CH-Y4		$CH(CH_3)_2$	H	H	H	H	H	0	2	4.04	402.3	401.4
B-5	CF_3	C	H	OCH_2CH_3	H	H	CH_2CH_3	H	H	H	H	H	0	2	3.61	332.2	331.3
B-6	CF_3	C	H	OCH_2CH_3	H	H	H	H	H	CH_2CH_3	H	H	0	2	3.62	332.2	331.3
B-7	CF_3	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	0	2	3.43	318.2	317.3
B-8	CF_3	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	H	H	0	2	3.45	317.8	317.3
B-9	CF_3	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	CH_3	H	0	2	3.73	331.8	331.3
B-10	CF_3	C	H	OCH_2CH_3	H	H	CO_2CH_3	H	H	H	H	H	0	2	3.33	361.1	360.3
B-11	CF_3	C	H	CH_3	CH_3	H	CH_2CH_3	H	H	H	H	H	0	2	5.04	316.2	315.3
B-12	CF_3	C	H	CH_3	CH_3	H	H	H	H	CH_2CH_3	H	H	0	2	4.59	316.2	315.3
B-13	CF_3	C	H	CH_3	CH_3	H	H	H	H	CH_3	H	H	0	2	3.91	301.8	301.3
B-14	CF_3	C	H	CH_3	CH_3	H	H	H	H	CH_3	CH_3	H	0	2	4.81	315.8	315.3
B-15	CF_3	N	-	H	CH_3	CH_2CH_3	CH_2CH_3	H	H	H	H	H	0	2	3.42	331.2	330.4
B-16	CF_3	N	-	H	CH_3	CH_2CH_3	H	H	H	CH_2CH_3	H	H	0	2	3.38	331.2	330.4
B-17	CF_3	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	0	2	3.27	317.2	316.3
B-18	CF_3	N	-	H	CH_3	CH_2CH_3	H	H	H	CH_3	H	H	0	2	3.22	317.2	316.3
B-19	CF_3	N	-	H	CH_3	CH_2CH_3	H	H	H	CH_3	CH_3	H	0	2	3.65	330.8	330.4
B-20	CF_3	N	-	H	CH_3	CH_2CH_3	CO_2CH_3	H	H	H	H	H	0	2	3.43	362.1	361.3
B-21	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_2CH_3	H	H	H	H	H	0	2	3.99	352.2	351.4
B-22	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	CH_2CH_3	H	H	0	2	4.02	352.2	351.4
B-23	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	0	2	3.80	338.2	337.3
B-24	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	CH_3	H	H	0	2	3.85	338.2	337.3
B-25	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	CH_3	CH_3	H	0	2	4.24	352.2	351.4

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^{6a}	R^{7a}	R^4	R^{6b}	R^{7b}	R^5	n	HPLC	Rt	m/z	MW
B-26	CHF_2	C	H	OCH_2CH_3	H	H	CH_2CH_3	H	H	H	H	H	0	2	3.33	313.8	313.3
B-27	CHF_2	C	H	OCH_2CH_3	H	H	H	H	H	CH_2CH_3	H	H	0	2	3.33	313.8	313.3
B-28	CHF_2	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	0	2	3.13	299.8	299.3
B-29	CHF_2	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	H	H	0	2	3.13	299.8	299.3
B-30	CHF_2	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	CH_3	H	0	2	3.42	313.8	313.3
B-31	CHF_2	C	H	OCH_2CH_3	H	H	CO_2CH_3	H	H	H	H	H	0	2	3.13	343.7	343.3
B-32	CF_2CF_3	C	H	OCH_2CH_3	H	H	CH_2CH_3	H	H	H	H	H	0	2	3.93	381.7	381.3
B-33	CF_2CF_3	C	H	OCH_2CH_3	H	H	H	H	H	CH_2CH_3	H	H	0	2	3.93	381.7	381.3
B-34	CF_2CF_3	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	0	2	3.77	367.7	367.3
B-35	CF_2CF_3	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	H	H	0	2	3.77	367.7	367.3
B-36	CF_2CF_3	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	CH_3	H	0	2	4.03	381.7	381.3
B-37	CF_2CF_3	C	H	OCH_2CH_3	H	H	CO_2CH_3	H	H	H	H	H	0	2	3.75	411.7	411.3
B-38	CF_2CHF_2	C	H	OCH_2CH_3	H	H	CH_2CH_3	H	H	H	H	H	0	2	3.64	363.8	363.4
B-39	CF_2CHF_2	C	H	OCH_2CH_3	H	H	H	H	H	CH_2CH_3	H	H	0	2	3.64	363.8	363.4
B-40	CF_2CHF_2	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	0	2	3.47	349.8	349.3
B-41	CF_2CHF_2	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	H	H	0	2	3.48	349.8	349.3
B-42	CF_2CHF_2	C	H	OCH_2CH_3	H	H	H	H	H	CH_3	CH_3	H	0	2	3.73	363.7	363.4
B-43	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		COOH	H	H	H	H	H	0	2	2.16	368.1	367.3
B-44	CF_3	C	H	H	Y3-CH=CH-O-Y4		=O		H	H	H	H	0	2	2.83	314.1	313.2
B-45	C_2F5	C	H	H	Y3-CH=CH-O-Y4		=O		H	H	H	H	0	2	3.25	364.1	363.2
B-46	CF_2CHF_2	C	H	H	Y3-CH=CH-O-Y4		=O		H	H	H	H	0	2	2.93	346.1	345.3
B-47	CHF_2	C	H	H	Y3-CH=CH-O-Y4		=O		H	H	H	H	0	2	2.49	296.1	295.2
B-48	CF_3	C	H	H	Y3-CH=CH-CH=CH-Y4		H	H	H	phenyl	H	H	0	2	4.01	400.2	399.4
B-49	CF_3	C	H	H	Y3-CH=CH-CH=CH-Y4		H	H	H	benzyl	H	H	0	2	4.19	414.2	413.4
B-50	CH3	C	H	CH3	H	H	H	H	-CH_2-		-CH_2-		1	2	2.96	258.2	257.3

Table B continued (X=CO; R^2 = H; R^3 = H; Y^2, Y^3, Y^4 = C)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-51	CF_3	C	H	OCH_2CH_3	H	H	H	H	CH_3	CH_3	H	H	2A-E; 12A-B;2H
B-52	CF_3	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-53	CF_3	C	H	CH_3	CH_3	H	H	H	CH_3	H	H	H	2A-E; 12A-B;2H
B-54	CF_3	C	H	CH_3	CH_3	H	H	H	CH_3	CH_3	H	H	2A-E; 12A-B;2H
B-55	CF_3	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-56	CF_3	C	H	CH_3	CH_3	H	H	H	CO_2CH_3	H	H	H	2A-E; 12A-B;2H
B-57	CF_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	CH_3	H	H	2A-E; 17A,12B;2H
B-58	CF_3	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	2A-E; 17A,12B;2H
B-59	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	CH_3	H	H	2A-E; 8A,12B;2H
B-60	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-61	CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CO_2CH_3	H	H	H	2A-E; 8A,12B;2H
B-62	CHF_2	C	H	OCH_2CH_3	H	H	H	H	CH_3	CH_3	H	H	10F-I; 12A-B;2H
B-63	CHF_2	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	10F-I; 8A,12B;2H
B-64	CHF_2	C	H	CH_3	CH_3	H	H	H	CH_2CH_3	H	H	H	10F-I; 12A-B;2H
B-65	CHF_2	C	H	CH_3	CH_3	H	H	H	H	H	CH_2CH_3	H	10F-I; 12A-B;2H
B-66	CHF_2	C	H	CH_3	CH_3	H	H	H	CH_3	H	H	H	10F-I; 12A-B;2H
B-67	CHF_2	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	H	10F-I; 8A,12B;2H
B-68	CHF_2	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	CH_3	10F-I; 8A,12B;2H
B-69	CHF_2	C	H	CH_3	CH_3	H	H	H	CH_3	CH_3	H	H	10F-I; 12A-B;2H
B-70	CHF_2	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	10F-I; 8A,12B;2H
B-71	CHF_2	C	H	CH_3	CH_3	H	H	H	CO_2CH_3	H	H	H	10F-I; 12A-B;2H
B-72	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CH_2CH_3	H	H	H	10F-I; 17A,12B;2H
B-73	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_2CH_3	H	10F-I; 17A,12B;2H
B-74	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	H	H	H	10F-I; 17A,12B;2H
B-75	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	H	10F-I; 17A,12B;2H

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-76	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	CH_3	10F-I; 17A,12B;2H
B-77	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	CH_3	H	H	10F-I; 17A,12B;2H
B-78	CHF_2	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	10F-I; 17A,12B;2H
B-79	CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CO_2CH_3	H	H	H	10F-I; 12A-B;2H
B-80	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_2CH_3	H	H	H	10F-I; 8A,12B;2H
B-81	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_2CH_3	H	10F-I; 8A,12B;2H
B-82	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	H	H	H	10F-I; 8A,12B;2H
B-83	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	H	10F-I; 8A,12B;2H
B-84	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	CH_3	10F-I; 8A,12B;2H
B-85	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	CH_3	H	H	10F-I; 8A,12B;2H
B-86	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	10F-I; 8A,12B;2H
B-87	CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CO_2CH_3	H	H	H	10F-I; 8A,12B;2H
B-88	CF_2CF_3	C	H	OCH_2CH_3	H	H	H	H	CH_3	CH_3	H	H	2A-E; 12A-B;2H
B-89	CF_2CF_3	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-90	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	CH_2CH_3	H	H	H	2A-E; 12A-B;2H
B-91	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_2CH_3	H	2A-E; 12A-B;2H
B-92	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	CH_3	H	H	H	2A-E; 12A-B;2H
B-93	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	H	2A-E; 8A, 12B;2H
B-94	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	CH_3	2A-E; 8A,12B;2H
B-95	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	CH_3	CH_3	H	H	2A-E; 12A-B;2H
B-96	CF_2CF_3	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-97	CF_2CF_3	C	H	CH_3	CH_3	H	H	H	CO_2CH_3	H	H	H	2A-E; 12A-B;2H
B-98	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_2CH_3	H	H	H	2A-E; 17A,12B;2H
B-99	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_2CH_3	H	2A-E; 17A,12B;2H
B-100	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	H	H	H	2A-E; 17A,12B;2H

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-101	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	H	2A-E; 17A,12B;2H
B-102	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	CH_3	2A-E; 17A,12B;2H
B-103	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	CH_3	H	H	2A-E; 17A,12B;2H
B-104	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	2A-E; 17A,12B;2H
B-105	CF_2CF_3	N	-	H	CH_3	CH_2CH_3	H	H	CO_2CH_3	H	H	H	2A-E; 12A-B;2H
B-106	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_2CH_3	H	H	H	2A-E; 8A,12B;2H
B-107	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_2CH_3	H	2A-E; 8A,12B;2H
B-108	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	H	H	H	2A-E; 8A,12B;2H
B-109	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	H	2A-E; 8A,12B;2H
B-110	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	CH_3	2A-E; 8A,12B;2H
B-111	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	CH_3	H	H	2A-E; 8A,12B;2H
B-112	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-113	CF_2CF_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CO_2CH_3	H	H	H	2A-E; 8A,12B;2H
B-114	CF_2CHF_2	C	H	OCH_2CH_3	H	H	H	H	CH_3	CH_3	H	H	2A-E; 12A-B;2H
B-115	CF_2CHF_2	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-116	CF_2CHF_2	C	H	OCH_2CH_3	H	H	H	H	CO_2CH_3	H	H	H	2A-E; 12A-B;2H
B-117	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	CH_2CH_3	H	H	H	2A-E; 12A-B;2H
B-118	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	H	H	CH_2CH_3	H	2A-E; 12A-B;2H
B-119	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	CH_3	H	H	H	2A-E; 12A-B;2H
B-120	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	H	2A-E; 8A,12B;2H
B-121	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	CH_3	2A-E; 8A,12B;2H
B-122	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	CH_3	CH_3	H	H	2A-E; 12A-B;2H
B-123	CF_2CHF_2	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-124	CF_2CHF_2	C	H	CH_3	CH_3	H	H	H	CO_2CH_3	H	H	H	2A-E; 12A-B;2H
B-125	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CH_2CH_3	H	H	H	2A-E; 17A,12B;2H

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-126	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_2CH_3	H	2A-E; 17A,12B;2H
B-127	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	H	H	H	2A-E; 17A,12B;2H
B-128	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	H	2A-E; 17A,12B;2H
B-129	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	CH_3	2A-E; 17A,12B;2H
B-130	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	CH_3	H	H	2A-E; 17A,12B;2H
B-131	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	2A-E; 17A,12B;2H
B-132	CF_2CHF_2	N	-	H	CH_3	CH_2CH_3	H	H	CO_2CH_3	H	H	H	2A-E; 12A-B;2H
B-133	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_2CH_3	H	H	H	2A-E; 8A,12B;2H
B-134	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_2CH_3	H	2A-E; 8A,12B;2H
B-135	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	H	H	H	2A-E; 8A,12B;2H
B-136	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	H	2A-E; 8A,12B;2H
B-137	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	CH_3	2A-E; 8A,12B;2H
B-138	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	CH_3	H	H	2A-E; 8A,12B;2H
B-139	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	2A-E; 8A,12B;2H
B-140	CF_2CHF_2	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CO_2CH_3	H	H	H	2A-E; 8A,12B;2H
B-141	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	CH_2CH_3	H	H	H	10F-I; 12A-B;2H
B-142	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	H	H	CH_2CH_3	H	10F-I; 8A,12B;2H
B-143	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	CH_3	H	H	H	10F-I; 12A-B;2H
B-144	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	H	H	CH_3	H	10F-I; 8A,12B;2H
B-145	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	H	H	CH_3	CH_3	10F-I; 12A-B;2H
B-146	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	CH_3	CH_3	H	H	10F-I; 12A-B;2H
B-147	CF_2CH_3	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	10F-I; 8A,12B;2H
B-148	CF_2CH_3	C	H	OCH_2CH_3	H	H	H	H	CO_2CH_3	H	H	H	10F-I; 12A-B;2H
B-149	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	CH_2CH_3	H	H	H	10F-I; 12A-B;2H
B-150	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_2CH_3	H	10F-I; 12A-B;2H

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-151	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	CH_3	H	H	H	10F-I; 12A-B;2H
B-152	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	H	10F-I; 8A,12B;2H
B-153	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	CH_3	10F-I; 8A,12B;2H
B-154	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	CH_3	CH_3	H	H	10F-I; 12A-B;2H
B-155	CF_2CH_3	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	10F-I; 8A,12B;2H
B-156	CF_2CH_3	C	H	CH_3	CH_3	H	H	H	CO_2CH_3	H	H	H	10F-I; 12A-B;2H
B-157	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_2CH_3	H	H	H	10F-I; 17A,12B;2H
B-158	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_2CH_3	H	10F-I; 17A,12B;2H
B-159	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	H	H	H	10F-I; 17A,12B;2H
B-160	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	H	10F-I; 17A,12B;2H
B-161	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	CH_3	10F-I; 17A,12B;2H
B-162	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	CH_3	H	H	10F-I; 17A,12B;2H
B-163	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	10F-I; 17A,12B;2H
B-164	CF_2CH_3	N	-	H	CH_3	CH_2CH_3	H	H	CO_2CH_3	H	H	H	10F-I; 12A-B;2H
B-165	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_2CH_3	H	H	H	10F-I; 8A,12B;2H
B-166	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_2CH_3	H	10F-I; 8A,12B;2H
B-167	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	H	H	H	10F-I; 8A,12B;2H
B-168	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	H	10F-I; 8A,12B;2H
B-169	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	CH_3	10F-I; 8A,12B;2H
B-170	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	CH_3	H	H	10F-I; 8A,12B;2H
B-171	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	10F-I; 8A,12B;2H
B-172	CF_2CH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CO_2CH_3	H	H	H	10F-I; 8A,12B;2H
B-173	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	CH_2CH_3	H	H	H	12A-B;2H
B-174	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	H	H	CH_2CH_3	H	8A,12B;2H
B-175	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	CH_3	H	H	H	12A-B;2H

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-176	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	H	H	CH_3	H	8A,12B;2H
B-177	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	H	H	CH_3	CH_3	12A-B;2H
B-178	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	CH_3	CH_3	H	H	12A-B;2H
B-179	CH_2OCH_3	C	H	OCH_2CH_3	H	H	CH_3	H	H	H	H	H	8A,12B;2H
B-180	CH_2OCH_3	C	H	OCH_2CH_3	H	H	H	H	CO_2CH_3	H	H	H	12A-B;2H
B-181	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	CH_2CH_3	H	H	H	12A-B;2H
B-182	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_2CH_3	H	12A-B;2H
B-183	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	CH_3	H	H	H	12A-B;2H
B-184	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	H	8A,12B;2H
B-185	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	H	H	CH_3	CH_3	8A,12B;2H
B-186	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	CH_3	CH_3	H	H	12A-B;2H
B-187	CH_2OCH_3	C	H	CH_3	CH_3	H	CH_3	H	H	H	H	H	8A,12B;2H
B-188	CH_2OCH_3	C	H	CH_3	CH_3	H	H	H	CO_2CH_3	H	H	H	12A-B;2H
B-189	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_2CH_3	H	H	H	17A,12B;2H
B-190	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_2CH_3	H	17A,12B;2H
B-191	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	H	H	H	17A,12B;2H
B-192	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	H	17A,12B;2H
B-193	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	H	H	CH_3	CH_3	17A,12B;2H
B-194	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	CH_3	CH_3	H	H	17A,12B;2H
B-195	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	CH_3	H	H	H	H	H	17A,12B;2H
B-196	CH_2OCH_3	N	-	H	CH_3	CH_2CH_3	H	H	CO_2CH_3	H	H	H	12A-B;2H
B-197	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_2CH_3	H	H	H	8A,12B;2H
B-198	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_2CH_3	H	8A,12B;2H
B-199	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	H	H	H	8A,12B;2H
B-200	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	H	8A,12B;2H

(continued)

No	R^1	Y^1	R^{12}	R^{13}	R^{14}	R^{15}	R^4	R^5	R^{6a}	R^{7a}	R^{6b}	R^{7b}	Synth. Method
B-201	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	H	H	CH_3	CH_3	8A,12B;2H
B-202	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CH_3	CH_3	H	H	8A,12B;2H
B-203	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		CH_3	H	H	H	H	H	8A,12B;2H
B-204	CH_2OCH_3	C	H	CH_3	Y3-CH=CH-CH=CH-Y4		H	H	CO_2CH_3	H	H	H	8A,12B;2H

[0409] Further examples of specific compounds of the present invention include each of the compounds of table B above wherein X = SO_2 instead of CO and each of the compounds of table B wherein X = CS instead of CO.

[0410] Further examples of specific compounds of the present invention include each of the compounds in table B and analogues wherein X = SO_2 or wherein X = CS, in form of its pyridine-N-oxide.

E Biological examples: Determining activity against *Ascaridia galli* and *Oesophagostomum dentatum.*

[0411] Anthelmintic effects of compounds of this invention were tested *in vitro* using gut-welling larval stages of two parasitic nematode species: *Ascaridia galli* (intestinal roundworm of chicken), larval stage 3 ("L3"); and *Oesophagostumum dentatum* (nodular worm of swine), larval stages 3 and 4 (respectively "L3" and "L4"). When conducting these experiments, DMSO-solutions of various concentrations of compounds of this invention were prepared and incubated in 96-well microtiter plates. The parasites were then distributed at 20 larvae per well. The anthelmintic effects were classified by microscopic examination. The microscopic examination included assessing mortality, damage, motility, progression of development, and neutral red uptake by the larvae in comparison to a DMSO-control. The anthelmintic effects were defined by the minimum effective concentration ("MEC"), which is the concentration by which at least one of the larvae shows mortality, damage, change in motility, change in progression of development, or no neutral red uptake. The following compounds showed at least some activity against one or more of the nematodes at an MEC of 50μM or less: A-1 - A-5, A-7-A-9, A-11 - A-14, A-17, A-19 - A-22, A-25 - A-27, A-29 - A-31, A-33 - A-35, A-41 - A-44, A-46 - A-52, A-55 - A-56, A-60 - A-75, A-78 - A-81, A-83, A-86 - A-89, A-91 - A-92, A-95-A-100, A-102 - A-103, A-105 - A-107, A-111, A-113 - A-119, A-121 - A-123, A-125, A-129 - A153, A-156 - A-159, A-163, A-166 - A-168, A-170 - A-180, A-182 - A-187, A-189 - A-190, A-192 - A-206, A-210 - A-226, A-229, A-231 - A-234, A-236 - A-248, A-251 - A-255, A-257 - A-267, A-269 - A-276, A-279 - A-290, A-292 - A-296, A-298 - A-303, A-305 - A-329, A-331, A-333 - A-352, A-354 - A-393, A-395 - A-404, A-406 - A-413, A-415 - A-421, A-428 - A-429, A-431 - A-432, A-434 - A-437, A-440 - A-446, Aa2, Aa3, Aa5, B-1 - B-9, B-11 - B-19, B-21 - B-49.

F Formulation examples

Formulation A: 5% Suspension:

[0412] 4.5 g of compound A (a compound according to this invention, but which may be any compound in line with the invention) was dissolved in DMSO, the resulting solution was mixed with a 0.1 % solution of methyl cellulose in isotonic NaCl to give a homogeneous suspension of compound A (5 % by weight).

Formulation B: 0.5 % Suspension:

[0413] 18.6 mg of compound B (a compound according to this invention, but which may be any compound in line with the invention) was dissolved in DMSO, the resulting solutioin was mixed with a 0.1 % solution of methyl cellulose in isotonic NaCl to give a homogeneous suspension of compound B (0.5% by weight).

Formulation C: 5% Solution:

[0414] 0.25 g of Compound C (a compound according to this invention, but which may be any compound in line with the invention) was dissolved in 1-methyl-2-pyrrolidinone (3.25 ml). 1,2-Propanediol (0.75 ml) and water was added until a total volume of 5.0 ml was reached to give a homogeneous solution with a content by weight of 5 % compound C.

[0415] The formulations can be used i.a. for parenteral and oral administration to animals, e.g. sheep or cattle.

DEFINITIONS

[0416] The term "acyl" (alone or in combination with (an)other term(s)) means a the radical derived from an oxo acid, preferably from a carboxylic acid, by removal of the OH-group. Preferred acyl groups have the formula R-CO, wherein R is H or an aromatic or heteroaromatic ring, preferably of 4 to 10 ring atoms, or an aliphatic hydrocarbon radical, preferably of 1 to 10 carbon atoms, more preferred are unsubstituted or substituted alkyl of 1 to 6 carbon atoms.

[0417] The term "alkyl" (alone or in combination with (an)other term(s)) means a straight-chain or branched-chain saturated hydrocarbyl substituent (*i.e.*, a substituent containing only carbon and hydrogen) which unless otherwise specified typically contains from 1 to 6 carbon atoms, and even more typically from 1 to about 4 carbon atoms. Examples of such substituents include methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, pentyl, *iso*-pentyl, hexyl, and octyl. For instance the term "C_1-C_6-alkyl" includes but is not limited to methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, *n*-pentyl, *iso*-pentyl, *neo*-pentyl, *n*-hexyl, *iso*-hexyl.

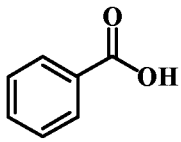
[0418] The term "alkenyl" (alone or in combination with (an)other term(s)) means a straight- or branched-chain hydrocarbyl substituent containing one or more double bonds and unless otherwise specified typically contains from 2 to 6 carbon atoms, even more typically from 2 to 4 carbon atoms. Examples of such substituents include ethenyl (vinyl); 2-propenyl; 3-propenyl; 1,4-pentadienyl; 1,4-butadienyl; 1-butenyl; 2-butenyl; 3-butenyl; and 2-hexenyl.

[0419] The term "alkynyl" (alone or in combination with (an)other term(s)) means a straight- or branched-chain hydrocarbyl substituent containing one or more triple bonds and unless otherwise specified typically from 2 to 6 atoms, even more typically from 2 to 4 carbon atoms. Examples of such substituents include ethynyl, 2-propynyl, 3-propynyl, 1-butynyl, 2-butynyl, 3-butynyl, and 2-hexynyl.

[0420] The term "cycloalkyl" (alone or in combination with (an)other term(s)) means a cyclic saturated hydrocarbyl substituent (*i.e.,* a substituent containing only carbon and hydrogen) which unless otherwise specified typically contains from 3 to 8 carbon atoms. The cycle or ring in the "cycloalkyl" substituent may be formed by all carbon atoms of the substituent, or may be formed by some, but not all of the carbon atoms of the substituent. In the latter case, the substituent may be connected at a carbon atom that is part of a cycle or that is not part of a cycle. Examples of such substituents include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, 2-methylcyclopropyl, cyclopropylmethyl, cyclohexylmethyl.

[0421] The term "halogen" (alone or in combination with (an)other term(s)) means a fluorine radical ("fluoro", which may be depicted as F), chlorine radical ("chloro", which may be depicted as Cl), bromine radical ("bromo", which may be depicted as Br), or iodine radical ("iodo", which may be depicted as I). Typically, fluoro or chloro is preferred.

[0422] When a chemical formula is used to describe a mono-valent substituent, the dash on the left side of the formula indicates the portion of the substituent that has the free valence. To illustrate, benzene substituted with -C(O)-OH has the following structure:

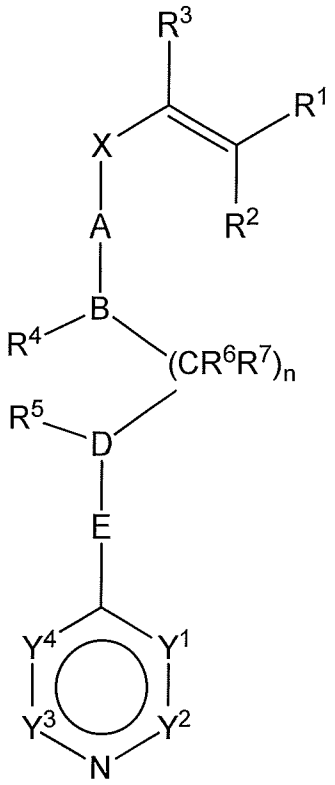


[0423] When a chemical formula is used to describe a di-valent (or "linking") component between two other components of a depicted chemical structure (the right and left components), the leftmost dash of the linking component indicates the portion of the linking component that is bound to the left component in the depicted structure. The rightmost dash, on the other hand, indicates the portion of the linking component that is bound to the right component in the depicted structure.

[0424] The term "pharmaceutically acceptable" is used adjectivally to mean that the modified noun is appropriate for use in a pharmaceutical product. When it is used, for example, to describe a salt, solvate, N-oxide, active compound or excipient, it characterizes the salt, solvate, N-oxide, active compound or excipient as being compatible with the other ingredients of the composition, and not deleterious to the intended recipient animal, e.g. to the extent that the benefit(s) outweigh(s) the deleterious effect(s).

Claims

1. A compound of the formula (I) and pharmaceutically acceptable salts, solvates, N-oxides



Formula (I)

, wherein

R^1 is halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, SF_5, C_1-C_6-alkyl sulfonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,

R^2 is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6- alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms,

R^3 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^4 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^5 is hydrogen, C_1-C_6-alkyl, cycloalkyl, acyl, cycloalkyloxycarbony or C_1-C_6-alkyloxycarbonyl,

R^6 is hydrogen, C_1-C_6-alkyl, cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy, cycloalkyloxy or C_1-C_6-alkyloxy,

R^7 is hydrogen, C_1-C_6-alkyl or cycloalkyl,

or R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cycloalkyl radicals,

n is an integer from 1 to 3,

X is a carbonyl, thiocarbonyl or sulfonyl group, preferably a carbonyl group,

A is a bond or NR^8, wherein R^8 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

E is a bond or NR^9, wherein R^9 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

B is N or CR^{10}, wherein R^{10} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

D is N or CR^{11}, wherein R^{11} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl,

Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl, Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system, and wherein at least one of B and D is a nitrogen atom.

2. A compound according to claim 1, wherein

R^1 is halogen, C_1-C_6-alkyl, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, C_1-C_6-alkyl carbonyl, C_2-C_6-alkenyl carbonyl, SF_5, C_1-C_6-alkyl sulfonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms
R^2 is hydrogen,
R^3 is hydrogen,
R^4 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,
R^5 is hydrogen, C_1-C_6-alkyl, acyl or C_1-C_6-alkyloxycarbonyl
$(CR^6R^7)_n$ is a C_1-C_3-alkylene group, preferably an ethylene group, which is optionally substituted by one or more C_1-C_6-alkyl radicals,
A is a bond or NR^8, wherein R^8 is H or C_1-C_6-alkyl,
E is a bond or NR^9, wherein R^9 is H or C_1-C_6-alkyl,
B is N or CR^{10}, wherein R^{10} is H or C_1-C_6-alkyl,
D is N or CR^{11}, wherein R^{11} is H or C_1-C_6-alkyl,
X is a carbonyl, thiocarbonyl or sulfonyl group, preferably a carbonyl group,
Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,
Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholi-

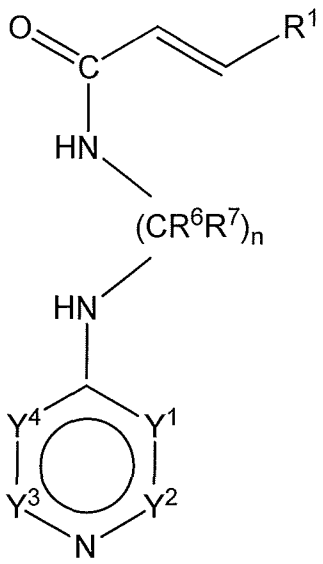
nyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, Cycloalkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, Cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(Cycloalkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-haloalkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system, and wherein at least one of B and D is a nitrogen atom.

3. A compound of the formula (II) according to claim 1 or 2,



Formula (II)

wherein

R^1 is C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, or C_1-C_6-alkylthio C_1-C_6-alkyl, wherein each of the carbon-containing radicals is unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms,

R^6 is hydrogen, C_1-C_6-alkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxy or C_1-C_6-alkyloxy, preferably R^6 is hydrogen,

C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), phenyl, phenyl C_1-C_6-alkyl, more preferably R^6 is hydrogen or C_1-C_6-alkyl, even more preferably hydrogen,

R^7 is hydrogen or C_1C_6-alkyl, preferably hydrogen,

n is 2 or 3,

Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, Cycloalkyl, Cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl,

Y^2 is C or N, preferably C, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, Cycloalkyl, Cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^3 is C or N, preferably C, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1C_6-haloalkoxy, Cycloalkyl, Cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl,

Y^4 is C or N, preferably C, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a 5- or 6-membered ring system.

4. A compound according to claim 3, wherein

R^1 is C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, or C_1-C_6-alkylthio C_1-C_6-alkyl, wherein each of the carbon-containing radicals is unsubstituted or substituted by one or more halogen atoms, preferably by one or more fluorine atoms, e.g. by 1 to 10, preferably by 1 to 5, fluorine atoms,

Y^1 is C or N, wherein C is substituted by R^{12} which is H, or C_1-C_6-alkyl,

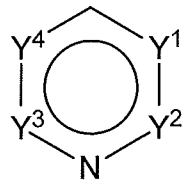
Y^2 is C, wherein C is substituted by R^{13} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkyl carbonyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-alkylthio

Y^3 is C, wherein C is substituted by R^{14} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkyl carbonyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-alkylthio

Y^4 is C, wherein C is substituted by R^{15} is H, C_1-C_6-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio

or Y^1 and Y^2 or Y^3 and Y^4 are joined together to form a 5- or 6-membered ring system.

5. A compound according to any of claims 1 to 4, wherein the group of the formula (A)



Formula (A)

represents a pyridine, pyrimidine, quinoline, quinazoline, thienopyrimidine, thienopyridine, triazolopyrimidine, pyridopyridine, pyrrolopyridine, pyrazolopyrimidine, pyrazolopyridine, furopyridine, 2,3-dihydrofuropyridine, 2,3-dihydro-1,4-dioxinopyridine, furopyrimidine, pyridazine or cinnoline group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, Cycloalkyl, Cy-

cloalkyloxy, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, halogen, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl , thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, dioxolane, dioxane, or dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl.

6. A compound according to any of claims 1 to 5, wherein

R^2 is hydrogen,
R^3 is hydrogen,
R^4 is hydrogen or C_1-C_6-alkyl,
R^5 is hydrogen or C_1-C_6-alkyl,
R^6 is hydrogen or C_1-C_6-alkyl,
R^7 is hydrogen,
X is a carbonyl group,
n is 2,

the group of formula (A) represents a pyridine, pyrimidine or quinoline group, preferably a pyridine or pyrimidine group, more preferably a pyridine group, wherein each group is optionally substituted by one or more radicals, preferably by one or two radicals, selected from the group of C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, Cycloalkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thio, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, dioxolane, dioxane, or dioxepane, wherein each ring is unsubstituted or substituted by C_1-C_6-alkyl, and one of A and B and one of D and E contains a nitrogen atom.

7. A pharmaceutical composition, wherein the composition comprises:

a) one or more compounds as defined in one or more of claims 1 to 6; and
b) one or more pharmaceutically acceptable excipients and/or one or more pharmaceutically acceptable active ingredients which differ in structure from component a).

8. A compound of formula (1-IV), wherein Y^1, Y^2, Y^3 and Y^4 are C, substituted by R^{12}, R^{13}, R^{14} and R^{15} respectively and which are selected from the group of halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl and phenyl, and wherein at least one of R^{12} and R^{13} is C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, and B is N, A is N or a bond, n is 2, R^6 and R^7 are H, and R^4 and R^5 are defined as in any of claims 1 to 6.

9. A compound of formula (3-IV), wherein Y^1, Y^2, Y^3 and Y^4 are C, substituted by R^{12}, R^{13} R^{14} and R^{15} respectively and which are selected from the group of halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl or phenyl, and wherein at least one of R^{12} and R^{13} is C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, and B is N, A is N or a bond, n is 2 or 3, R^6 and R^7 are H, and R^4 and R^5 are defined as in any of claims 1 to 6.

10. A compound of formula (**4-II**), wherein Y^1, Y^2, Y^3 and Y^4 are C, substituted by R^{12}, R^{13}, R^{14} and R^{15} respectively and which are selected from the group of halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl or phenyl, and wherein at least one of $R^{12}$and R^{13} are C_1-C_6-alkoxy or C_1-C_6-haloalkoxy, and B is N, A is N or a bond, n is 2 or 3, R^6 and R^7 are H, and R^4 and R^5 are defined as in any of claims 1 to 6.

11. A compound as defined in any of claims 1 to 6, or a pharmaceutical composition as defined in claim 7, for use as a medicament.

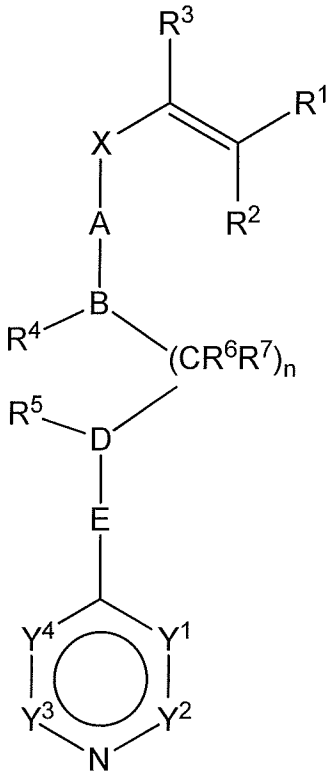
12. A compound as defined in any of claims 1 to 6, or a pharmaceutical composition as defined in claim 7, for use in the treatment of parasite infections.

13. Use of a compound, as defined in any of claims 1 to 6, or a pharmaceutical composition as defined in claim 7, in the manufacture of a medicament for the treatment of parasite infections of non-human animals.

14. A kit, wherein the kit comprises:

a) one or more compounds as defined in one or more of claims 1 to 6, and
b) one or more other components selected from the group consisting of an excipient, an active ingredient, an apparatus for combining the compound of component a) with an excipient and/or active ingredient, an apparatus for administering the compound of component a) to an animal, and a diagnostic tool.

15. A compound of the formula (I a) and pharmaceutically acceptable solvates, N-oxides and salts thereof,



Formula (I a)

, wherein

R^1 is hydrogen, halogen, C_1-C_6-alkyl, cycloalkyl, C_1-C_6-alkyloxy, cycloalkyloxy, C_1-C_6-alkylthio, cycloalkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, cycloalkyloxy C_1-C_6-alkyl, C_1-C_6-alkyloxy cycloalkyl, cycloalkyloxy cycloalkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, cycloalkylthio C_1-C_6-alkyl, C_1-C_6-alkylthio cycloalkyl, cycloalkylthio cycloalkyl, amino, C_1-C_6-alkylamino, cycloalkylamino, di-(C_1-C_6-alkyl)amino, di-(cycloalkyl)amino, C_1-C_6-alkyl-cycloalkylamino, C_1-C_6-alkylamino-C_1-C_6-alkyl, cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-alkylamino-cycloalkyl, cycloalkylamino-cycloalkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-cycloalkyl, di-(cycloalkyl)amino-C_1-C_6-alkyl, di-(cycloalkyl)amino-cycloalkyl, C_1-C_6-alkyl-cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-alkyl-cycloalkylamino-cycloalkyl, C_1-C_6-alkyl carbonyl, cycloalkylcarbonyl, C_1-C_6-alkyloxy carbonyl, cycloalkoxy carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms, or R^1 is phenyl, furanyl, imidazolinyl, or thiophenyl, wherein each of the rings optionally is substituted by one or more radicals from the group of C_1-C_6-alkyl, cycloalkyl and halogen, preferably fluorine,
R^2 is hydrogen, halogen, C_1-C_6-alkyl, cycloalkyl, C_1-C_6-alkyloxy, cycloalkyloxy, C_1-C_6-alkylthio, cycloalkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, cycloalkyloxy C_1-C_6-alkyl, C_1-C_6-alkyloxy cycloalkyl, cycloalkyloxy cycloalkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, cycloalkylthio C_1-C_6-alkyl, C_1-C_6-alkylthio cycloalkyl, cy-

cloalkylthio cycloalkyl, amino, C_1-C_6-alkylamino, cycloalkylamino, di-(C_1-C_6-alkyl)amino, di-(cycloalkyl)amino, C_1-C_6-alkyl-cycloalkylamino, C_1-C_6-alkylamino-C_1-C_6-alkyl, cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-alkylamino-cycloalkyl, cycloalkylamino-cycloalkyl, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, di-(C_1-C_6-alkyl)amino-cycloalkyl, di-(cycloalkyl)amino-C_1-C_6-alkyl, di-(cycloalkyl)amino-cycloalkyl, C_1-C_6-alkyl-cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-alkyl-cycloalkylamino-cycloalkyl, C_1-C_6-alkyl carbonyl, cycloalkylcarbonyl, C_1-C_6-alkyloxy carbonyl, cycloalkoxy carbonyl, C_2-C_6-alkenyl carbonyl, wherein each of the carbon-containing radicals optionally is substituted by one or more halogen atoms, preferably fluorine atoms, or R^2 is phenyl, furanyl, imidazolinyl, or thiophenyl, wherein each of the rings optionally is substituted by one or more radicals from the group of C_1-C_6-alkyl, cycloalkyl and halogen, preferably fluorine, preferably R^2 is hydrogen,

R^3 is hydrogen, C_1-C_6-alkyl or cycloalkyl, preferably hydrogen,

R^4 is hydrogen, C_1-C_6-alkyl or cycloalkyl preferably hydrogen,

R^5 is hydrogen, C_1-C_6-alkyl, cycloalkyl or acyl,

R^6 is hydrogen, C_1-C_6-alkyl, cycloalkyl, hydroxy, C_1-C_6-alkyloxy, phenyl C_1-C_6-alkyloxy, hydroxy C_1-C_6-alkyl, C_1-C_6-alkyloxy C_1-C_6-alkyl, phenyl C_1-C_6-alkyloxy C_1-C_6-alkyl, thiol C_1-C_6-alkyl, C_1-C_6-alkylthio C_1-C_6-alkyl, phenyl C_1-C_6-alkylthio C_1-C_6-alkyl, hydroxycarbonyl, hydroxycarbonyl C_1-C_6-alkyl, C_1-C_6-alkyloxycarbonyl, C_1-C_6-alkyloxycarbonyl C_1-C_6-alkyl, aminocarbonyl, aminocarbonyl C_1-C_6-alkyl, C_1-C_6-alkylaminocarbonyl, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di(C_1-C_6-alkyl)aminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylamino C_1-C_6-alkyl, di(C_1-C_6-alkyl)amino C_1-C_6-alkyl, phenyl, phenyl C_1-C_6-alkyl, wherein each phenyl group is optionally substituted by hydroxyl, C_1-C_6-alkyloxy or cycloalkyloxy,

R^7 is hydrogen, C_1-C_6-alkyl or cycloalkyl,

or R^6 and R^7 together represent an oxo-group or a thioxo-group, or R^6 is joined together with R^8 to form a C_1-C_3-alkylene group and R^7 is joined together with R^9 to form a C_1-C_3-alkylene group, wherein one or both of said C_1-C_3-alkylene groups are optionally substituted by one or more C_1-C_6-alkyl or cycloalkyl radicals,

n is an integer from 1 to 3,

X is a carbonyl or sulfonyl group, preferably a carbonyl group,

A is a bond or NR^8, wherein R^8 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

E is a bond or NR^9, wherein R^9 is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

B is N or CR^{10}, wherein R^{10} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

D is N or CR^{11}, wherein R^{11} is hydrogen or C_1-C_6-alkyl, preferably hydrogen,

Y^1 is C or N, wherein C is substituted by R^{12} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

Y^2 is C or N, wherein C is substituted by R^{13} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkylcarbonylamino, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

Y^3 is C or N, wherein C is substituted by R^{14} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

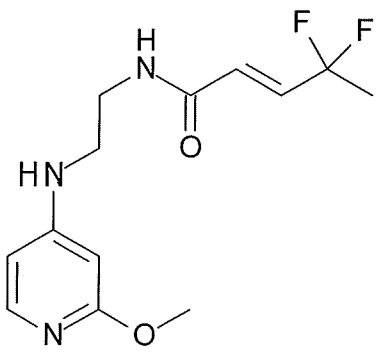
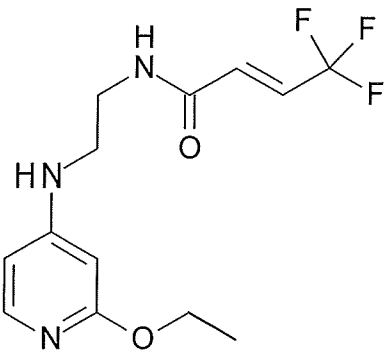
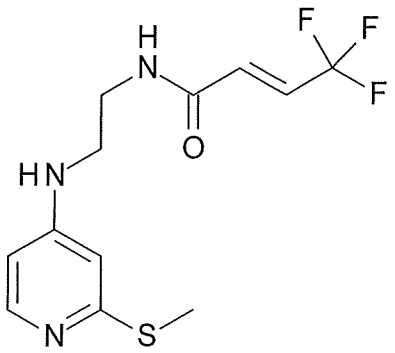
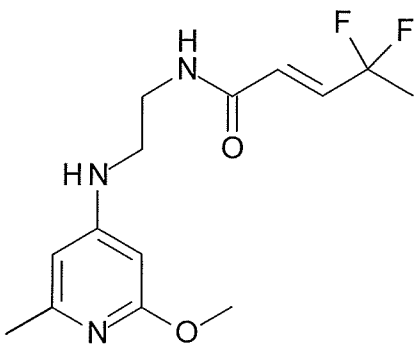
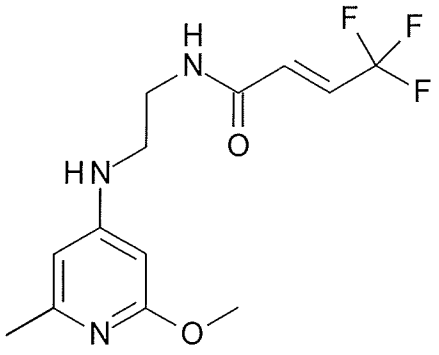
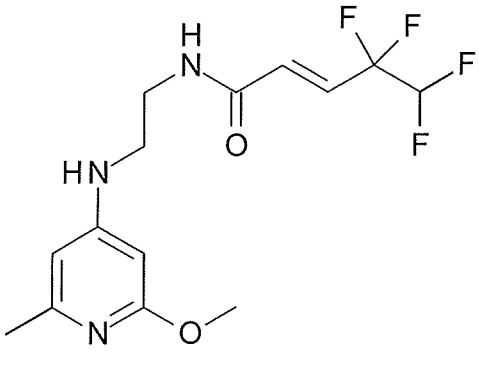
Y^4 is C or N, wherein C is substituted by R^{15} which is hydrogen, halogen, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-alkoxy, C_1-C_6-haloalkoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyl, N-piperidinyl, N-morpholinyl, C_1-C_6-alkylthio, C_1-C_6-alkyl carbonyl, C_1-C_6-haloalkyl carbonyl, C_1-C_6-alkylcarbonylamino, aminocarbonyl, C_1-C_6-alkylaminocarbonyl, di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-alkoxycarbonyl, cycloalkyl, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, phenyl, dioxolane such as 1,3-dioxolane, dioxane such as 1,3-dioxane, or dioxepane such as 1,3-dioxepane, each said ring being unsubstituted or substituted by C_1-C_6-alkyl or cycloalkyl,

or Y^1 and Y^2 and/or Y^3 and Y^4 are joined together to form a ring system,
and wherein at least one of B and D is a nitrogen atom, for use in treating a helminth infection.

16. An anthelmintic composition, wherein the composition comprises:

a) one or more compounds as defined in claim 15; and
b) one or more pharmaceutically acceptable excipients and/or one or more pharmaceutically acceptable active ingredients which differ from the said one or more compounds as defined in claim 15.

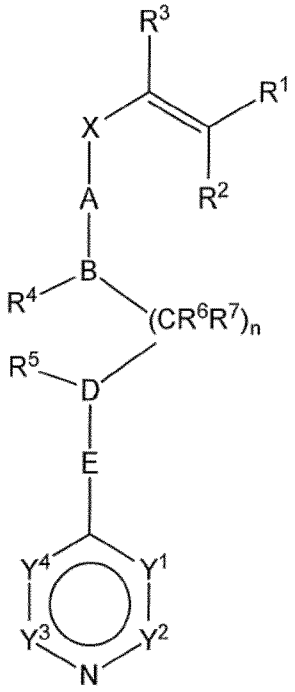
17. A compound according to claim 1, wherein the compound has a structure chosen from the group consisting of

, or

Patentansprüche

1. Verbindung der Formel (I) und pharmazeutisch verträgliche Salze, Solvate und N-Oxide,



Formel (I)

wobei

R^1 Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkyloxy, C_1-C_6-Alkylthio, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, C_1-C_6-Alkylcarbonyl, C_2-C_6-Alkenylcarbonyl, SF_5, C_1-C_6-Alkylsulfonyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste gegebenenfalls mit einem oder mehreren Halogenatomen, vorzugsweise Fluoratomen, substituiert ist,

R^2 Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkyloxy, C_1-C_6-Alkylthio, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, C_1-C_6-Alkylcarbonyl, C_2-C_6-Alkenylcarbonyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste gegebenenfalls mit einem oder mehreren Halogenatomen, vorzugsweise Fluoratomen, substituiert ist,

R^3 Wasserstoff, C_1-C_6-Alkyl oder Cycloalkyl ist, vorzugsweise Wasserstoff,

R^4 Wasserstoff, C_1-C_6-Alkyl oder Cycloalkyl ist, vorzugsweise Wasserstoff,

R^5 Wasserstoff, C_1-C_6-Alkyl, Cycloalkyl, Acyl, Cycloalkyloxycarbonyl oder C_1-C_6-Alkyloxycarbonyl ist,

R^6 Wasserstoff, C_1-C_6-Alkyl, Cycloalkyl, Hydroxy, C_1-C_6-Alkyloxy, Phenyl-C_1-C_6-alkyloxy, Hydroxy-C_1-C_6-alkyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, Phenyl-C_1-C_6-alkyloxy-C_1-C_6-alkyl, Thiol-C_1-C_6-alkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, Phenyl-C_1-C_6-alkylthio-C_1-C_6-alkyl, Hydroxycarbonyl, Hydroxycarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkyloxycarbonyl, C_1-C_6-Alkyloxycarbonyl-C_1-C_6-alkyl, Aminocarbonyl, Aminocarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkylaminocarbonyl, C_1-C_6-Alkylaminocarbonyl-(C_1-C_6-alkyl), Di(C_1-C_6-alkyl)aminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl-(C_1-C_6-alkyl), C_1-C_6-Alkylamino-C_1-C_6-alkyl, Di(C_1-C_6-alkyl) amino-C_1-C_6-alkyl, Phenyl, Phenyl-C_1-C_6-alkyl ist, wobei jede Phenylgruppe gegebenenfalls mit Hydroxy, Cycloalkyloxy oder C_1-C_6-Alkyloxy substituiert ist,

R^7 Wasserstoff, C_1-C_6-Alkyl oder Cycloalkyl ist,

oder R^6 mit R^8 verbunden ist, um eine C_1-C_3-Alkylengruppe zu bilden, und R^7 mit R^9 verbunden ist, um eine C_1-C_3-Alkylengruppe zu bilden, wobei eine oder beide der C_1-C_3-Alkylengruppen gegebenenfalls mit einem oder mehreren C_1-C_6-Alkyl- oder Cycloalkylresten substituiert sind,

n eine ganze Zahl von 1 bis 3 ist,

X eine Carbonyl-, Thiocarbonyl- oder Sulfonylgruppe ist, vorzugsweise eine Carbonylgruppe,

A eine Bindung oder NR^8 ist, wobei R^8 Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,

E eine Bindung oder NR^9 ist, wobei R^9 Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,

B N oder CR^{10} ist, wobei R^{10} Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,

D N oder CR^{11} ist, wobei R^{11} Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,

Y^1 C oder N ist, wobei C mit R^{12} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl) amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-

Morpholinyl, C_1-C_6-Alkylthio, Cycloalkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Phenyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

Y^2 C oder N ist, wobei C mit R^{13} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, Cycloalkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkylcarbonylamino, C_1-C_6-Alkoxycarbonyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

Y^3 C oder N ist, wobei C mit R^{14} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, Cycloalkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

Y^4 C oder N ist, wobei C mit R^{15} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Phenyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

oder Y^1 und Y^2 und/oder Y^3 und Y^4 miteinander verbunden sind, um ein Ringsystem zu bilden,
und wobei wenigstens eines von B und D ein Stickstoffatom ist.

2. Verbindung gemäß Anspruch 1, wobei

R^1 Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkyloxy, C_1-C_6-Alkylthio, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, C_1-C_6-Alkylcarbonyl, C_2-C_6-Alkenylcarbonyl, SF_5, C_1-C_6-Alkylsulfonyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste gegebenenfalls mit einem oder mehreren Halogenatomen, vorzugsweise Fluoratomen, substituiert ist,
R^2 Wasserstoff ist,
R^3 Wasserstoff ist,
R^4 Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,
R^5 Wasserstoff, C_1-C_6-Alkyl, Acyl oder C_1-C_6-Alkyloxycarbonyl ist,
$(CR^6R^7)_n$ eine C_1-C_3-Alkylengruppe ist, vorzugsweise eine Ethylengruppe, die gegebenenfalls mit einem oder mehreren C_1-C_6-Alkylresten substituiert ist,
A eine Bindung oder NR^8 ist, wobei R^8 H oder C_1-C_6-Alkyl ist,
E eine Bindung oder NR^9 ist, wobei R^9 H oder C_1-C_6-Alkyl ist,
B N oder CR^{10} ist, wobei R^{10} H oder C_1-C_6-Alkyl ist,
D N oder CR^{11} ist, wobei R^{11} H oder C_1-C_6-Alkyl ist,
X eine Carbonyl-, Thiocarbonyl- oder Sulfonylgruppe ist, vorzugsweise eine Carbonylgruppe,
Y^1 C oder N ist, wobei C mit R^{12} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl) amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, Cycloalkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Phenyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,
Y^2 C oder N ist, wobei C mit R^{13} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl) amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-

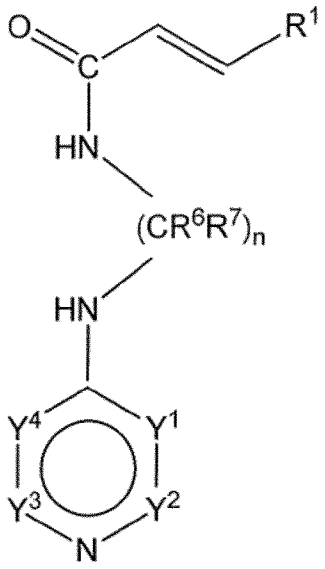
Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, Cycloalkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkylcarbonylamino, C_1-C_6-Alkoxycarbonyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

Y^3 C oder N ist, wobei C mit R^{14} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, Cycloalkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

Y^4 C oder N ist, wobei C mit R^{15} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Alkenyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, C_1-C_6-Halogenalkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Phenyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,

oder Y^1 und Y^2 und/oder Y^3 und Y^4 miteinander verbunden sind, um ein Ringsystem zu bilden,
und wobei wenigstens eines von B und D ein Stickstoffatom ist.

3. Verbindung der Formel (II) gemäß Anspruch 1 oder 2,



Formel (II)

wobei

R^1 C_1-C_6-Alkyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl oder C_1-C_6-Alkylthio-C_1-C_6-alkyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste unsubstituiert oder mit einem oder mehreren Halogenatomen, vorzugsweise mit einem oder mehreren Fluoratomen, substituiert ist, beispielsweise mit 1 bis 10, vorzugsweise mit 1 bis 5, Fluoratomen,
R^6 Wasserstoff, C_1-C_6-Alkyl, Hydroxy, C_1-C_6-Alkyloxy, Phenyl-C_1-C_6-alkyloxy, Hydroxy-C_1-C_6-alkyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, Phenyl-C_1-C_6-alkyloxy-C_1-C_6-alkyl, Thiol-C_1-C_6-alkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, Phenyl-C_1-C_6-alkylthio-C_1-C_6-alkyl, Hydroxycarbonyl, Hydroxycarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkyloxycarbonyl, C_1-C_6-Alkyloxycarbonyl-C_1-C_6-alkyl, Aminocarbonyl, Aminocarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkylaminocarbonyl, C_1-C_6-Alkylaminocarbonyl-(C_1-C_6-alkyl), Di(C_1-C_6-alkyl)aminocarbonyl, Di(C_1-C_6-alkyl) aminocarbo-

nyl-(C_1-C_6-alkyl), C_1-C_6-Alkylamino-C_1-C_6-alkyl, Di(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, Phenyl, Phenyl-C_1-C_6-alkyl ist, wobei jede Phenylgruppe gegebenenfalls mit Hydroxy oder C_1-C_6-Alkyloxy substituiert ist, wobei R^6 vorzugsweise Wasserstoff, C_1-C_6-Alkyl, Hydroxycarbonyl, Hydroxycarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkyloxycarbonyl, C_1-C_6-Alkyloxycarbonyl-C_1-C_6-alkyl, Aminocarbonyl, Aminocarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkylaminocarbonyl, C_1-C_6-Alkylaminocarbonyl-(C_1-C_6-alkyl), Di(C_1-C_6-alkyl)aminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl-(C_1-C_6-alkyl), Phenyl, Phenyl-C_1-C_6-alkyl ist, wobei R^6 bevorzugter Wasserstoff oder C_1-C_6-Alkyl ist, noch bevorzugter Wasserstoff,
R^7 Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,
n 2 oder 3 ist,
Y^1 C oder N ist, wobei C mit R^{12} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Cycloalkyl, Cycloalkyloxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl ist,
Y^2 C oder N ist, vorzugsweise C, wobei C mit R^{13} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Cycloalkyl, Cycloalkyloxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,
Y^3 C oder N ist, vorzugsweise C, wobei C mit R^{14} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Cycloalkyl, Cycloalkyloxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist,
Y^4 C oder N ist, vorzugsweise C, wobei C mit R^{15} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl ist,

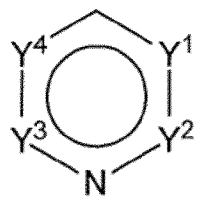
oder Y^1 und Y^2 und/oder Y^3 und Y^4 miteinander verbunden sind, um ein 5- oder 6-gliedriges Ringsystem zu bilden.

4. Verbindung gemäß Anspruch 3, wobei

R^1 C_1-C_6-Alkyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl oder C_1-C_6-Alkylthio-C_1-C_6-alkyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste unsubstituiert oder mit einem oder mehreren Halogenatomen substituiert ist, vorzugsweise mit einem oder mehreren Fluoratomen, beispielsweise mit 1 bis 10, vorzugsweise mit 1 bis 5, Fluoratomen,
Y^1 C oder N ist, wobei C mit R^{12} substituiert ist, das H oder C_1-C_6-Alkyl ist,
Y^2 C ist, wobei C mit R^{13} substituiert ist, das H, C_1-C_6-Alkyl, C_1-C_6-Alkoxy, C_1-C_6-Alkylcarbonyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Alkylthio ist,
Y^3 C ist, wobei C mit R^{14} substituiert ist, das H, C_1-C_6-Alkyl, C_1-C_6-Alkoxy, C_1-C_6-Alkylcarbonyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Alkylthio ist,
Y^4 C ist, wobei C mit R^{15} substituiert ist, das H, C_1-C_6-Alkyl, C_1-C_6-Alkoxy, C_1-C_6-Alkylthio ist,

oder Y^1 und Y^2 oder Y^3 und Y^4 miteinander verbunden sind, um ein 5- oder 6-gliedriges Ringsystem zu bilden.

5. Verbindung gemäß einem der Ansprüche 1 bis 4, wobei die Gruppe der Formel (A)



Formel (A)

eine Pyridin-, Pyrimidin-, Chinolin-, Chinazolin-, Thienopyrimidin-, Thienopyridin-, Triazolopyrimidin-, Pyridopyridin-, Pyrrolopyridin-, Pyrazolopyrimidin-, Pyrazolopyridin-, Furopyridin-, 2,3-Dihydrofuropyridin-, 2,3-Dihydro-1,4-dioxinopyridin-, Furopyrimidin-, Pyridazin- oder Cinnolingruppe darstellt, wobei jede Gruppe gegebenenfalls mit einem oder mehreren Resten substituiert ist, vorzugsweise mit einem oder zwei Resten, ausgewählt aus der Gruppe von C_1-C_6-Alkyl, Cycloalkyl, Cycloalkyloxy, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Halogen, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Dioxolan, Dioxan und Dioxepan, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist.

6. Verbindung gemäß einem der Ansprüche 1 bis 5, wobei

R^2 Wasserstoff ist,
R^3 Wasserstoff ist,
R^4 Wasserstoff oder C_1-C_6-Alkyl ist,
R^5 Wasserstoff oder C_1-C_6-Alkyl ist,
R^6 Wasserstoff oder C_1-C_6-Alkyl ist,
R^7 Wasserstoff ist,
X eine Carbonylgruppe ist,
n 2 ist,

die Gruppe der Formel (A) eine Pyridin-, Pyrimidin- oder Chinolingruppe darstellt, vorzugsweise eine Pyridin- oder Pyrimidingruppe, bevorzugter eine Pyridingruppe, wobei jede Gruppe gegebenenfalls mit einem oder mehreren Resten substituiert ist, vorzugsweise mit einem oder zwei Resten, ausgewählt aus der Gruppe von C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, Cycloalkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thio, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, Dioxolan, Dioxan und Dioxepan, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl substituiert ist, und
eines von A und B und eines von D und E ein Stickstoffatom enthält.

7. Pharmazeutische Zusammensetzung, wobei die Zusammensetzung umfasst:

a) eine oder mehrere Verbindungen gemäß einem oder mehreren der Ansprüche 1 bis 6; und
b) einen oder mehrere pharmazeutisch verträgliche Hilfsstoffe und/oder einen oder mehrere pharmazeutisch verträgliche Wirkstoffe, die in ihrer Struktur von Komponente a) verschieden sind.

8. Verbindung der Formel (**1-IV**), wobei Y^1 Y^2, Y^3 und Y^4 C sind, substituiert mit R^{12}, R^{13}, R^{14} bzw. R^{15}, die ausgewählt sind aus der Gruppe von Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl und Phenyl, und wobei wenigstens eines von R^{12} und R^{13} C_1-C_6-Alkoxy oder C_1-C_6-Halogenalkoxy ist, und B N ist, A N oder eine Bindung ist, n 2 ist, R^6 und R^7 H sind und R^4 und R^5 wie in einem der Ansprüche 1 bis 6 definiert sind.

9. Verbindung der Formel (**3-IV**), wobei Y^1, Y^2, Y^3 und Y^4 C sind, substituiert mit R^{12}, R^{13}, R^{14} bzw. R^{15}, die ausgewählt sind aus der Gruppe von Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl und Phenyl, und wobei wenigstens eines von R^{12} und R^{13} C_1-C_6-Alkoxy oder C_1-C_6-Halogenalkoxy ist, und B N ist, A N oder eine Bindung ist, n 2 oder 3 ist, R^6 und R^7 H sind und R^4 und R^5 wie in einem der Ansprüche 1 bis 6 definiert sind.

10. Verbindung der Formel (**4-II**), wobei Y^1, Y^2, Y^3 und Y^4 C sind, substituiert mit R^{12}, R^{13}, R^{14} bzw. R^{15}, die ausgewählt sind aus der Gruppe von Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl und Phenyl, und wobei wenigstens eines von R^{12} und R^{13} C_1-C_6-Alkoxy oder C_1-C_6-Halogenalkoxy ist, und B N ist, A N oder eine Bindung ist, n 2 oder 3 ist, R^6 und R^7 H sind und R^4 und R^5 wie in einem der Ansprüche 1 bis 6 definiert sind.

11. Verbindung gemäß einem der Ansprüche 1 bis 6 oder pharmazeutische Zusammensetzung gemäß Anspruch 7 für

die Verwendung als Medikament.

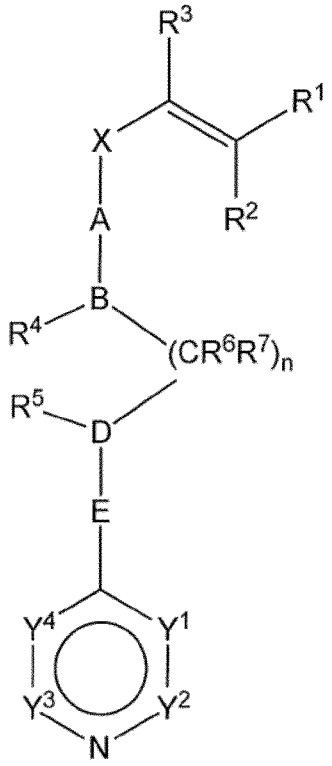
12. Verbindung gemäß einem der Ansprüche 1 bis 6 oder pharmazeutische Zusammensetzung gemäß Anspruch 7 für die Verwendung bei der Behandlung von Parasiteninfektionen.

13. Verwendung einer Verbindung gemäß einem der Ansprüche 1 bis 6 oder einer pharmazeutischen Zusammensetzung gemäß Anspruch 7 bei der Herstellung eines Medikaments für die Behandlung von Parasiteninfektionen von nicht-menschlichen Tieren.

14. Kit, wobei das Kit umfasst:

a) eine oder mehrere Verbindungen gemäß einem oder mehreren der Ansprüche 1 bis 6; und
b) eine oder mehrere andere Komponenten ausgewählt aus der Gruppe bestehend aus einem Hilfsstoff, einem Wirkstoff, einer Vorrichtung zum Kombinieren der Verbindung von Komponente a) mit einem Hilfsstoff und/oder Wirkstoff, einer Vorrichtung zum Verabreichen der Verbindung von Komponente a) an ein Tier, und einem diagnostischen Werkzeug.

15. Verbindung der Formel (Ia) und pharmazeutisch verträgliche Solvate, N-Oxide und Salze davon,



Formel (Ia)

wobei

R^1 Wasserstoff, Halogen, C_1-C_6-Alkyl, Cycloalkyl, C_1-C_6-Alkyloxy, Cycloalkyloxy, C_1-C_6-Alkylthio, Cycloalkylthio, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, Cycloalkyloxy-C_1-C_6-alkyl, C_1-C_6-Alkyloxycycloalkyl, Cycloalkyloxycycloalkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, Cycloalkylthio-C_1-C_6-alkyl, C_1-C_6-Alkylthiocycloalkyl, Cycloalkylthiocycloalkyl, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, Di(cycloalkyl)amino, C_1-C_6-Alkylcycloalkylamino, C_1-C_6-Alkylamino-C_1-C_6-alkyl, Cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-Alkylaminocycloalkyl, Cycloalkylaminocycloalkyl, Di(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, Di(C_1-C_6-alkyl)aminocycloalkyl, Di(cycloalkyl)amino-C_1-C_6-alkyl, Di(cycloalkyl)aminocycloalkyl, C_1-C_6-Alkylcycloalkylamino-C_1-C_6-alkyl, C_1-C_6-Alkylcycloalkylaminocycloalkyl, C_1-C_6-Alkylcarbonyl, Cycloalkylcarbonyl, C_1-C_6-Alkyloxycarbonyl, Cycloalkoxycarbonyl, C_2-C_6-Alkenylcarbonyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste ge-

gebenenfalls mit einem oder mehreren Halogenatomen, vorzugsweise Fluoratomen, substituiert ist, oder R^1 Phenyl, Furanyl, Imidazolinyl oder Thiophenyl ist, wobei jeder der Ringe gegebenenfalls mit einem oder mehreren Resten aus der Gruppe von C_1-C_6-Alkyl, Cycloalkyl und Halogen, vorzugsweise Fluor, substituiert ist,
R^2 Wasserstoff, Halogen, C_1-C_6-Alkyl, Cycloalkyl, C_1-C_6-Alkyloxy, Cycloalkyloxy, C_1-C_6-Alkylthio, Cycloalkylthio, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, Cycloalkyloxy-C_1-C_6-alkyl, C_1-C_6-Alkyloxycycloalkyl, Cycloalkyloxycycloalkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, Cycloalkylthio-C_1-C_6-alkyl, C_1-C_6-Alkylthiocycloalkyl, Cycloalkylthiocycloalkyl, Amino, C_1-C_6-Alkylamino, Cycloalkylamino, Di(C_1-C_6-alkyl)amino, Di(cycloalkyl)amino, C_1-C_6-Alkylcycloalkylamino, C_1-C_6-Alkylamino-C_1-C_6-alkyl, Cycloalkylamino-C_1-C_6-alkyl, C_1-C_6-Alkylaminocycloalkyl, Cycloalkylaminocycloalkyl, Di(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, Di(C_1-C_6-alkyl)aminocycloalkyl, Di(cycloalkyl)amino-C_1-C_6-alkyl, Di(cycloalkyl)aminocycloalkyl, C_1-C_6-Alkylcycloalkylamino-C_1-C_6-alkyl, C_1-C_6-Alkylcycloalkylaminocycloalkyl, C_1-C_6-Alkylcarbonyl, Cycloalkylcarbonyl, C_1-C_6-Alkyloxycarbonyl, Cycloalkoxycarbonyl, C_2-C_6-Alkenylcarbonyl ist, wobei jeder der Kohlenstoff-enthaltenden Reste gegebenenfalls mit einem oder mehreren Halogenatomen, vorzugsweise Fluoratomen, substituiert ist, oder R^2 Phenyl, Furanyl, Imidazolinyl oder Thiophenyl ist, wobei jeder der Ringe gegebenenfalls mit einem oder mehreren Resten aus der Gruppe von C_1-C_6-Alkyl, Cycloalkyl und Halogen, vorzugsweise Fluor, substituiert ist, wobei R^2 vorzugsweise Wasserstoff ist,
R^3 Wasserstoff, C_1-C_6-Alkyl oder Cycloalkyl ist, vorzugsweise Wasserstoff,
R^4 Wasserstoff, C_1-C_6-Alkyl oder Cycloalkyl ist, vorzugsweise Wasserstoff,
R^5 Wasserstoff, C_1-C_6-Alkyl, Cycloalkyl oder Acyl ist,
R^6 Wasserstoff, C_1-C_6-Alkyl, Cycloalkyl, Hydroxy, C_1-C_6-Alkyloxy, Phenyl-C_1-C_6-alkyloxy, Hydroxy-C_1-C_6-alkyl, C_1-C_6-Alkyloxy-C_1-C_6-alkyl, Phenyl-C_1-C_6-alkyloxy-C_1-C_6-alkyl, Thiol-C_1-C_6-alkyl, C_1-C_6-Alkylthio-C_1-C_6-alkyl, Phenyl-C_1-C_6-alkylthio-C_1-C_6-alkyl, Hydroxycarbonyl, Hydroxycarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkyloxycarbonyl, C_1-C_6-Alkyloxycarbonyl-C_1-C_6-alkyl, Aminocarbonyl, Aminocarbonyl-C_1-C_6-alkyl, C_1-C_6-Alkylaminocarbonyl, C_1-C_6-Alkylaminocarbonyl-(C_1-C_6-alkyl), Di(C_1-C_6-alkyl)aminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl-(C_1-C_6-alkyl), C_1-C_6-Alkylamino-C_1-C_6-alkyl, Di(C_1-C_6-alkyl)amino-C_1-C_6-alkyl, Phenyl, Phenyl-C_1-C_6-alkyl ist, wobei jede Phenylgruppe gegebenenfalls mit Hydroxy, C_1-C_6-Alkyloxy oder Cycloalkyloxy substituiert ist,
R^7 Wasserstoff, C_1-C_6-Alkyl oder Cycloalkyl ist,
oder R^6 und R^7 zusammen eine Oxogruppe oder eine Thioxogruppe darstellen oder R^6 mit R^8 verbunden ist, um eine C_1-C_3-Alkylengruppe zu bilden, und R^7 mit R^9 verbunden ist, um eine C_1-C_3-Alkylengruppe zu bilden, wobei eine oder beide der C_1-C_3-Alkylengruppen gegebenenfalls mit einem oder mehreren C_1-C_6-Alkyl- oder Cycloalkylresten substituiert sind,
n eine ganze Zahl von 1 bis 3 ist,
X eine Carbonyl- oder Sulfonylgruppe ist, vorzugsweise eine Carbonylgruppe,
A eine Bindung oder NR^8 ist, wobei R^8 Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,
E eine Bindung oder NR^9 ist, wobei R^9 Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,
B N oder CR^{10} ist, wobei R^{10} Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,
D N oder CR^{11} ist, wobei R^{11} Wasserstoff oder C_1-C_6-Alkyl ist, vorzugsweise Wasserstoff,
Y^1 C oder N ist, wobei C mit R^{12} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Cycloalkyl, Cycloalkyloxy, Cycloalkylamino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, Cycloalkylthio, Phenyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl oder Cycloalkyl substituiert ist,
Y^2 C oder N ist, wobei C mit R^{13} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkylcarbonylamino, C_1-C_6-Alkoxycarbonyl, Cycloalkyl, Cycloalkyloxy, Cycloalkylamino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, Cycloalkylthio, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl oder Cycloalkyl substituiert ist,
Y^3 C oder N ist, wobei C mit R^{14} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, Thiol, Hydroxy, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Cycloalkyl, Cycloalkyloxy, Cycloalkylamino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, Cycloalkylthio, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl oder Cycloalkyl substituiert ist,

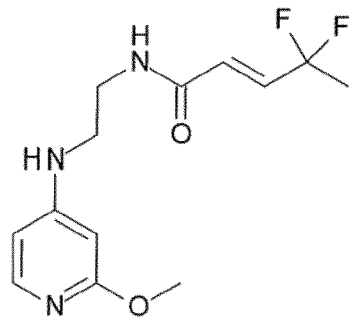
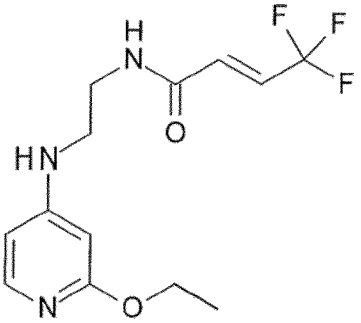
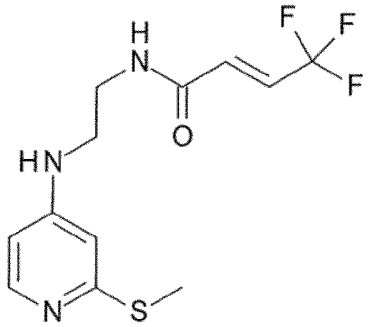
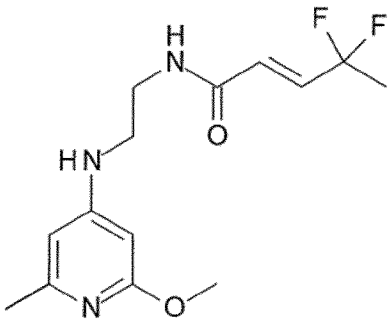
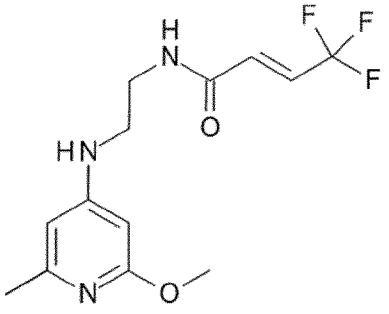
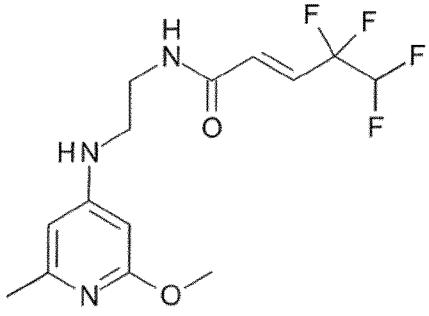
Y^4 C oder N ist, wobei C mit R^{15} substituiert ist, das Wasserstoff, Halogen, C_1-C_6-Alkyl, C_1-C_6-Halogenalkyl, C_1-C_6-Alkoxy, C_1-C_6-Halogenalkoxy, Nitrilo, Nitro, Amino, C_1-C_6-Alkylamino, Di(C_1-C_6-alkyl)amino, N-Pyrrolidinyl, N-Piperidinyl, N-Morpholinyl, C_1-C_6-Alkylthio, C_1-C_6-Alkylcarbonyl, C_1-C_6-Halogenalkylcarbonyl, C_1-C_6-Alkylcarbonylamino, Aminocarbonyl, C_1-C_6-Alkylaminocarbonyl, Di(C_1-C_6-alkyl)aminocarbonyl, C_1-C_6-Alkoxycarbonyl, Cycloalkyl, Cycloalkyloxy, Cycloalkylamino, (C_1-C_6-Alkyl)-(cycloalkyl)amino, Cycloalkylthio, Phenyl, Dioxolan, wie z. B. 1,3-Dioxolan, Dioxan, wie z. B. 1,3-Dioxan, oder Dioxepan, wie z. B. 1,3-Dioxepan, ist, wobei jeder Ring unsubstituiert oder mit C_1-C_6-Alkyl oder Cycloalkyl substituiert ist,

oder Y^1 und Y^2 und/oder Y^3 und Y^4 miteinander verbunden sind, um ein Ringsystem zu bilden,
und wobei wenigstens eines von B und D ein Stickstoffatom ist,
für die Verwendung bei der Behandlung einer Helminthen-Infektion.

16. Antihelminthische Zusammensetzung, wobei die Zusammensetzung umfasst:

a) eine oder mehrere Verbindungen gemäß Anspruch 15; und
b) einen oder mehrere pharmazeutisch verträgliche Hilfsstoffe und/oder einen oder mehrere pharmazeutisch verträgliche Wirkstoffe, die von der einen oder den mehreren Verbindungen gemäß Anspruch 15 verschieden sind.

17. Verbindung gemäß Anspruch 1, wobei die Verbindung eine Struktur aufweist, die ausgewählt ist aus der Gruppe bestehend aus

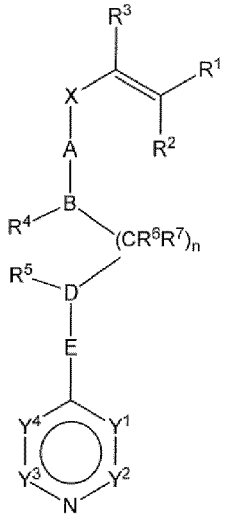







und

.

Revendications

1. Composé de formule (I) et les sels, solvates et N-oxydes pharmaceutiquement acceptables,



Formule (I)

dans lequel

R^1 est halogène, C_1-C_6-alkyle, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alcényle, C_2-C_6-alcynyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, C_1-C_6-alkylcarbonyle, C_2-C_6-alcénylcarbonyle, SF_5, C_1-C_6-alkylsulfonyle, où chacun des radicaux carbonés est éventuellement substitué par un ou plusieurs atomes d'halogène, préférablement des atomes de fluor,
R^2 est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alcényle, C_2-C_6-alcynyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, C_1-C_6-alkylcarbonyle, C_2-C_6-alcénylcarbonyle, où chacun des radicaux carbonés est éventuellement substitué par un ou plusieurs atomes d'halogène, préférablement des atomes de fluor,
R^3 est hydrogène, C_1-C_6-alkyle ou cycloalkyle, préférablement hydrogène,
R^4 est hydrogène, C_1-C_6-alkyle ou cycloalkyle, préférablement hydrogène,
R^5 est hydrogène, C_1-C_6-alkyle, cycloalkyle, acyle, cycloalkyloxycarbonyle ou C_1-C_6-alkyloxycarbonyle,
R^6 est hydrogène, C_1-C_6-alkyle, cycloalkyle, hydroxy, C_1-C_6-alkyloxy, phénylC_1-C_6-alkyloxy, hydroxyC_1-C_6-alkyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, phénylC_1-C_6-alkyloxyC_1-C_6-alkyle, thioC_1-C_6-alkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, phénylC_1-C_6-alkylthioC_1-C_6-alkyle, hydroxycarbonyle, hydroxycarbonylC_1-C_6-alkyle, C_1-C_6-alkyloxycarbonyle, C_1-C_6-alkyloxycarbonylC_1-C_6-alkyle, aminocarbonyle, aminocarbonylC_1-C_6-alkyle, C_1-C_6-alkylaminocarbonyle, C_1-C_6-alkylaminocarbonyl (C_1-C_6-alkyl), di (C_1-C_6-alkyl)-aminocarbonyle, di (C_1-C_6-alkyl) aminocarbonyl (C_1-C_6-alkyl), C_1-C_6-alkylaminoC_1-C_6-alkyle, di (C_1-C_6-alkyl)-aminoC_1-C_6-alkyle, phényle, phénylC_1-C_6-alkyle, où chaque groupement phényle est éventuellement substitué par hydroxy, cycloalkyloxy ou C_1-C_6-alkyloxy,
R^7 est hydrogène, C_1-C_6-alkyle ou cycloalkyle,
ou R^6 est lié ensemble avec R^8 pour former un groupement C_1-C_3-alkylène et R^7 est lié ensemble avec R^9 pour former un groupement C_1-C_3-alkylène, où un, ou les deux, parmi lesdits groupements C_1-C_3-alkylène sont éventuellement substitués par un ou plusieurs radicaux C_1-C_6-alkyle ou cycloalkyle,
n est un nombre entier allant de 1 à 3,
X est un groupement carbonyle, thiocarbonyle ou sulfonyle, préférablement un groupement carbonyle,
A est une liaison ou NR^8, où R^8 est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
E est une liaison ou NR^9, où R^9 est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
B est N ou CR^{10}, où R^{10} est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
D est N ou CR^{11}, où R^{11} est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
Y^1 est C ou N, où C est substitué par R^{12} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-

morpholinyle, C_1-C_6-alkylthio, cycloalkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, phényle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,

Y^2 est C ou N, où C est substitué par R^{13} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thiol, hydroxy, C_1-C_6-alkylthio, cycloalkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di (C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alkylcarbonylamino, C_1-C_6-alcoxycarbonyle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,

Y^3 est C ou N, où C est substitué par R^{14} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thiol, hydroxy, C_1-C_6-alkylthio, cycloalkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,

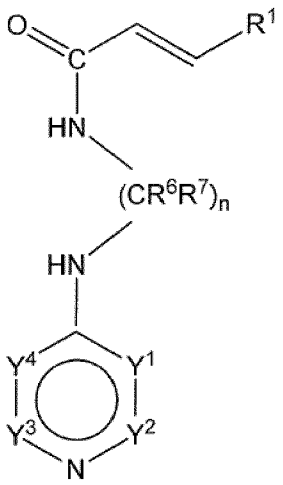
Y^4 est C ou N, où C est substitué par R^{15} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, phényle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,

ou Y^1 et Y^2 et/ou Y^3 et Y^4 sont liés ensemble pour former un noyau,
et au moins l'un parmi B et D est un atome d'azote.

2. Composé selon la revendication 1, dans lequel
R^1 est halogène, C_1-C_6-alkyle, C_1-C_6-alkyloxy, C_1-C_6-alkylthio, C_2-C_6-alcényle, C_2-C_6-alcynyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, C_1-C_6-alkylcarbonyle, C_2-C_6-alcénylcarbonyle, SF_5, C_1-C_6-alkylsulfonyle, où chacun des radicaux carbonés est éventuellement substitué par un ou plusieurs atomes d'halogène, préférablement des atomes de fluor,
R^2 est hydrogène,
R^3 est hydrogène,
R^4 est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
R^5 est hydrogène, C_1-C_6-alkyle, acyle ou C_1-C_6-alkyloxycarbonyle,
$(CR^6R^7)_n$ est un groupement C_1-C_3-alkylène, préférablement un groupement éthylène, qui est éventuellement substitué par un ou plusieurs radicaux C_1-C_6-alkyle,
A est une liaison ou NR^8, où R^8 est H ou C_1-C_6-alkyle,
E est une liaison ou NR^9, où R^9 est H ou C_1-C_6-alkyle,
B est N ou CR^{10}, où R^{10} est H ou C_1-C_6-alkyle,
D est N ou CR^{11}, où R^{11} est H ou C_1-C_6-alkyle,
X est un groupement carbonyle, thiocarbonyle ou sulfonyle, préférablement un groupement carbonyle,
Y^1 est C ou N, où C est substitué par R^{12} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, cycloalkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, phényle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,
Y^2 est C ou N, où C est substitué par R^{13} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholi-

nyle, thiol, hydroxy, C_1-C_6-alkylthio, cycloalkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alkylcarbonylamino, C_1-C_6-alcoxycarbonyle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,
Y^3 est C ou N, où C est substitué par R^{14} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thiol, hydroxy, C_1-C_6-alkylthio, cycloalkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,
Y^4 est C ou N, où C est substitué par R^{15} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-alcényle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, cycloalkylamino, di(C_1-C_6-alkyl)amino, (C_1-C_6-alkyl)-(cycloalkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, C_1-C_6-halogénoalkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, phényle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,
ou Y^1 et Y^2 et/ou Y^3 et Y^4 sont liés ensemble pour former un noyau,
et au moins l'un parmi B et D est un atome d'azote.

3. Composé de formule (II) selon la revendication 1 ou 2,



Formule (II)

dans lequel

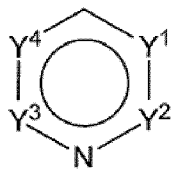
R^1 est C_1-C_6-alkyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, ou C_1-C_6-alkylthioC_1-C_6-alkyle, où chacun des radicaux carbonés est non substitué ou substitué par un ou plusieurs atomes d'halogène, préférablement par un ou plusieurs atomes de fluor, par exemple par de 1 à 10, préférablement par de 1 à 5, atomes de fluor,
R^6 est hydrogène, C_1-C_6-alkyle, hydroxy, C_1-C_6-alkyloxy, phénylC_1-C_6-alkyloxy, hydroxyC_1-C_6-alkyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, phénylC_1-C_6-alkyloxyC_1-C_6-alkyle, thioC_1-C_6-alkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, phénylC_1-C_6-alkylthioC_1-C_6-alkyle, hydroxycarbonyle, hydroxycarbonylC_1-C_6-alkyle, C_1-C_6-alkyloxycarbonyle, C_1-C_6-alkyloxycarbonylC_1-C_6-alkyle, aminocarbonyle, aminocarbonylC_1-C_6-alkyle, C_1-C_6-alkylaminocarbonyle, C_1-C_6-alkylaminocarbonyl(C_1-C_6-alkyl), di(C_1-C_6-alkyl)-aminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyl(C_1-C_6-alkyl), C_1-C_6-alkylaminoC_1-C_6-alkyle, di(C_1-C_6-alkyl)-aminoC_1-C_6-alkyle, phényle, phénylC_1-C_6-alkyle, où chaque groupement phényle est éventuellement substitué par hydroxy ou C_1-C_6-alkyloxy, préférablement
R^6 est hydrogène, C_1-C_6-alkyle, hydroxycarbonyle, hydroxycarbonylC_1-C_6-alkyle, C_1-C_6-alkyloxycarbonyle, C_1-C_6-alkyloxycarbonylC_1-C_6-alkyle, aminocarbonyle, aminocarbonylC_1-C_6-alkyle, C_1-C_6-alkylaminocarbonyle, C_1-C_6-alkylaminocarbonyl(C_1-C_6-alkyl), di(C_1-C_6-alkyl)-aminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyl(C_1-C_6-alkyl), phényle, phénylC_1-C_6-alkyle, plus préférablement R^6 est hydrogène ou C_1-C_6-alkyle, encore

plus préférablement hydrogène,
R^7 est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
n vaut 2 ou 3,
Y^1 est C ou N, où C est substitué par R^{12} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, cycloalkyle, cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle,
Y^2 est C ou N, préférablement C, où C est substitué par R^{13} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, cycloalkyle, cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,
Y^3 est C ou N, préférablement C, où C est substitué par R^{14} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, cycloalkyle, cycloalkyloxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle,
Y^4 est C ou N, préférablement C, où C est substitué par R^{15} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl) amino, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle,

ou Y^1 et Y^2 et/ou Y^3 et Y^4 sont liés ensemble pour former un noyau de 5 ou 6 chaînons.

4. Composé selon la revendication 3, dans lequel
R^1 est C_1-C_6-alkyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, ou C_1-C_6-alkylthioC_1-C_6-alkyle, où chacun des radicaux carbonés est non substitué ou substitué par un ou plusieurs atomes d'halogène, préférablement par un ou plusieurs atomes de fluor, par exemple par de 1 à 10, préférablement par de 1 à 5, atomes de fluor,
Y^1 est C ou N, où C est substitué par R^{12} qui est H, ou C_1-C_6-alkyle,
Y^2 est C, où C est substitué par R^{13} est H, C_1-C_6-alkyle, C_1-C_6-alcoxy, C_1-C_6-alkylcarbonyle, cycloalkyle, cycloalkyloxy, C_1-C_6-alkylthio,
Y^3 est C, où C est substitué par R^{14} est H, C_1-C_6-alkyle, C_1-C_6-alcoxy, C_1-C_6-alkylcarbonyle, cycloalkyle, cycloalkyloxy, C_1-C_6-alkylthio,
Y^4 est C, où C est substitué par R^{15} est H, C_1-C_6-alkyle, C_1-C_6-alcoxy, C_1-C_6-alkylthio,
ou Y^1 et Y^2 ou Y^3 et Y^4 sont liés ensemble pour former un noyau de 5 ou 6 chaînons.

5. Composé selon l'une quelconque des revendications 1 à 4, dans lequel le groupement de formule (A)



Formule (A)

représente un groupement pyridine, pyrimidine, quinoléine, quinazoline, thiénopyrimidine, thiénopyridine, triazolopyrimidine, pyridopyridine, pyrrolopyridine, pyrazolopyrimidine, pyrazolopyridine, furopyridine, 2,3-dihydrofuropyridine, 2,3-dihydro-1,4-dioxinopyridine, furopyrimidine, pyridazine ou cinnoline, où chaque groupement est éventuellement substitué par un ou plusieurs radicaux, préférablement par un ou deux radicaux, choisis dans le groupe constitué par C_1-C_6-alkyle, cycloalkyle, cycloalkyloxy, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, halogène, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, dioxolane, dioxane, ou dioxépane, où chaque cycle est non substitué ou substitué par C_1-C_6-alkyle.

6. Composé selon l'une quelconque des revendications 1 à 5, dans lequel
R^2 est hydrogène,
R^3 est hydrogène,
R^4 est hydrogène ou C_1-C_6-alkyle,
R^5 est hydrogène ou C_1-C_6-alkyle,
R^6 est hydrogène ou C_1-C_6-alkyle,
R^7 est hydrogène,
X est un groupement carbonyle,
n vaut 2,
le groupement de formule (A) représente un groupement pyridine, pyrimidine ou quinoléine, préférablement un groupement pyridine ou pyrimidine, plus préférablement un groupement pyridine, où chaque groupement est éventuellement substitué par un ou plusieurs radicaux, préférablement par un ou deux radicaux, choisis dans le groupe constitué par C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, cycloalcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thio, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, dioxolane, dioxane, ou dioxépane, où chaque cycle est non substitué ou substitué par C_1-C_6-alkyle, et
l'un parmi A et B et l'un parmi D et E contient un atome d'azote.

7. Composition pharmaceutique, où la composition comprend :

a) un ou plusieurs composés tels que définis selon l'une ou plusieurs parmi les revendications 1 à 6 ; et
b) un ou plusieurs excipients pharmaceutiquement acceptables et/ou un ou plusieurs ingrédients actifs pharmaceutiquement acceptables dont la structure diffère de celle du composant a).

8. Composé de formule (1-IV), dans lequel Y^1, Y^2, Y^3 et Y^4 sont C, substitué par R^{12}, R^{13}, R^{14} et R^{15} respectivement et qui sont choisis dans le groupe constitué par halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl) amino, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle et phényle, et où au moins l'un parmi R^{12} et R^{13} est C_1-C_6-alcoxy ou C_1-C_6-halogénoalcoxy, et B est N, A est N ou une liaison, n vaut 2, R^6 et R^7 sont H, et R^4 et R^5 sont tels que définis selon l'une quelconque des revendications 1 à 6.

9. Composé de formule (3-IV), dans lequel Y^1, Y^2, Y^3 et Y^4 sont C, substitué par R^{12}, R^{13} R^{14} et R^{15} respectivement et qui sont choisis dans le groupe constitué par halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl) amino, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle ou phényle, et où au moins l'un parmi R^{12} et R^{13} est C_1-C_6-alcoxy ou C_1-C_6-halogénoalcoxy, et B est N, A est N ou une liaison, n vaut 2 ou 3, R^6 et R^7 sont H, et R^4 et R^5 sont tels que définis selon l'une quelconque des revendications 1 à 6.

10. Composé de formule (4-II), dans lequel Y^1, Y^2, Y^3 et Y^4 sont C, substitué par R^{12}, R^{13}, R^{14} et R^{15} respectivement et qui sont choisis dans le groupe constitué par halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl) amino, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle ou phényle, et où au moins l'un parmi R^{12} et R^{13} est C_1-C_6-alcoxy ou C_1-C_6-halogénoalcoxy, et B est N, A est N ou une liaison, n vaut 2 ou 3, R^6 et R^7 sont H, et R^4 et R^5 sont tels que définis selon l'une quelconque des revendications 1 à 6.

11. Composé tel que défini selon l'une quelconque des revendications 1 à 6, ou composition pharmaceutique telle que définie selon la revendication 7, pour une utilisation comme médicament.

12. Composé tel que défini selon l'une quelconque des revendications 1 à 6, ou composition pharmaceutique telle que définie selon la revendication 7, pour une utilisation dans le traitement d'infections parasitaires.

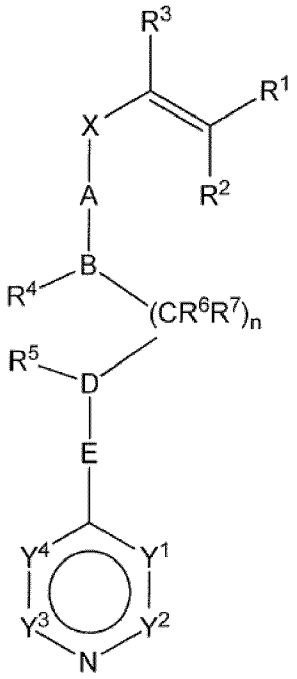
13. Utilisation d'un composé tel que défini selon l'une quelconque des revendications 1 à 6, ou d'une composition pharmaceutique telle que définie selon la revendication 7, dans l'élaboration d'un médicament destiné au traitement d'infections parasitaires chez des animaux non humains.

14. Kit, où le kit comprend :

a) un ou plusieurs composés tels que définis selon l'une ou plusieurs parmi les revendications 1 à 6, et

b) un ou plusieurs autres composants choisis dans le groupe constitué par un excipient, un ingrédient actif, un appareil pour combiner le composé du composant a) avec un excipient et/ou un ingrédient actif, un appareil pour administrer le composé du composant a) à un animal, et un outil de diagnostic.

15. Composé de formule (Ia) et des solvates, N-oxydes et sels pharmaceutiquement acceptables de celui-ci,



Formule (Ia)

dans lequel

R^1 est hydrogène, halogène, C_1-C_6-alkyle, cycloalkyle, C_1-C_6-alkyloxy, cycloalkyloxy, C_1-C_6-alkylthio, cycloalkylthio, C_2-C_6-alcényle, C_2-C_6-alcynyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, cycloalkyloxyC_1-C_6-alkyle, C_1-C_6-alkyloxycycloalkyle, cycloalkyloxycycloalkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, cycloalkylthioC_1-C_6-alkyle, C_1-C_6-alkylthiocycloalkyle, cycloalkylthiocycloalkyle, amino, C_1-C_6-alkylamino, cycloalkylamino, di-(C_1-C_6-alkyl)amino, di-(cycloalkyl)amino, C_1-C_6-alkyl-cycloalkylamino, C_1-C_6-alkylaminoC_1-C_6-alkyle, cycloalkylamino-C_1-C_6-alkyle, C_1-C_6-alkylamino-cycloalkyle, cycloalkylaminocycloalkyle, di-(C_1-C_6-alkyl)aminoC_1-C_6-alkyle, di-(C_1-C_6-alkyl)-aminocycloalkyle, di-(cycloalkyl)amino-C_1-C_6-alkyle, di-(cycloalkyl)aminocycloalkyle, C_1-C_6-alkyl-cycloalkylamino-C_1-C_6-alkyle, C_1-C_6-alkylcycloalkylaminocycloalkyle, C_1-C_6-alkylcarbonyle, cycloalkylcarbonyle, C_1-C_6-alkyloxycarbonyle, cycloalcoxycarbonyle, C_2-C_6-alcénylcarbonyle, où chacun des radicaux carbonés est éventuellement substitué par un ou plusieurs atomes d'halogène, préférablement des atomes de fluor, ou R^1 est phényle, furanyle, imidazolinyle, ou thiophényle, où chacun parmi les cycles est éventuellement substitué par un ou plusieurs radicaux choisis dans le groupe constitué par C_1-C_6-alkyle, cycloalkyle et halogène, préférablement fluor,

R^2 est hydrogène, halogène, C_1-C_6-alkyle, cycloalkyle, C_1-C_6-alkyloxy, cycloalkyloxy, C_1-C_6-alkylthio, cycloalkylthio, C_2-C_6-alcényle, C_2-C_6-alcynyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, cycloalkyloxyC_1-C_6-alkyle, C_1-C_6-alkyloxycycloalkyle, cycloalkyloxycycloalkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, cycloalkylthioC_1-C_6-alkyle, C_1-C_6-alkylthiocycloalkyle, cycloalkylthiocycloalkyle, amino, C_1-C_6-alkylamino, cycloalkylamino, di-(C_1-C_6-alkyl)amino, di-(cycloalkyl)amino, C_1-C_6-alkylcycloalkylamino, C_1-C_6-alkylamino-C_1-C_6-alkyle, cycloalkylamino-C_1-C_6-alkyle, C_1-C_6-alkylamino-cycloalkyle, cycloalkylamino-cycloalkyle, di-(C_1-C_6-alkyl)amino-C_1-C_6-alkyle, di-(C_1-C_6-alkyl)aminocycloalkyle, di-(cycloalkyl)amino-C_1-C_6-alkyle, di-(cycloalkyl)aminocycloalkyle, C_1-C_6-alkyl-cycloalkylamino-C_1-C_6-alkyle, C_1-C_6-alkyl-cycloalkylamino-cycloalkyle, C_1-C_6-alkylcarbonyle, cycloalkylcarbonyle, C_1-C_6-alkyloxycarbonyle, cycloalcoxycarbonyle, C_2-C_6-alcénylcarbonyle, où chacun des radicaux carbonés est éventuellement substitué par un ou plusieurs atomes d'halogène, préférablement des atomes de fluor, ou R^2 est phényle, furanyle, imidazolinyle, ou thiophényle, où chacun parmi les cycles est éventuellement substitué par un ou plusieurs radicaux choisis dans le groupe constitué par C_1-C_6-alkyle, cycloalkyle et halogène, préfé-

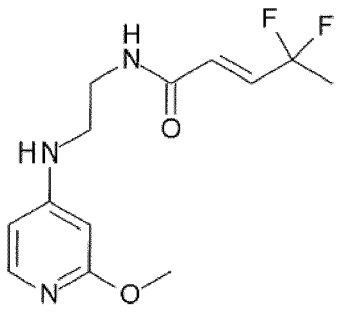
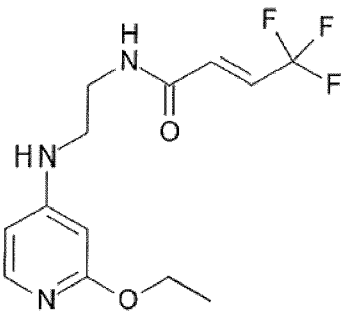
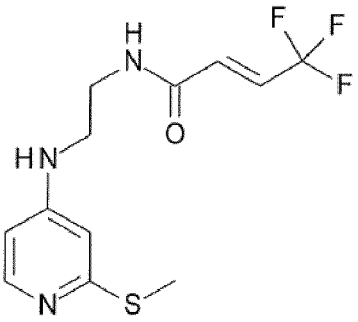
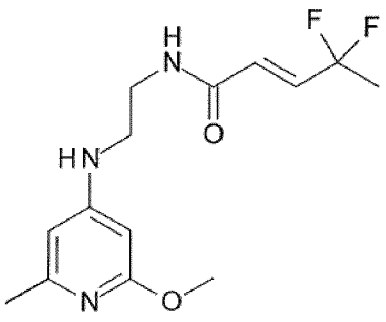
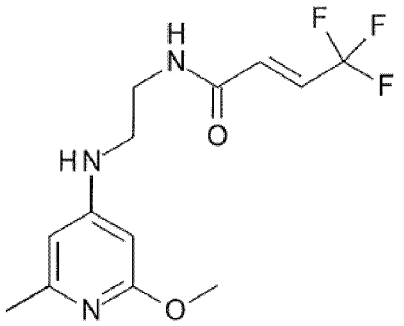
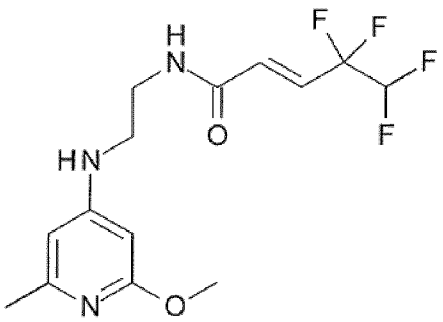
rablement fluor, préférablement R^2 est hydrogène,
R^3 est hydrogène, C_1-C_6-alkyle ou cycloalkyle, préférablement hydrogène,
R^4 est hydrogène, C_1-C_6-alkyle ou cycloalkyle, préférablement hydrogène,
R^5 est hydrogène, C_1-C_6-alkyle, cycloalkyle ou acyle,
R^6 est hydrogène, C_1-C_6-alkyle, cycloalkyle, hydroxy, C_1-C_6-alkyloxy, phénylC_1-C_6-alkyloxy, hydroxyC_1-C_6-alkyle, C_1-C_6-alkyloxyC_1-C_6-alkyle, phénylC_1-C_6-alkyloxyC_1-C_6-alkyle, thioC_1-C_6-alkyle, C_1-C_6-alkylthioC_1-C_6-alkyle, phénylC_1-C_6-alkylthioC_1-C_6-alkyle, hydroxycarbonyle, hydroxycarbonylC_1-C_6-alkyle, C_1-C_6-alkyloxycarbonyle, C_1-C_6-alkyloxycarbonylC_1-C_6-alkyle, aminocarbonyle, aminocarbonylC_1-C_6-alkyle, C_1-C_6-alkylaminocarbonyle, C_1-C_6-alkylaminocarbonyl(C_1-C_6-alkyl), di(C_1-C_6-alkyl)-aminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyl(C_1-C_6-alkyl), C_1-C_6-alkylaminoC_1-C_6-alkyle, di(C_1-C_6-alkyl)-aminoC_1-C_6-alkyle, phényle, phénylC_1-C_6-alkyle, où chaque groupement phényle est éventuellement substitué par hydroxyle, C_1-C_6-alkyloxy ou cycloalkyloxy,
R^7 est hydrogène, C_1-C_6-alkyle ou cycloalkyle,
ou R^6 et R^7 représentent ensemble un groupement oxo ou un groupement thioxo, ou R^6 est lié ensemble avec R^8 pour former un groupement C_1-C_3-alkylène et R^7 est lié ensemble avec R^9 pour former un groupement C_1-C_3-alkylène, où un, ou les deux, parmi lesdits groupements C_1-C_3-alkylène sont éventuellement substitués par un ou plusieurs radicaux C_1-C_6-alkyle ou cycloalkyle,
n est un nombre entier allant de 1 à 3,
X est un groupement carbonyle ou sulfonyle, préférablement un groupement carbonyle,
A est une liaison ou NR^8, où R^8 est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
E est une liaison ou NR^9, où R^9 est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
B est N ou CR^{10}, où R^{10} est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
D est N ou CR^{11}, où R^{11} est hydrogène ou C_1-C_6-alkyle, préférablement hydrogène,
Y^1 est C ou N, où C est substitué par R^{12} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di (C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)-aminocarbonyle, C_1-C_6-alcoxycarbonyle, cycloalkyle, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, phényle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle ou cycloalkyle,
Y^2 est C ou N, où C est substitué par R^{13} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alkylcarbonylamino, C_1-C_6-alcoxycarbonyle, cycloalkyle, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle ou cycloalkyle,
Y^3 est C ou N, où C est substitué par R^{14} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di (C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, thiol, hydroxy, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, cycloalkyle, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)-(cycloalkyl)amino, cycloalkylthio, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle ou cycloalkyle,
Y^4 est C ou N, où C est substitué par R^{15} qui est hydrogène, halogène, C_1-C_6-alkyle, C_1-C_6-halogénoalkyle, C_1-C_6-alcoxy, C_1-C_6-halogénoalcoxy, nitrilo, nitro, amino, C_1-C_6-alkylamino, di(C_1-C_6-alkyl)amino, N-pyrrolidinyle, N-pipéridinyle, N-morpholinyle, C_1-C_6-alkylthio, C_1-C_6-alkylcarbonyle, C_1-C_6-halogénoalkylcarbonyle, C_1-C_6-alkylcarbonylamino, aminocarbonyle, C_1-C_6-alkylaminocarbonyle, di(C_1-C_6-alkyl)aminocarbonyle, C_1-C_6-alcoxycarbonyle, cycloalkyle, cycloalkyloxy, cycloalkylamino, (C_1-C_6-alkyl)(cycloalkyl)amino, cycloalkylthio, phényle, dioxolane tel que 1,3-dioxolane, dioxane tel que 1,3-dioxane, ou dioxépane tel que 1,3-dioxépane, chacun parmi lesdits cycles étant non substitué ou substitué par C_1-C_6-alkyle ou cycloalkyle,

ou Y^1 et Y^2 et/ou Y^3 et Y^4 sont liés ensemble pour former un noyau,
et au moins l'un parmi B et D est un atome d'azote, pour une utilisation dans le traitement d'une infection par des helminthes.

16. Composition anthelminthique, où la composition comprend :

a) un ou plusieurs composés tels que définis selon la revendication 15 ; et
b) un ou plusieurs excipients pharmaceutiquement acceptables et/ou un ou plusieurs ingrédients actifs pharmaceutiquement acceptables qui diffèrent desdits un ou plusieurs composés tels que définis selon la revendication 15.

17. Composé selon la revendication 1, où le composé possède une structure choisie dans le groupe constitué par

, ou

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- WO 2008028689 A1 **[0005]**
- WO 2008028691 A1 **[0005]**
- WO 201075591 A **[0257]**
- WO 2010053517 A **[0258]**
- EP 0539588 A **[0259]**
- WO 2007115643 A **[0259]**
- US 5399582 A **[0260]**
- US 5945317 A **[0260]**
- US 5962499 A **[0260]**
- US 5834260 A **[0260]**
- US 6221894 B **[0260]**
- US 5595991 A **[0260]**
- US 20050182059 A **[0261]**
- US 7361689 B **[0261]**
- US 7312248 B **[0261]**
- US 20060281695 A **[0261]**
- US 20060128779 A **[0261]**
- WO 2005085216 A **[0261]**
- WO 2007026965 A **[0261]**
- WO 2007070606 A **[0261]**
- WO 2007075459 A **[0261]**
- WO 2007079162 A **[0261]**
- WO 2007105814 A **[0261]**
- WO 2007125984 A **[0261]**
- WO 2008019760 A **[0261]**
- WO 2008122375 A **[0261]**
- WO 2008150393 A **[0261]**
- WO 2009002809 A **[0261]**
- WO 2009003075 A **[0261]**
- WO 2009022746 A **[0261]**
- WO 2009035004 A **[0261]**
- WO 2009045999 A **[0261]**
- WO 2009051956 A **[0261]**
- WO 200660461 A **[0284]**
- EP 1574504 A **[0284]**
- WO 2006127203 A **[0292]**
- US 200350222 B **[0292]**
- WO 200448347 A **[0294]**
- US 5098462 A **[0296]**
- WO 2008125839 A **[0300]**

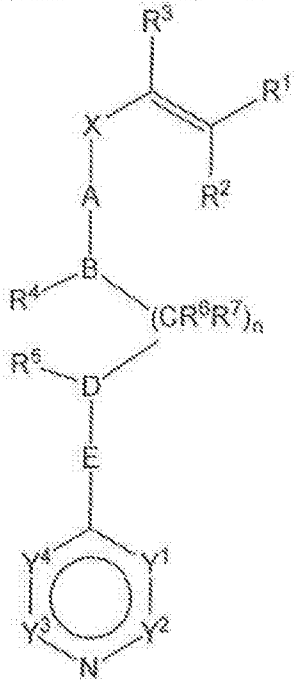
Non-patent literature cited in the description

- **MCKELLAR, Q.A. et al.** Veterinary anthelmintics: old and new. *Review: Trends in Parasitology,* October 2004, vol. 20 (10), 456-61 **[0003]**
- **JABBAR, A. et al.** Anthelmintic resistance: the state of play revisited. *Life Sciences,* 2006, vol. 79, 2413-31 **[0004]**
- **S. K. DAVIDSEN et al.** *J. of Med. Chem.,* 1994, vol. 37, 4423-4429 **[0103]**
- **S. C. ALLEY.** *Bioconjugate Chem.,* 2008, vol. 19, 759-765 **[0104]**
- **D. LOPEZ.** *Abstracts of Papers, 231st National Meeting, Atlanta, GA, United States, March 26-30, 2006, MEDI-292* **[0104]**
- Remington: The Science and Practice of Pharmacy. Lippincott Williams & Wilkins, 2000 **[0165]**
- Pharmaceutical Dosage Forms. Marcel Decker, 1980 **[0165]**
- The Pesticide Manual. British Crop Protection Council, 2003 **[0254]**
- **GREEN ; WUTS.** Protective Groups in Organic Synthesis. John Wiley & Sons, 1999 **[0278]**
- **GOODMAN, M. ; FELIX, A. ; MORODER, L. ; TONIOLO, C.** Methods of Organic Chemistry (Houben-Weyl), Synthesis of Peptides and Peptidomimetics. Georg Thieme Verlag, 2002, vol. E22a **[0278]**
- **SMITH, M.B. ; MARCH, J.** March's Advanced Organic Chemistry. John Wiley & Sons, 2007, 1277-1280 **[0278] [0287] [0298]**
- Methods of Organic Chemistry (Houben-Weyl), Hetarenes II. Georg Thieme Verlag, 1991, vol. E7a **[0279] [0305]**
- **SMITH, M.B. ; MARCH, J.** March's Advanced Organic Chemistry. John Wiley & Sons, 2007, 1841-1842 **[0284]**
- **J. FALBE.** Methods of Organic Chemistry (Houben-Weyl), Carboxylic acids. Georg Thieme Verlag, 1985, vol. E5 **[0290]**
- **M. JAGODZINSKA et al.** *Tetrahedron,* 2007, vol. 63, 2042-2046 **[0290] [0291]**
- **P.F. BEVILAQUA.** *J. Org. Chem.,* 1984, vol. 94, 1430-1434 **[0290]**
- **T. KITAZUME.** *J. Fluorine Chemistry,* 1989, vol. 42, 17-29 **[0291]**
- **V. K. BREL.** *Synthesis,* 2006, 339-343 **[0292]**

- **J. T. MOON.** *Bioorg. Med. Chem. Letters,* 2010, vol. 20, 52-55 **[0292]**
- **O. TSUGE ; T. HATTA ; R. MIZUGUCHI.** *Heterocycles,* 1994, vol. 38, 235-241 **[0294]**
- **G. SHAW ; R. N. WARRENER.** *J. Chem. Soc.,* 1958, 157-161 **[0294]**
- **G. SHAW ; R. N. WARRENER.** *J. Chem. Soc.,* 1958, 153-156 **[0294]**
- **SMITH, M.B. ; MARCH, J.** March's Advanced Organic Chemistry. John Wiley & Sons, 2007, 1288-1292 **[0298]**
- **SAKAMOTO, T.** *Synthesis,* 1988, 485-486 **[0298]**
- **ADGER, B. M.** *J. Chem. Soc. Perkin Trans.,* 1988, 2791-2796 **[0298]**
- **CLAUDI, F. et al.** *Eur. J. Med. Chem.,* 1995, vol. 30 (5), 415-421 **[0300]**
- **MONTI, D. et al.** *Farmaco,* 1981, vol. 36 (6), 412-418 **[0300]**
- **Z. WRÓBEL.** *Tetrahedron,* 2001, vol. 57, 7899-7907 **[0302]**
- **BURCKHARD, J. ; CARREIRA, E.M.** *Organic Lett.,* 2008, vol. 10, 3525-3526 **[0304]**
- **BURCKHARD, J. ; GUEROT, C. ; KNUST, H. ; ROGERS-EVANS, M. ; CARREIRA, E.M.** *Organic Lett.,* 2010, vol. 12, 1944-1947 **[0304]**
- Methods of Organic Chemistry (Houben-Weyl), Hetarenes II. Georg Thieme Verlag, 1992, vol. E7b **[0305]**
- Methods of Organic Chemistry (Houben-Weyl), Hetarenes IV. Georg Thieme Verlag, 1998, vol. E9b **[0305]**
- Methods of Organic Chemistry (Houben-Weyl), Hetarenes IV. Georg Thieme Verlag, 1997, vol. E9b **[0305]**
- Methods of Organic Chemistry (Houben-Weyl), Hetarenes IV. Georg Thieme Verlag, 1997, vol. E9a **[0305]**
- The Naphthyridines. The Chemistry of Heterocyclic Compounds. John Wiley & Sons, 2007, vol. 63 **[0305]**
- Comprehensive Heterocyclic Chemistry II. Elsevier Science Ltd, 1996, vol. 7 **[0305]**
- **S. SHIOTANI ; K. TANAGUCHI.** *J. Heterocyclic Chem.,* 1996, vol. 33, 1051-1056 **[0305]**
- **S. SHIOTANI ; K. TANAGUCHI.** *J. Heterocyclic Chem.,* 1997, vol. 34, 925-929 **[0305]**
- **F. SUZENET ; M. KHOUILI ; S. LAZAR ; G. GUILLAUMENT.** *Synlett,* 2009, 92-96 **[0305]**
- **B. JOSEPH ; A. BENARAB ; G. GUILLAUMENT.** *Heterocycles,* 1994, vol. 38, 1355-1360 **[0305]**
- Methods of Organic Chemistry (Houben-Weyl), Carboxylic acids and Derivatives, part I. Georg Thieme Verlag, 1985, vol. E5 **[0306]**
- Methods of Organic Chemistry (Houben-Weyl), Aldehydes. Georg Thieme Verlag, 1983, vol. E3 **[0306]**
- Methods of Organic Chemistry (Houben-Weyl), Ketones I-III. Georg Thieme Verlag, 1973, vol. VII **[0306]**

Szabadalmi igénypontok

1. Képlet (I) szerinti vegyület, és gyógyszerészetileg elfogadható sók, szolvátok, N-oxidok



képlet (I)

, ahol

R^1 halogén, C_1-C_6-alkil, C_1-C_6-alkiloxi, C_1-C_6-alkiltio, C_2-C_6-alkenil, C_2-C_6-alkynil, C_1-C_6-alkiloxi C_1-C_6-alkil, C_1-C_6-alkiltio C_1-C_6-alkil, C_1-C_6-alkil karbonil, C_2-C_6-alkenil karbonil, SF_5, C_1-C_6-alkil szulfonil, ahol széntartalmú gyökök mindegyike opcionálisan szubsztituálva van egy vagy több halogén atommal, előnyösen fluor atommal,

R^2 hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkiloxi, C_1-C_6- alkiltio, C_2-C_6-alkenil, C_2-C_6-alkynil, C_1-C_6-alkiloxi C_1-C_6-alkil, C_1-C_6-alkiltio C_1-C_6-alkil, C_1-C_6-alkil karbonil, C_2-C_6-alkenil karbonil, ahol széntartalmú gyökök mindegyike opcionálisan szubsztituálva van egy vagy több halogén atommal, előnyösen fluor atommal,

R^3 hidrogén, C_1-C_6-alkil vagy cikloalkil, előnyösen hidrogén,

R^4 hidrogén, C_1-C_6-alkil vagy cikloalkil, előnyösen hidrogén,

R^5 hidrogén, C_1-C_6-alkil, cikloalkil, acil, cikloalkiloxikarbonil vagy C_1-C_6-alkiloxikarbonil,

R^6 hidrogén, C_1-C_6-alkil, cikloalkil, hidroxi, C_1-C_6-alkiloxi, fenil C_1-C_6-alkiloxi, hidroxi C_1-C_6-alkil, C_1-C_6-alkiloxi C_1-C_6-alkil, fenil C_1-C_6-alkiloxi C_1-C_6-alkil, tiol C_1-C_6-alkil, C_1-C_6-alkiltio C_1-C_6-alkil, fenil C_1-C_6-alkiltio C_1-C_6-alkil, hidroxikarbonil, hidroxikarbonil C_1-C_6-alkil, C_1-C_6-alkiloxikarbonil, C_1-C_6-alkiloxikarbonil C_1-C_6-alkil, aminokarbonil, aminokarbonil C_1-C_6-alkil, C_1-C_6-alkilaminokarbonil, C_1-C_6-alkilaminokarbonil (C_1-C_6-alkil), di(C_1-C_6-alkil)aminokarbonil, di(C_1-C_6-alkil)aminokarbonil (C_1-C_6-alkil), C_1-C_6-alkilamino C_1-C_6-alkil, di(C_1-C_6-alkil)amino C_1-C_6-alkil, fenil, fenil C_1-C_6-alkil, ahol mindegyik fenil csoport opcionálisan szubsztituálva van a következővel: hidroxi, cikloalkiloxi vagy C_1-C_6-alkiloxi,

R^7 hidrogén, C_1-C_6-alkil vagy cikloalkil,

vagy R^6 össze van kapcsolva R^8-al, hogy C_1-C_3-alkilén csoportot alkosson és R^7 össze van kapcsolva R^9-el, hogy C_1-C_3-alkilén csoportot alkosson, ahol az egy vagy mindkettő C_1-C_3-alkilén csoport opcionálisan szubsztituálva van egy vagy több C_1-C_6-alkillal vagy cikloalkil gyökkel,

n egész 1-től 3-ig,

X karbonil, tiokarbonil vagy szulfonil csoport, előnyösen karbonil csoport,

A kötés vagy NR^8, ahol R^8 hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

E kötés vagy NR^9, ahol R^9 hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

B N vagy CR^{10}, ahol R^{10} hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

D N vagy CR^{11}, ahol R^{11} hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

Y^1 C vagy N, ahol C szubsztituálva van R^{12}-vel, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, Cikloalkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, fenil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

Y^2 C vagy N, ahol C szubsztituálva van R^{13}-al, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tiol, hidroxi, C_1-C_6-alkiltio, Cikloalkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkilkarbonilamino, C_1-C_6-alkoxikarbonil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

Y^3 C vagy N, ahol C szubsztituálva van R^{14}-el, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tiol, hidroxi, C_1-C_6-alkiltio, Cikloalkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

Y^4 C vagy N, ahol C szubsztituálva van R^{15}-el, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, fenil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C1-C6-alkillal,

vagy Y^1 és Y^2 és/vagy Y^3 és Y^4 össze vannak kapcsolva, hogy gyűrű rendszert alkossanak, és ahol B és D legalább egyike nitrogén atom.

2. Az 1. igénypont szerinti vegyület, ahol

R^1 halogén, C_1-C_6-alkil, C_1-C_6-alkiloxi, C_1-C_6-alkiltio, C_2-C_6-alkenil, C_2-C_6-alkynil, C_1-C_6-alkiloxi C_1-C_6-alkil, C_1-C_6-alkiltio C_1-C_6-alkil, C_1-C_6-alkil karbonil, C_2-C_6-alkenil karbonil, SF_5, C_1-C_6-alkil szulfonil, ahol széntartalmú gyökök mindegyike opcionálisan szubsztituálva van egy vagy több halogén atommal, előnyösen fluor atommal

R^2 hidrogén,

R^3 hidrogén,

R^4 hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

R^5 hidrogén, C_1-C_6-alkil, acil vagy C_1-C_6-alkiloxikarbonil

$(CR^6R^7)_n$ C_1-C_3-alkilén csoport, előnyösen etilén csoport, amely opcionálisan szubsztituált egy vagy több C_1-C_6-alkil gyökkel,

A kötés vagy NR^8, ahol R^8 H vagy C_1-C_6-alkil,

E kötés vagy NR^9, ahol R^9 H vagy C_1-C_6-alkil,

B N vagy CR^{10}, ahol R^{10} H vagy C_1-C_6-alkil,

D N vagy CR^{11}, ahol R^{11} H vagy C_1-C_6-alkil,

X karbonil, tiokarbonil vagy szulfonil csoport, előnyösen karbonil csoport,

Y^1 C vagy N, ahol C szubsztituálva van R^{12}-vel, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, Cikloalkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, fenil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C1-C6-alkillal,

Y^2 C vagy N, ahol C szubsztituálva van R^{13}-al, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tiol, hidroxi, C_1-C_6-alkiltio, Cikloalkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkilkarbonilamino, C_1-C_6-alkoxikarbonil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

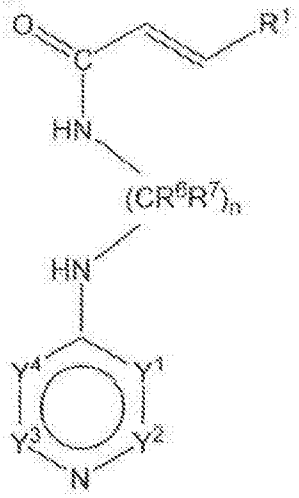
Y^3 C vagy N, ahol C szubsztituálva van R^{14}-el, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tiol, hidroxi, C_1-C_6-alkiltio, Cikloalkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

Y^4 C vagy N, ahol C szubsztituálva van R^{15}-el, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-alkenil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-

C_6-alkilamino, Cikloalkilamino, di(C_1-C_6-alkil)amino, (C_1-C_6-alkil)-(Cikloalkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, C_1-C_6-haloalkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, fenil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

vagy Y^1 és Y^2 és/vagy Y^3 és Y^4 össze vannak kapcsolva, hogy gyűrű rendszert alkossanak, és ahol B és D legalább egyike nitrogén atom.

3. Képlet (II) szerinti 1. vagy 2. vegyület,



képlet (II)

ahol

R^1 C_1-C_6-alkil, C_1-C_6-alkiloxi C_1-C_6-alkil, vagy C_1-C_6-alkiltio C_1-C_6-alkil, ahol széntartalmú gyökök mindegyike szubsztituálatlan vagy szubsztituált egy vagy több halogén atommal, előnyösen egy vagy több fluor atommal, pl., 1-től 10-ig, előnyösen 1-től 5-ig, fluor atommal,

R^6 hidrogén, C_1-C_6-alkil, hidroxi, C_1-C_6-alkiloxi, fenil C_1-C_6-alkiloxi, hidroxi C_1-C_6-alkil, C_1-C_6-alkiloxi C_1-C_6-alkil, fenil C_1-C_6-alkiloxi C_1-C_6-alkil, tiol C_1-C_6-alkil, C_1-C_6-alkiltio C_1-C_6-alkil, fenil C_1-C_6-alkiltio C_1-C_6-alkil, hidroxikarbonil, hidroxikarbonil C_1-C_6-alkil, C_1-C_6-alkiloxikarbonil, C_1-C_6-alkiloxikarbonil C_1-C_6-alkil, aminokarbonil, aminokarbonil C_1-C_6-alkil, C_1-C_6-alkilaminokarbonil, C_1-C_6-alkilaminokarbonil (C_1-C_6-alkil), di(C_1-C_6-alkil)aminokarbonil, di(C_1-C_6-alkil)aminokarbonil (C_1-C_6-alkil), C_1-C_6-alkilamino C_1-C_6-alkil, di(C_1-C_6-alkil)amino C_1-C_6-alkil, fenil, fenil C_1-C_6-alkil, ahol mindegyik fenil csoport opcionálisan szubsztituált hidroxival vagy C_1-C_6-alkiloxi, előnyösen R^6 hidrogén, C_1-C_6-alkil, hidroxikarbonil, hidroxikarbonil C_1-C_6-alkil, C_1-C_6-alkiloxikarbonil, C_1-C_6-alkiloxikarbonil C_1-C_6-alkil, aminokarbonil, aminokarbonil C_1-C_6-alkil, C_1-C_6-alkilaminokarbonil, C_1-C_6-alkilaminokarbonil (C_1-C_6-alkil), di(C_1-C_6-alkil)aminokarbonil, di(C_1-C_6-alkil)aminokarbonil (C_1-C_6-alkil), fenil, fenil C_1-C_6-alkil, előnyösebben R^6 hidrogén vagy C_1-C_6-alkil, még előnyösebben hidrogén,

R^7 hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

n 2 vagy 3,

Y^1 C vagy N, ahol C szubsztituálva van R^{12}-vel, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, Cikloalkil, Cikloalkiloxi, nitrilo, nitro, amino, C_1-C_6-alkilamino,

di(C_1-C_6-alkil)amino, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil,

Y^2 C vagy N, előnyösen C, ahol C szubsztituálva van R^{15}-al, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, Cikloalkil, Cikloalkiloxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

Y^3 C vagy N, előnyösen C, ahol C szubsztituálva van R^{15}-el, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, Cikloalkil, Cikloalkiloxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal,

Y^4 C vagy N, előnyösen C, ahol C szubsztituálva van R^{15}-el, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil,

vagy Y^1 és Y^2 és/vagy Y^3 és Y^4 össze vannak kapcsolva, hogy 5- vagy 6-tagú gyűrű rendszert alkossanak.

4. A 3. igénypont szerinti vegyület, ahol

R^1 C_1-C_6-alkil, C_1-C_6-alkiloxi C_1-C_6-alkil, vagy C_1-C_6-alkiltio C_1-C_6-alkil, ahol szénatomos gyökök mindegyike szubsztituálatlan vagy szubsztituált egy vagy több halogén atommal, előnyösen egy vagy több fluor atommal, pl. 1-től 10-ig, előnyösen 1-től 5-ig, fluor atommal,

Y^1 C vagy N, ahol C szubsztituálva van R^{15}-el, amely H, vagy C_1-C_6-alkil,

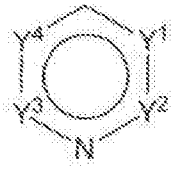
Y^2 C, ahol C szubsztituálva van R^{15}-al, amely H, C_1-C_6-alkil, C_1-C_6-alkoxi, C_1-C_6-alkil karbonil, Cikloalkil, Cikloalkiloxi, C_1-C_6-alkiltio

Y^3 C, ahol C szubsztituálva van R^{15}-el, amely H, C_1-C_6-alkil, C_1-C_6-alkoxi, C_1-C_6-alkil karbonil, Cikloalkil, Cikloalkiloxi, C_1-C_6-alkiltio

Y^4 C, ahol C szubsztituálva van R^{15}-el, amely H, C_1-C_6-alkil, C_1-C_6-alkoxi, C_1-C_6-alkiltio

vagy Y^1 és Y^2 vagy Y^3 és Y^4 össze vannak kapcsolva, hogy 5- vagy 6-tagú gyűrű rendszert alkosson.

5. Az 1-4. igénypontok bármelyike szerinti vegyület, ahol a képlet (A) szerinti csoport



képlet (A)

piridin, pirimidin, kinolin, kinazolin, thienopirimidin, thienopiridin, triazolopirimidin, piridopiridin, pirrolopiridin, pirazolopirimidin, pirazolopiridin, furopiridin, 2,3-dihidrofuropiridin, 2,3-dihidro-1,4-dioxinopiridin, furopirimidin, piridazin vagy cinnolin csoport, ahol mindegyik csoport opcionálisan szubsztituált egy vagy több gyökkel, előnyösen egy vagy két gyökkel,, amely ki van választva a következőkből álló csoportból: C_1-C_6-alkil, Cikloalkil, Cikloalkiloxi, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, halogén, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil , tiol, hidroxi, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, dioxolán, dioxán, vagy dioxepán, ahol mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal.

6. Az 1-5. igénypontok bármelyike szerinti vegyület, ahol

R^2 hidrogén,

R^3 hidrogén,

R^4 hidrogén vagy C_1-C_6-alkil,

R^5 hidrogén vagy C_1-C_6-alkil,

R^6 hidrogén vagy C_1-C_6-alkil,

R^7 hidrogén,

X karbonil csoport,

n 2,

a képlet (A) szerinti csoport a következőket reprezentálja: piridin, pirimidin vagy kinolin csoport, előnyösen piridin vagy pirimidin csoport, előnyösebben piridin csoport, ahol mindegyik csoport opcionálisan szubsztituált egy vagy több gyökkEl, előnyösen egy vagy két gyökkel, amely ki van választva a következőkből álló csoportból: C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, Cikloalkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tio, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, dioxolán, dioxán, vagy dioxepán, ahol mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal, és

A és B közül egy és D és E közül egy tartalmaz nitrogén atomot.

7. A gyógyszerészeti kompozíció, ahol a kompozíció tartalmaz:

a) egy vagy több vegyületet, amelyeket az 1-6. igénypontok közül egy vagy több definiál, és

b) egy vagy több gyógyszerészetileg elfogadható excipienst és/vagy egy vagy több gyógyszerészetileg elfogadható hatóanyagot, amelyek különböznek szerkezetben a) komponenstől.

8. A képlet (I-IV) szerinti vegyület, ahol Y^1, Y^2, Y^3 és Y^4 C, amely szubsztituálva van a következővel: R^{12}, R^{13}, R^{14} ill. R^{15} és amelyek ki vannak választva a következőkből álló csoportból: halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil és fenil, és ahol R^{12} és R^{13} legalább egyike, C_1-C_6-alkoxi vagy C_1-C_6-haloalkoxi, és B N, A N vagy kötés, n 2, R^6 és R^7 H, és R^4 és R^5 az 1-6. igénypontok bármelyikében van definiálva.

9. A képlet (3-IV) szerinti vegyület, ahol Y^1, Y^2, Y^3 és Y^4 C, amely szubsztituálva van a következővel: R^{12}, R^{13} R^{14} ill. R^{15} és amelyek ki vannak választva a következőkből álló csoportból: halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil vagy fenil, és ahol R^{12} és R^{13} legalább egyike C_1-C_6-alkoxi vagy C_1-C_6-haloalkoxi, és B N, A N vagy kötés, n 2 vagy 3, R^6 és R^7 H, és R^4 és R^5 az 1-6. igénypontok bármelyikében van definiálva.

10. A képlet (4-II) szerinti vegyület, ahol Y^1, Y^2, Y^3 és Y^4 C, amely szubsztituálva van a következővel: R^{12}, R^{13}, R^{14} ill. R^{15} és amelyek ki vannak választva a következőkből álló csoportból: halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil vagy fenil, és ahol R^{12}és R^{13} legalább egyike C_1-C_6-alkoxi vagy C_1-C_6-haloalkoxi, és B N, A N vagy kötés, n 2 vagy 3, R^6 és R^7 H, és R^4 és R^5 az 1-6. igénypontok bármelyikében van definiálva.

11. Az 1-6. igénypontok bármelyike szerinti vegyület, vagy a 7. igénypont szerinti gyógyszerészeti kompozíció, felhasználásra gyógyszer készítésére.

12. Az 1-6. igénypontok bármelyike szerinti vegyület, vagy a 7. igénypont szerinti gyógyszerészeti kompozíció, felhasználásra parazita fertőzések kezelésére.

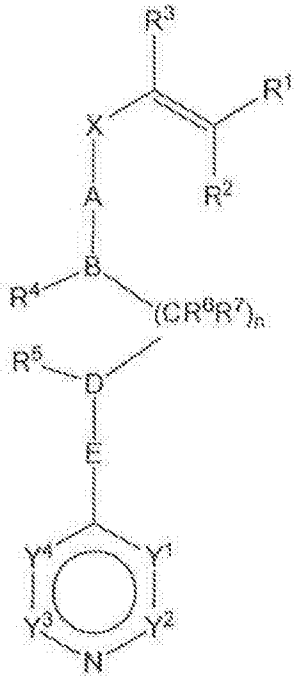
13. Az 1-6. igénypontok bármelyike szerinti vegyület felhasználása vagy a 7. igénypont szerinti gyógyszerészeti kompozíció felhasználása, gyógyszer előállítására, amely nem emberi állatok parazita fertőzéseinek kezelésére szolgál.

14. Készlet, ahol a készlet tartalmaz:

a) egy vagy több vegyületet, amely az 1-6. igénypontok egyike vagy többike szerint van definiálva, és

b) egy vagy több más összetevőt, amely ki van választva a következőkből álló csoportból: excipiens, hatóanyag, berendezés a) összetevő szerinti vegyület kombinálására excipienssel és/vagy hatóanyaggal, berendezés a) összetevő szerinti vegyület adagolására állat számára, és diagnosztikai eszköz.

15. Képlet (I a) szerinti vegyület és annak gyógyszerészetileg elfogadható szolvátjai, N-oxidjai és sói



képlet (I a)

, ahol

R^1 hidrogén, halogén, C_1-C_6-alkil, cikloalkil, C_1-C_6-alkiloxi, cikloalkiloxi, C_1-C_6-alkiltio, cikloalkiltio, C_2-C_6-alkenil, C_2-C_6-alkynil, C_1-C_6-alkiloxi C_1-C_6-alkil, cikloalkiloxi C_1-C_6-alkil, C_1-C_6-alkiloxi cikloalkil, cikloalkiloxi cikloalkil, C_1-C_6-alkiltio C_1-C_6-alkil, cikloalkiltio C_1-C_6-alkil, C_1-C_6-alkiltio cikloalkil, cikloalkiltio cikloalkil, amino, C_1-C_6-alkilamino, cikloalkilamino, di-(C_1-C_6-alkil)amino, di-(cikloalkil)amino, C_1-C_6-alkil-cikloalkilamino, C_1-C_6-alkilamino-C_1-C_6-alkil, cikloalkilamino-C_1-C_6-alkil, C_1-C_6-alkilamino-cikloalkil, cikloalkilamino-cikloalkil, di-(C_1-C_6-alkil)amino-C_1-C_6-alkil, di-(C_1-C_6-alkil)amino-cikloalkil, di-(cikloalkil)amino-C_1-C_6-alkil, di-(cikloalkil)amino-cikloalkil, C_1-C_6-alkil-cikloalkilamino-C_1-C_6-alkil, C_1-C_6-alkil-cikloalkilamino-cikloalkil, C_1-C_6-alkil karbonil, cikloalkilkarbonil, C_1-C_6-alkiloxi karbonil, cikloalkoxi karbonil, C_2-C_6-alkenil karbonil, ahol szénatartalmú gyökök mindegyike opcionálisan szubsztituálva van egy vagy több halogén atommal, előnyösen fluor atommal, vagy R^1 fenil, furanil, imidazolinil, vagy tiofenil, ahol a gyűrűk mindegyike opcionálisan szubsztituálva van egy vagy több gyökkel a következő csoportból: C_1-C_6-alkil, cikloalkil és halogén, előnyösen fluor,

R^2 hidrogén, halogén, C_1-C_6-alkil, cikloalkil, C_1-C_6-alkiloxi, cikloalkiloxi, C_1-C_6-alkiltio, cikloalkiltio, C_2-C_6-alkenil, C_2-C_6-alkynil, C_1-C_6-alkiloxi C_1-C_6-alkil, cikloalkiloxi C_1-C_6-alkil, C_1-C_6-alkiloxi cikloalkil, cikloalkiloxi cikloalkil, C_1-C_6-alkiltio C_1-C_6-alkil, cikloalkiltio C_1-C_6-alkil, C_1-C_6-alkiltio cikloalkil, cikloalkiltio cikloalkil, amino, C_1-C_6-alkilamino, cikloalkilamino, di-(C_1-C_6-alkil)amino, di-(cikloalkil)amino, C_1-C_6-alkil-cikloalkilamino, C_1-C_6-alkilamino-C_1-C_6-alkil, cikloalkilamino-C_1-C_6-alkil, C_1-C_6-alkilamino-cikloalkil, cikloalkilamino-cikloalkil, di-(C_1-C_6-alkil)amino-C_1-C_6-alkil, di-(C_1-C_6-

alkil)amino-cikloalkil, di-(cikloalkil)amino-C_1-C_6-alkil, di-(cikloalkil)amino-cikloalkil, C_1-C_6-alkil-cikloalkilamino-C_1-C_6-alkil, C_1-C_6-alkil-cikloalkilamino-cikloalkil, C_1-C_6-alkil karbonil, cikloalkilkarbonil, C_1-C_6-alkiloxi karbonil, cikloalkoxi karbonil, C_2-C_6-alkenil karbonil, ahol széntartalmú gyökök mindegyike opcionálisan szubsztituálva van egy vagy több halogén atommal, előnyösen fluor atommal, vagy R^2 fenil, furanil, imidazolinil, vagy tiofenil, ahol a gyűrűk mindegyike opcionálisan szubsztituálva van egy vagy több gyökkel, a következő csoportból: C_1-C_6-alkil, cikloalkil és halogén, előnyösen fluor, előnyösen R^2 hidrogén,

R^3 hidrogén, C_1-C_6-alkil vagy cikloalkil, előnyösen hidrogén,

R^4 hidrogén, C_1-C_6-alkil vagy cikloalkil előnyösen hidrogén,

R^5 hidrogén, C_1-C_6-alkil, cikloalkil vagy acil,

R^6 hidrogén, C_1-C_6-alkil, cikloalkil, hidroxi, C_1-C_6-alkiloxi, fenil C_1-C_6-alkiloxi, hidroxi C_1-C_6-alkil, C_1-C_6-alkiloxi C_1-C_6-alkil, fenil C_1-C_6-alkiloxi C_1-C_6-alkil, tiol C_1-C_6-alkil, C_1-C_6-alkiltio C_1-C_6-alkil, fenil C_1-C_6-alkiltio C_1-C_6-alkil, hidroxikarbonil, hidroxikarbonil C_1-C_6-alkil, C_1-C_6-alkiloxikarbonil, C_1-C_6-alkiloxikarbonil C_1-C_6-alkil, aminokarbonil, aminokarbonil C_1-C_6-alkil, C_1-C_6-alkilaminokarbonil, C_1-C_6-alkilaminokarbonil (C_1-C_6-alkil), di(C_1-C_6-alkil)aminokarbonil, di(C_1-C_6-alkil)aminokarbonil (C_1-C_6-alkil), C_1-C_6-alkilamino C_1-C_6-alkil, di(C_1-C_6-alkil)amino C_1-C_6-alkil, fenil, fenil C_1-C_6-alkil, ahol mindegyik fenil csoport opcionálisan szubsztituálva van a következővel: hidroxil, C_1-C_6-alkiloxi vagy cikloalkiloxi,

R^7 hidrogén, C_1-C_6-alkil vagy cikloalkil,

vagy R^6 és R^7 együtt reprezentál oxo-csoportot vagy tioxo-csoportot, vagy R^5 össze van kapcsolva R^8-al, hogy C_1-C_3-alkilén csoportot alakosson és R^7 össze van kapcsolva R^8-el, hogy C_1-C_3-alkilén csoportot alkosson, ahol a C_1-C_3-alkilén csoportok közül egy vagy mindkettő opcionálisan szubsztituálva van egy vagy több C_1-C_6-alkil vagy cikloalkil gyökkel,

n egész 1-től 3-ig,

X karbonil vagy szulfonil csoport, előnyösen karbonil csoport,

A kötés vagy NR^8, ahol R^8 hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

E kötés vagy NR^9, ahol R^9 hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

B N vagy CR^{10}, ahol R^{10} hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

D N vagy CR^{11}, ahol R^{11} hidrogén vagy C_1-C_6-alkil, előnyösen hidrogén,

Y^1 C vagy N, ahol C szubsztituálva van R^{12}-vel, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, cikloalkil, cikloalkiloxi, cikloalkilamino, (C_1-C_6-alkil)-(cikloalkil)amino, cikloalkiltio, fenil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal vagy cikloalkillal,

Y^2 C vagy N, ahol C szubsztituálva van R^{13}-al, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tiol, hidroxi, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-

alkilkarbonilamino, C_1-C_6-alkoxikarbonil, cikloalkil, cikloalkiloxi, cikloalkilamino, (C_3-C_6-alkil)-(cikloalkil)amino, cikloalkiltio, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal vagy cikloalkillal,

Y^3 C vagy N, ahol C szubsztituálva van R^{14}, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, tiol, hidroxi, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, cikloalkil, cikloalkiloxi, cikloalkilamino, (C_1-C_6-alkil)-(cikloalkil)amino, cikloalkiltio, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal vagy cikloalkillal,

Y^4 C vagy N, ahol C szubsztituálva van R^{15}, amely hidrogén, halogén, C_1-C_6-alkil, C_1-C_6-haloalkil, C_1-C_6-alkoxi, C_1-C_6-haloalkoxi, nitrilo, nitro, amino, C_1-C_6-alkilamino, di(C_1-C_6-alkil)amino, N-pirrolidinil, N-piperidinil, N-morfolinil, C_1-C_6-alkiltio, C_1-C_6-alkil karbonil, C_1-C_6-haloalkil karbonil, C_1-C_6-alkilkarbonilamino, aminokarbonil, C_1-C_6-alkilaminokarbonil, di(C_1-C_6-alkil)aminokarbonil, C_1-C_6-alkoxikarbonil, cikloalkil, cikloalkiloxi, cikloalkilamino, (C_1-C_6-alkil)-(cikloalkil)amino, cikloalkiltio, fenil, dioxolán, mint 1,3-dioxolán, dioxán, mint 1,3-dioxán, vagy dioxepán, mint 1,3-dioxepán, mindegyik gyűrű szubsztituálatlan vagy szubsztituált C_1-C_6-alkillal vagy cikloalkillal,

vagy Y^1 és Y^2 és/vagy Y^3 és Y^4 össze vannak kapcsolva, hogy gyűrű rendszert alkossanak,

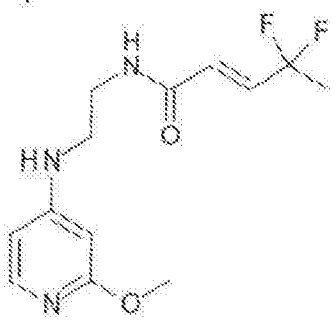
és ahol B és D legalább egyike nitrogén atom, felhasználásra helmint infekció kezelésére.

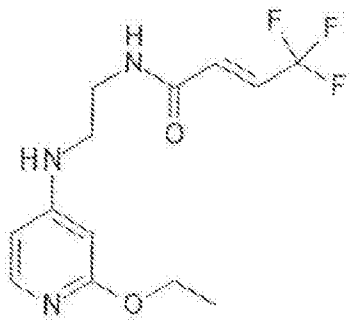
16. Antihelmint kompozíció, ahol a kompozíció tartalmaz:

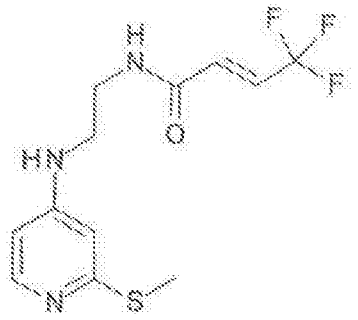
a) a 15. igénypont szerinti egy vagy több vegyületet; és

b) egy vagy több gyógyszerészetileg elfogadható excipienst és/vagy egy vagy több gyógyszerészetileg elfogadható hatóanyagot, amelyek különböznek a 15. igénypont szerinti egy vagy több vegyülettől.

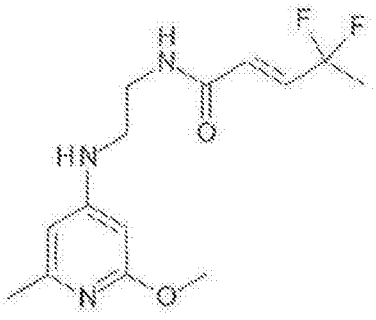
17. Az 1. igénypont szerinti vegyület, ahol vegyületnek szerkezete van, amely ki van választva következőkből álló csoportból:



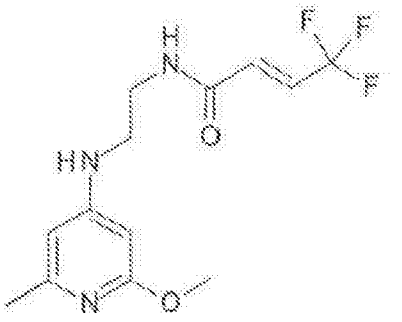




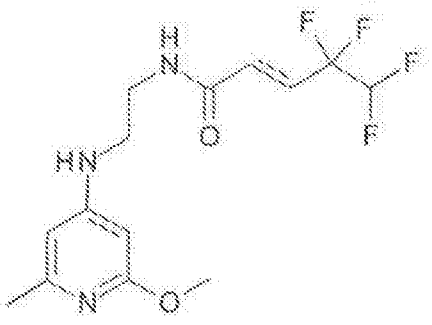
,



,



,



, vagy