

ANTHELMINTIC PYRROLOPYRIDAZINE COMPOUNDS

FIELD OF THE INVENTION

This patent application relates to new antiparasitic compounds, compositions comprising the compounds, and methods of using the compounds to prevent, treat and/or control parasites that
5 harm animals and humans.

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of priority to U.S. Provisional Application No. 63/263,367 filed on November 1, 2021, which is incorporated herein by reference in its entirety.

INCORPORATION BY REFERENCE

10 All references cited herein, are incorporated by reference herein, in their entirety.

BACKGROUND OF THE INVENTION

Animals, such as mammals and birds, are often susceptible to parasite infestations. These parasites may be ectoparasites, such as fleas and ticks. Animals and humans also suffer from endoparasitic infections including, for example, helminthiasis which is most frequently caused by
15 a group of parasitic worms described as nematodes or roundworms. These parasites cause severe economic losses in pigs, sheep, horses, and cattle as well as affecting companion animals (e.g. cats and dogs) and poultry. Endoparasites include those which occur in the gastrointestinal tract of animals and humans such as from the genera *Ancylostoma*, *Necator*, *Ascaris*, *Strongyloides*, *Trichinella*, *Capillaria*, *Toxocara*, *Toxascaris*, *Trichuris* and *Enterobius*. Other parasites which
20 are found in the blood or other tissues and organs include filarial worms and the extra intestinal stages of *Strongyloides* and *Trichinella*.

One type of endoparasite which seriously harms mammals is *Dirofilaria immitis*, also known as Heartworm. Other filarial endoparasites include *Dirofilaria repens* and *Dirofilaria honkongensis*, which can also infect humans. The most common hosts are dogs and cats but other
25 mammals such as ferrets and raccoons may also be infected. Heartworms go through several life stages before they become adults infecting the pulmonary artery of the host mammal. The worms require the mosquito as an intermediate host to complete their life cycle. The period between the

initial infection when the dog is bitten by a mosquito and the maturation of the worms into adults living in the heart and pulmonary arteries is six to seven months in dogs and is known as the "prepatent period." L3 larvae migrate during blood feeding of the mosquito to the tip of the mosquito's mouth parts (labium), leave the mosquito, and are deposited on the skin of the dog where they then migrate through the bite wound into the host. Most L3 larvae molt to fourth-stage larvae (L4s) in canine subcutaneous tissues within 1-3 days after infection. Then, they migrate to the muscles of the chest and abdomen, and 45 to 60 days after infection, molt to the fifth stage (L5, immature adult). Between 75 and 120 days after infection, these immature heartworms then enter the bloodstream and are carried through the heart to reside in the pulmonary artery. Around seven months after infection, *Dirofilaria immitis* adults reach maturity and sexually reproduce in the pulmonary arteries and right ventricle. Adult males are around 15cm in length, and females are around 25cm in length and their normal life span as adults is calculated to be about 5 years.

Heartworm infection is a severe and life-threatening disease. Canine heartworm infection is preventable and prophylaxis treatment is a priority in heartworm endemic areas. Treatment of mature heartworm infection with an adulticide (e.g. melarsomine dihydrochloride) is costly and can cause serious adverse side effects, thus prevention by monthly administration of drugs that interrupt larvae development is widely used. The goal of marketed heartworm preventive therapies in dogs is to prevent the development of the parasite to adult heartworms by interrupting the *Dirofilaria immitis* life cycle post-infection.

The macrocyclic lactones (MLs, e.g. ivermectin, eprinomectin, milbemycin oxime, moxidectin, and selamectin) are the most commonly used chemoprophylaxis agents and are administered at monthly or six-month intervals. These drugs have been effective against *Dirofilaria immitis* infective third-stage larvae (L3) deposited by the mosquito as well as maturing fourth-stage larvae (L4). When administered monthly, MLs kill L3 and L4 larvae acquired within the previous 30 days, and thus prevent disease caused by adult worms. MLs can also be used monthly in infected dogs to suppress reproduction in adult worms and remove microfilariae, thereby reducing transmission and gradually causing the attrition of adult worms (*Vet. Parasitol.* 2005 Oct 24 133(2-3) 197-206).

In recent years, an increased number of lack of efficacy (LOE) cases have been reported, in which dogs develop mature heartworm infections despite receiving monthly prophylactic doses of macrocyclic lactone drugs. For example, Atkins et al., (*Vet. Parasitol.* 206 (2014) 106–113) recently reported that an increasing number of cases of dogs that tested heartworm antigen positive while receiving heartworm preventive medication which suggests that some populations of *Dirofilaria immitis* have developed selectional resistance to heartworm preventives (see also Blagburn et al., “Evidence of genetic selection following treatment of heartworm-infected, microfilaremic dog with increasing dosages of ivermectin,” 58th annual meeting of American Association of Veterinary Parasitologists, p. 64, 20-23 July, 2013 American Heartworm Society, 2010. Heartworm Preventive Resistance. Is it Possible, vol. 37. Bulletin of the American Heartworm Society, pp. 5.). Bowman also reviews various studies in which LOE to macrocyclic lactone treatment have been observed from peer-reviewed journals, reports to the Center for Veterinary Medicine (CVM) of the Food and Drug Administration in the U.S. (Bowman, *Parasites & Vectors* **2012**, 5:138). Pulaski et al. described the establishment of macrocyclic lactone resistant *Dirofilaria immitis* isolates in experimentally infected dogs (Pulaski et al., *Parasites & Vectors* 2014, 7:494). Similarly, Snyder et al. report a controlled laboratory study with a recent isolate of *Dirofilaria immitis*, in which treatment with ivermectin and milbemycin oxime did not prevent maturation of inoculated L3 stage larvae. Blagburn et al. describe the comparison of four commercial heartworm preventative therapies against the MP3 laboratory strain of *Dirofilaria immitis* in which three of four products failed to prevent infections with adult heartworms (Blagburn et al., *Veterinary Parasitology*, 2011, 176, 189-194. Further reports of evidence of macrocyclic lactone resistant isolates of *Dirofilaria immitis* are reported in Bourguinat et al., *Veterinary Parasitology*, 2011, 181, 388-392; Geary et al., *Topics in Companion Animal Medicine*, 2011, vol. 26, no. 4, p. 187; *Trends in Parasitology*, October 2004, vol. 20, no. 10, p. 477; Bourguinat et al., *Veterinary Parasitology*, 2011, 176, p. 374-381. In addition, WO 2016/161369 describes in the examples a study in which treatment of dogs infected with L3 stage *Dirofilaria immitis* of the JYD-34 isolate were treated with an ivermectin oral solution, Profender[®] Tablets (emodepside + praziquantel) or a combination of an ivermectin oral solution and Profender[®] Tablets at two dosages. The ivermectin and Profender[®] Tablet groups resulted in less than 50% efficacy and the lower dosage of the ivermectin + Profender[®] Tablet group resulted in only 81%

efficacy. Thus, there is an ongoing need to develop new anthelmintic agents with improved activity against *Dirofilaria immitis* and other endoparasites.

WO 2017/178416 A1 provides pyrazolopyrimidine derivatives for the control, treatment and/or prevention of helminths. This publication describes anthelmintic compounds having a
5 different 5-6 fused nitrogen-containing heteroaryl core.

WO 2018/197401 A1 provides bicyclic pyrazole derivatives for the control, treatment and/or prevention of helminths.

WO 2018/087036 A1 provides quinolone-3-carboxamide derivatives for the control, treatment and/or prevention of helminths.

10 WO 2019/025341 provides quinoline compounds for the treatment, control and/or prevention of helminth infections and WO 2019/002132 A1 describes azaquinone derivatives for the control, treatment and/or prevention of helminths. WO 2019/215182 A1 also describes quinoline derivatives for the treatment and control of helminth infections.

15 WO 2020/083971 A2 describes additional carboxamide compounds substituted with bicyclic ring systems for the treatment and control of parasitic infections.

WO 2021/204930 describes substituted condensed azines containing a bicyclic nitrogen-containing bicyclic ring system that have anthelmintic properties.

20 WO 2021/018839 A1 describes isoquinoline derivatives for use in the treatment of parasite infections; and WO 2019/115768 A1 describes a process for preparing anthelmintic 4-amino-quinoline-3-carboxamide derivatives.

WO 2020/131629 A1, WO 2020/131631 A1 and WO 2020/247747 A1 describes bicyclic derivatives which are useful in the control of endoparasites, including heartworm, in warm-blooded animals.

25 WO 2021/122906 A1 describes anthelmintic compounds comprising azaindole compounds and WO 2021/122911 A1 describes quinoline compounds that are useful for the treatment of disease caused by helminths such as *Dirofilaria immitis*.

WO 2020/014068 A1 describes anthelmintic heterocyclic compounds having a core having a core bicyclic pyrazolo[1,5-a]pyridine ring system that were found to be active against *Dirofilaria immitis*. The pyrazolo[1,5-a]pyridine ring system of the compounds described in this publication is a 5-6-fused ring system having two nitrogen atoms, one at the 5-6 ring junction and the other in the 5-membered ring.

WO 2020/191091 A1 describes aza-benzothiophene and aza-benzofuran compounds that are useful for the control or prevention of parasitic infections, including against infections by *Dirofilaria immitis*.

WO 2022/106469 A2 describes N-(2,3-Dihydro-1,4-benzoxazin-4-yl)-3-isopropyl-7-(2,3,5-trifluorophenyl)benzo-thiophene-2-carboxamide derivatives and similar compounds for the treatment of heartworm infections.

WO 2022/117783 A1 describes bicyclic compounds of formula (I) and (I') disclosed for the treatment and/or control of endoparasite infections in warm-blooded animals.

WO 2022/122987 A1 describes anthelmintic compounds comprising a pyridine structure for the treatment of heartworm disease caused by *Dirofilaria immitis*.

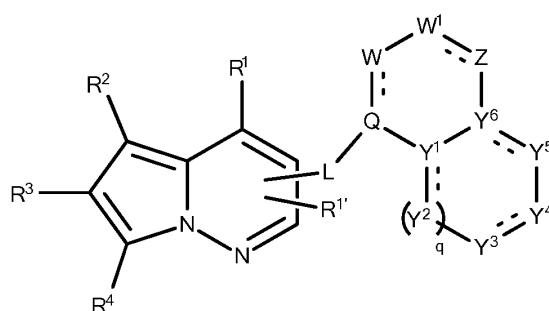
WO 2022/122988 A1 describes anthelmintic compounds comprising a thienopyridine structure for the treatment of heartworm disease caused by *Dirofilaria immitis*.

WO 2022/152918 A1 describes azaquinazoline derivatives for use in treating or preventing *Dirofilaria immitis* infections in a mammal.

SUMMARY OF THE INVENTION

The present application provides for novel anthelmintic and antiparasitic pyrrolopyridazine heterocyclic compounds with improved activity against endoparasites. The application is also directed to compositions comprising the compounds, methods and uses of the compounds for eradicating, controlling, and/or preventing a parasitic infection and/or infestation in animals including humans. The compounds may be administered to animals, particularly mammals, fish and birds, to treat, control and/or prevent parasitic infections.

An aspect of the present invention includes a compound of Formula (I):



(I)

or salt thereof, wherein variables R¹, R^{1'}, R², R³, R⁴, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, L, Q, W, W¹, Z and q are defined herein, and the dashed bonds (---) signifies a single or double bond.

5 The invention also includes a composition comprising a compound of Formula (I), or a salt thereof, and a pharmaceutically acceptable carrier. The compounds and compositions of the invention may be administered to animals, particularly mammals, fish and birds, to prevent, control and/or treat parasitic infections in animals. In particular, the compounds and compositions of the invention may be administered to cats, dogs, horses, chickens, pigs, sheep and cattle, with the aim
10 of substantially ridding these hosts of endoparasites.

In an embodiment, compounds of Formula (I) and compositions comprising said compounds are effective against endoparasites, such as filariae (e.g. *Dirofilaria immitis*), and nematodes including, but not limited to, hookworms, whipworms and roundworms of the digestive tract of animals and humans. In certain embodiments, compounds of Formula (I) and compositions
15 comprising said compounds are effective against *Dirofilaria immitis* (heartworm) isolates that are less sensitive to treatment with macrocyclic lactones. In another embodiment, the compounds and compositions of the invention are effective for treating, controlling and/or preventing infections of animals with nematodes that are less sensitive to treatment with commercially available or known active agents.

20 In an embodiment, the invention includes a combination of a compound of Formula (I) with at least a second active agent, which may broaden the scope of protection afforded to animals against endoparasites and/or ectoparasites.

Another embodiment includes a method for the treatment, control and/or prevention of a parasitic infection in an animal comprising administering a compound of Formula (I) to the animal. Another embodiment includes a use of a compound of Formula (I) for the treatment, control and/or prevention of a parasitic infection in an animal and the use of the compound of Formula (I) in the preparation of a medicament for the treatment, control and/or prevention of a parasitic infection in an animal.

Thus, the invention includes the following non-limiting embodiments:

- (a) a compound of Formula (I), or a salt thereof, which is an active endoparasiticide;
- 10 (b) a veterinary composition comprising a parasitically effective amount of a compound of Formula (I), or a salt thereof, in combination with a pharmaceutically acceptable carrier or diluent;
- (c) a veterinary composition comprising a parasitically effective amount of a compound of Formula (I), or a salt thereof, in combination with one or more additional active agents (*i.e.*, active ingredient not encompassed by Formula (I)) and a pharmaceutically acceptable carrier or diluent;
- 15 (d) a method for treating a parasitic infection and/or infestation in or on an animal comprising administering a parasitically effective amount a compound of Formula (I), or a salt thereof, optionally with one or more additional active agents (*i.e.*, active ingredient not encompassed by Formula (I)), to the animal in need thereof;
- 20 (e) a method for the prevention of a parasitic infection and/or infestation of an animal, which comprises administering a parasitically effective amount of a compound of Formula (I), or a salt thereof, optionally with one or more additional active agents (*i.e.*, active ingredient not encompassed by Formula (I)), to the animal in need thereof;
- 25 (f) a compound of Formula (I), or a salt thereof, optionally with one or more additional active agents (*i.e.*, active ingredient not encompassed by Formula (I)),

for use in the treatment, control and/or prevention of a parasitic infection and possibly also a parasitic infestation in an animal;

- 5 (g) a use of a compound of Formula (I), or a salt thereof, optionally with one or more additional active agents (*i.e.*, active ingredient not encompassed by Formula (I)), for the manufacture of a veterinary medicament for the treatment, control and/or prevention of a parasitic infection and/or infestation in an animal; and
- (h) a method of preparation of the compounds of Formula (I).

DEFINITIONS:

10 It is noted that in this disclosure and particularly in the claims and/or paragraphs, terms such as "comprises", "comprised", "comprising" and the like can be interpreted as "includes", "included", "including", and the like; and that terms such as "consisting essentially of" and "consists essentially of" are interpreted as allowing for elements not explicitly recited, but excluding elements that are found in the prior art or that affect a basic or novel characteristic of the invention.

15 Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this invention belongs at the time of filing. Terms not specifically defined herein should be given the meanings that would be given to them by one of skill in the art in light of the disclosure and the context. The meaning and scope of terms should be clear; however, in the event of any latent ambiguity, definitions

20 provided herein take precedent over any dictionary or extrinsic definition. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Herein, the use of "or" means "and/or" unless stated otherwise. Furthermore, the use of the term "including", as well as other forms such as "includes" and "included" is not limiting. As used in the specification, however, unless specified to the contrary, the following terms have

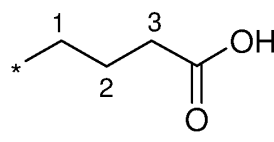
25 the meaning indicated and the following conventions are adhered to.

In the groups, radicals, or moieties defined herein, the number of carbon atoms is often specified preceding the group, for example, C₁₋₆-alkyl means an alkyl group or radical having 1 to 6 carbon atoms. In general, in groups like HO, H₂N, (O)S, (O)₂S, NC (cyano), HOOC, F₃C or the

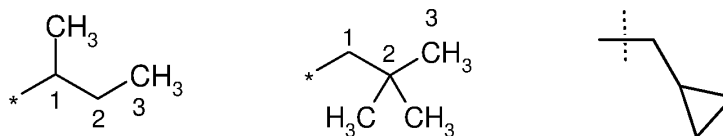
like, the skilled artisan can see the radical attachment point(s) to the molecule from the free valences of the group itself. For combined groups comprising two or more subgroups, the last-named subgroup is the radical attachment point, for example, the substituent "aryl-C₁₋₃-alkylene" means an aryl group which is bound to a C₁₋₃-alkyl-group, the latter of which is bound to the core or to the group to which the substituent is attached.

In case a compound of the present invention is depicted in the form of a chemical name and as a formula, in case of any discrepancy the formula shall prevail. An asterisk may be used in sub-formulas to indicate the bond which is connected to the core molecule as defined.

The numeration of the atoms of a substituent starts with the atom which is closest to the core or to the group to which the substituent is attached. For example, the term "3-carboxypropyl-group" represents the following substituent:



wherein the carboxy group is attached to the third carbon atom of the propyl group. The terms "1-methylpropyl-", "2,2-dimethylpropyl-" or "cyclopropylmethyl-" group represent the following groups:



The asterisk or “*” may be used in sub-formulas to indicate the bond which is connected to the core molecule as defined.

The term "substituted" as used herein, means that one or more hydrogens on the designated atom are replaced by a group selected from a defined group of substituents, provided that the designated atom's normal valence is not exceeded, and that the substitution results in a stable compound. Likewise, the term “substituted” may be used in connection with a chemical moiety instead of a single atom, e.g. “substituted alkyl”, “substituted aryl” or the like.

- Unless indicated otherwise for a specific embodiment of the invention, the term “optionally substituted” as used herein is meant to indicate that a given radical is optionally substituted by one or more of the following moieties: halogen, hydroxyl, oxo (C=O), alkyl, haloalkyl, cycloalkyl, cycloalkenyl, carboxyl, acyl, acyloxy, acetyl, alkylcarbonyl, haloalkylcarbonyl, alkoxy carbonyl, haloalkoxy carbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, haloalkylaminocarbonyl, dihaloalkylaminocarbonyl, amino, alkyl- or dialkylamino, amido, arylamino, alkoxy, haloalkoxy, aryloxy, alkylthio, haloalkylthio, nitro, cyano, azido, thiol, thioamido, imino, amidino, guanidino, carbonate, R₃Si- or R₃SiO- where R is C₁-C₆-alkyl, C₁-C₆-haloalkyl or aryl, SF₅, sulfate, alkylsulfonyl, haloalkylsulfonyl, alkoxy sulfonyl, haloalkoxy sulfonyl, arylsulfonyl, alkylsulfinyl, haloalkylsulfinyl, arylsulfinyl, sulfamoyl, sulfoximine, sulfinimine, sulfonimidamide, sulfonediimine, phosphonyl, phosphinyl, phosphoryl, phosphine, phosphonamidate, phosphinamidate, phosphinate, phosphine oxide, thioester, anhydride, oxime, hydrazine, carbamate, phosphate, phosphonate, aryl, heteroaryl and heterocyclyl.
- In some embodiments, unless indicated otherwise for a specific embodiment of the invention, the term “optionally substituted” includes substitution of a core group with halogen (chloro, fluoro, bromo, iodo), hydroxyl, oxo, C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3- to 8-membered cycloalkyl, 5- to 8-membered cycloalkenyl, carboxyl, amino, amido, thioamide, imino, amidino, guanidino, carbonate, tri-C₁-C₆-alkylsilyl, tri-C₁-C₆-alkylsiloxyl, sulfate, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, phenylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, phenoxy, cyano, azido, thiol, nitro, SF₅, acetyl, C₁-C₆-alkoxy carbonyl, C₁-C₆-alkoxy carbonyloxy, C₁-C₆-haloalkoxy carbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylcarbonyloxy, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, aminocarbonyloxy, C₁-C₆-alkylaminocarbonyloxy, C₁-C₆-dialkylaminocarbonyloxy, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, phenylsulfinyl, C₁-C₆-alkylsulfonyl, phenylsulfonyl, C₁-C₆-alkoxy sulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl, C₁-C₆-haloalkylsulfonyl, C₁-C₆-haloalkoxy sulfonyl, phenyl, 5- or 6-membered heteroaryl, 5- or 6-membered heterocyclyl, sulfamoyl, sulfoximine, sulfinimine, sulfonimidamide, sulfonediimine, phosphonyl, phosphinyl, phosphoryl, phosphine, phosphonamidate, phosphinamidate, phosphinate, phosphine oxide, thioester, anhydride, oxime, hydrazine, carbamate, phosphate or phosphonate.

In other embodiments, unless indicated otherwise for a specific embodiment of the invention, the term “optionally substituted” includes substitution of a core group with halogen (chloro, fluoro, bromo, iodo), hydroxyl, C₁-C₃-alkyl, C₁-C₃-haloalkyl, 3- to 8-membered cycloalkyl, 5-8-membered cycloalkenyl, amino, C₁-C₃-alkylamino, C₁-C₃-dialkylamino, C₁-C₃-alkoxy, C₁-C₃-haloalkoxy, cyano, nitro, SF₅, acetyl, C₁-C₃-alkoxycarbonyl, C₁-C₃-haloalkoxycarbonyl, C₁-C₃-alkylcarbonyl, C₁-C₃-haloalkylcarbonyl, aminocarbonyl, C₁-C₃-alkylaminocarbonyl, C₁-C₃-dialkylaminocarbonyl, C₁-C₃-haloalkylaminocarbonyl, C₁-C₃-dihaloalkylaminocarbonyl, C₁-C₃-alkylthio, C₁-C₃-alkylsulfinyl, C₁-C₃-alkylsulfonyl, C₁-C₃-haloalkylthio, C₁-C₃-haloalkylsulfinyl, C₁-C₃-haloalkylsulfonyl, phenyl, 5- or 6-membered heteroaryl, 5- or 6-membered heterocyclyl.

In certain embodiments, unless indicated otherwise for a specific embodiment of the invention, the term “optionally substituted” includes substitution by halogen (chloro, fluoro, bromo and iodo), methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, hydroxyl, thiol, amino, methylamino, ethylamino, propylamino, butylamino, dimethylamino, diethylamino, methoxy, ethoxy, propoxy, CF₃, CF₂CF₃, -OCF₃, -OCF₂CF₃, -SCH₃, -SCF₃, -S(O)CH₃, -S(O)CF₃, -S(O)₂CH₃, -S(O)₂CF₃, aziridinyl, azetidiny, morpholino, piperidinyl, pyridyl and phenyl.

Unless specifically indicated, throughout the specification and the appended claims, a given chemical formula or name shall encompass tautomers and all stereo, optical and geometrical isomers (e.g. enantiomers, diastereomers, E/Z isomers etc.) and racemates thereof as well as mixtures in different proportions of the separate enantiomers, mixtures of diastereomers, or mixtures of any of the foregoing forms where such isomers and enantiomers exist, as well as solvates thereof such as for instance hydrates.

Unless specifically indicated, also “pharmaceutically acceptable salts” as defined in more detail below shall encompass solvates thereof such as for instance hydrates.

In general, substantially pure stereoisomers can be obtained according to synthetic principles known to a person skilled in the field, e.g. by separation of corresponding mixtures, by using stereochemically pure starting materials and/or by stereoselective synthesis. It is known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis, e.g. starting from optically active starting materials and/or by using chiral reagents.

Enantiomerically pure compounds of this invention or intermediates may be prepared via asymmetric synthesis, for example by preparation and subsequent separation of appropriate diastereomeric compounds or intermediates which can be separated by known methods (e.g. by chromatographic separation or crystallization) and/or by using chiral reagents, such as chiral starting materials, chiral catalysts or chiral auxiliaries.

Further, it is known to the person skilled in the art how to prepare enantiomerically pure compounds from the corresponding racemic mixtures, such as by chromatographic separation of the corresponding racemic mixtures on chiral stationary phases; or by resolution of a racemic mixture using an appropriate resolving agent, e.g. by means of diastereomeric salt formation of the racemic compound with optically active acids or bases, subsequent resolution of the salts and release of the desired compound from the salt; or by derivatization of the corresponding racemic compounds with optically active chiral auxiliary reagents, subsequent diastereomer separation and removal of the chiral auxiliary group; or by kinetic resolution of a racemate (e.g. by enzymatic resolution); by enantioselective crystallization from a conglomerate of enantiomorphous crystals under suitable conditions; or by (fractional) crystallization from a suitable solvent in the presence of an optically active chiral auxiliary.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of animals without excessive toxicity, irritation, allergic response, or other problem or complication, and commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salt" refers to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like.

For example, such salts include salts from benzenesulfonic acid, benzoic acid, citric acid, ethanesulfonic acid, fumaric acid, gentisic acid, hydrobromic acid, hydrochloric acid, maleic acid, malic acid, malonic acid, mandelic acid, methanesulfonic acid, 4-methyl-benzenesulfonic acid,

phosphoric acid, salicylic acid, succinic acid, sulfuric acid and tartaric acid. Further pharmaceutically acceptable salts can be formed with cations from ammonia, L-arginine, calcium, 2,2'-iminobisethanol, L-lysine, magnesium, *N*-methyl-D-glucamine, potassium, sodium and tris(hydroxymethyl)-aminomethane.

5 The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a sufficient amount of the appropriate base or acid in water or in an organic diluent such as ether, ethyl acetate, ethanol, isopropanol, or acetonitrile, or a mixture thereof.

10 Salts of other acids than those mentioned above which for example are useful for purifying or isolating the compounds of the present invention (e.g. trifluoro acetate salts,) also comprise a part of the invention.

The term "halogen" denotes fluorine, chlorine, bromine and iodine.

The term "C_{1-n}-alkyl", wherein n is an integer selected from 2, 3, 4, 5 or 6, preferably 4, 5,
15 or 6, either alone or in combination with another radical, denotes an acyclic, saturated, branched or linear hydrocarbon radical with 1 to n C atoms. For example the term C₁₋₅-alkyl embraces the radicals H₃C-, H₃C-CH₂-, H₃C-CH₂-CH₂-, H₃C-CH(CH₃)-, H₃C-CH₂-CH₂-CH₂-, H₃C-CH₂-CH(CH₃)-, H₃C-CH(CH₃)-CH₂-, H₃C-C(CH₃)₂-, H₃C-CH₂-CH₂-CH₂-CH₂-, H₃C-CH₂-CH₂-CH(CH₃)-, H₃C-CH₂-CH(CH₃)-CH₂-, H₃C-CH(CH₃)-CH₂-CH₂-,
20 H₃C-CH₂-C(CH₃)₂-, H₃C-C(CH₃)₂-CH₂-, H₃C-CH(CH₃)-CH(CH₃)- and H₃C-CH₂-CH(CH₂CH₃)-.

The term "C_{1-n}-alkylene", wherein n is an integer selected from 2, 3, 4, 5 or 6, preferably 4, 5 or 6, either alone or in combination with another radical, denotes an acyclic, saturated, branched or linear chain divalent alkyl radical containing from 1 to n carbon atoms. For example, the term C₁₋₄-alkylene
25 includes -CH₂-, -CH₂-CH₂-, -CH(CH₃)-, -CH₂-CH₂-CH₂-, -C(CH₃)₂-, -CH(CH₂CH₃)-, -CH(CH₃)-CH₂-, -CH₂-CH(CH₃)-, -CH₂-CH₂-CH₂-CH₂-, -CH₂-CH₂-CH(CH₃)-, -CH(CH₃)-CH₂-CH₂-, -CH₂-CH(CH₃)-CH₂-, -CH₂-C(CH₃)₂-, -C(CH₃)₂-CH₂-, -CH(CH₃)-CH(CH₃)-, -CH₂-CH(CH₂CH₃)-, -CH(CH₂CH₃)-CH₂-, -CH(CH₂CH₂CH₃)-, -CH(CH(CH₃))₂- and -C(CH₃)(CH₂CH₃)-.

The term “C_{2-m}-alkenyl” is used for a group “C_{2-m}-alkyl”, wherein m is an integer selected from 3, 4, 5 or 6, preferably 4, 5 or 6, if at least two carbon atoms of said group are bonded to each other by a double bond.

5 The term “C_{2-m}-alkenylene” is used for a group “C_{2-m}-alkylene”, wherein m is an integer selected from 3, 4, 5 or 6, preferably 4, 5 or 6, if at least two carbon atoms of said group are bonded to each other by a double bond.

The term “C_{2-m}-alkynyl” is used for a group “C_{2-m}-alkyl”, wherein m is an integer selected from 3, 4, 5 or 6, preferably 4, 5 or 6, if at least two carbon atoms of said group are bonded to each other by a triple bond.

10 The term “C_{2-m}-alkynylene” is used for a group “C_{2-m}-alkylene”, wherein m is an integer selected from 3, 4, 5 or 6, preferably 4, 5 or 6, if at least two of those carbon atoms of said group are bonded to each other by a triple bond.

15 The term “C_{3-k}-cycloalkyl”, wherein k is an integer selected from 4, 5, 6, 7 or 8, preferably 4, 5 or 6, either alone or in combination with another radical, denotes a cyclic, saturated, unbranched hydrocarbon radical with 3 to k C atoms. For example the term C₃₋₇-cycloalkyl includes cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl.

20 The term “C_{3-k}-cycloalkenyl”, wherein k is an integer selected from 4, 5, 6, 7 or 8, preferably 4, 5 or 6, either alone or in combination with another radical, denotes a cyclic, unsaturated, but non-aromatic, unbranched hydrocarbon radical with 3 to k C atoms, at least two of which are bonded to each other by a double bond. For example the term C₃₋₇-cycloalkenyl includes cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentadienyl, cyclohexenyl, cyclohexadienyl, cycloheptenyl, cycloheptadienyl and cycloheptatrienyl.

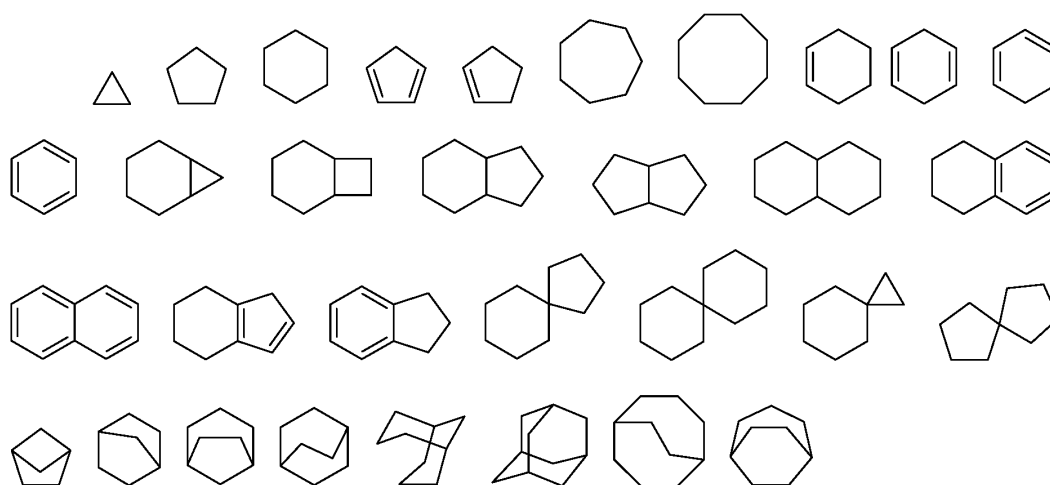
25 The term “halo” added to an “alkyl”, “alkylene”, “alkenyl”, “alkenylene”, “alkynyl”, “alkynylene”, “cycloalkyl”, “cycloalkenyl” or “alkoxy” group defines an alkyl, alkylene, alkenyl, alkenylene, alkynyl, alkynylene, cycloalkyl, cycloalkenyl or alkoxy group, wherein one or more hydrogen atoms are replaced by a halogen atom selected from among fluorine, chlorine, bromine or iodine, preferably fluorine and chlorine, particularly preferred is fluorine. For example C₁-C₄-

haloalkyl includes, but is not limited to, chloromethyl, bromomethyl, dichloromethyl, trichloromethyl, fluoromethyl, difluoromethyl, trifluoromethyl, chlorofluoromethyl, dichlorofluoromethyl, chlorodifluoromethyl, 1-chloroethyl, 1-bromoethyl, 1-fluoroethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 2-chloro-2-fluoroethyl, 2-chloro-2,2-difluoroethyl, 2,2-dichloro-2-fluoroethyl, 2,2,2-trichloroethyl, pentafluoroethyl and the like.

The term “fluoroalkyl” as used herein refers to an alkyl in which one or more of the hydrogen atoms is replaced with fluorine atoms, for example difluoromethyl, trifluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 1,1,2,2-tetrafluoroethyl or pentafluoroethyl.

The term “alkoxy” refers to an alkyl-*O*-, wherein alkyl is as defined above. Similarly, the terms “alkenyloxy”, “alkynyloxy”, “haloalkoxy”, “haloalkenyloxy”, “haloalkynyloxy”, “cycloalkoxy”, “cycloalkenyloxy”, “halocycloalkoxy”, and “halocycloalkenyloxy” refer to the groups alkenyl-*O*-, alkynyl-*O*-, haloalkyl-*O*-, haloalkenyl-*O*-, haloalkynyl-*O*-, cycloalkyl-*O*-, cycloalkenyl-*O*-, halocycloalkyl-*O*-, and halocycloalkenyl-*O*-, respectively, wherein alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, cycloalkyl, cycloalkenyl, halocycloalkyl, and halocycloalkenyl are as defined herein. Examples of C₁-C₆-alkoxy include, but are not limited to, methoxy, ethoxy, OCH₂-C₂H₅, OCH(CH₃)₂, n-butoxy, OCH(CH₃)-C₂H₅, OCH₂-CH(CH₃)₂, OC(CH₃)₃, n-pentoxy, 1-methylbutoxy, 2-methylbutoxy, 3-methylbutoxy, 1,1-dimethylpropoxy, 1,2-dimethylpropoxy, 2,2-dimethyl-propoxy, 1-ethylpropoxy, n-hexoxy, 1-methylpentoxy, 2-methylpentoxy, 3-methylpentoxy, 4-methylpentoxy, 1,1-dimethylbutoxy, 1,2-dimethylbutoxy, 1,3-dimethylbutoxy, 2,2-dimethylbutoxy, 2,3-dimethylbutoxy, 3,3-dimethylbutoxy, 1-ethylbutoxy, 2-ethylbutoxy, 1,1,2-trimethylpropoxy, 1,2,2-trimethylpropoxy, 1-ethyl-1-methylpropoxy, 1-ethyl-2-methylpropoxy and the like.

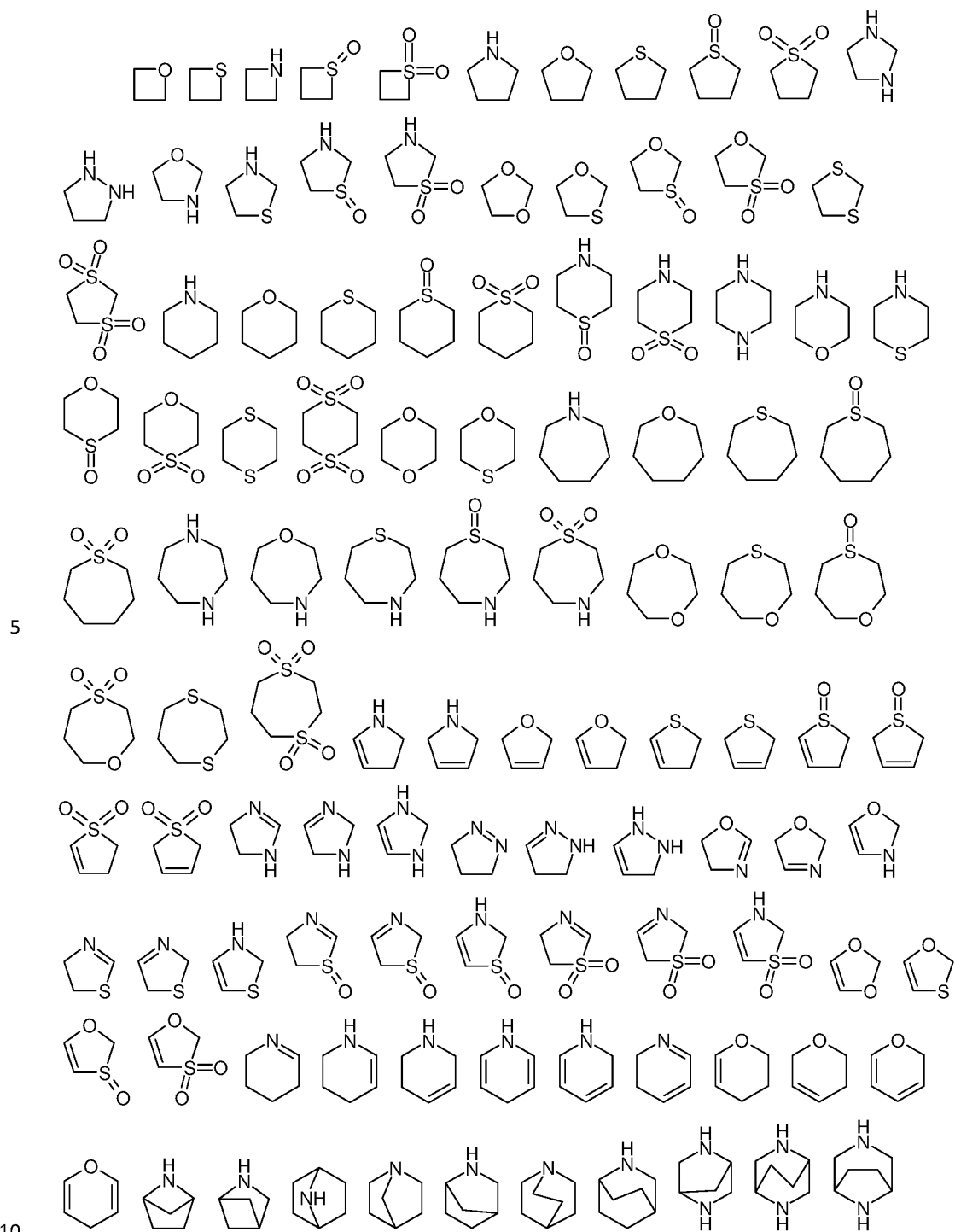
The term “carbocyclyl” or “carbocycle”, either alone or in combination with another radical, means a mono-, bi- or tricyclic ring structure consisting of 3 to 14 carbon atoms. The term “carbocyclyl” or “carbocycle” refers to fully saturated, partially saturated and aromatic ring systems. The term “carbocyclyl” or “carbocycle” encompasses fused, bridged and spirocyclic systems. Examples include:

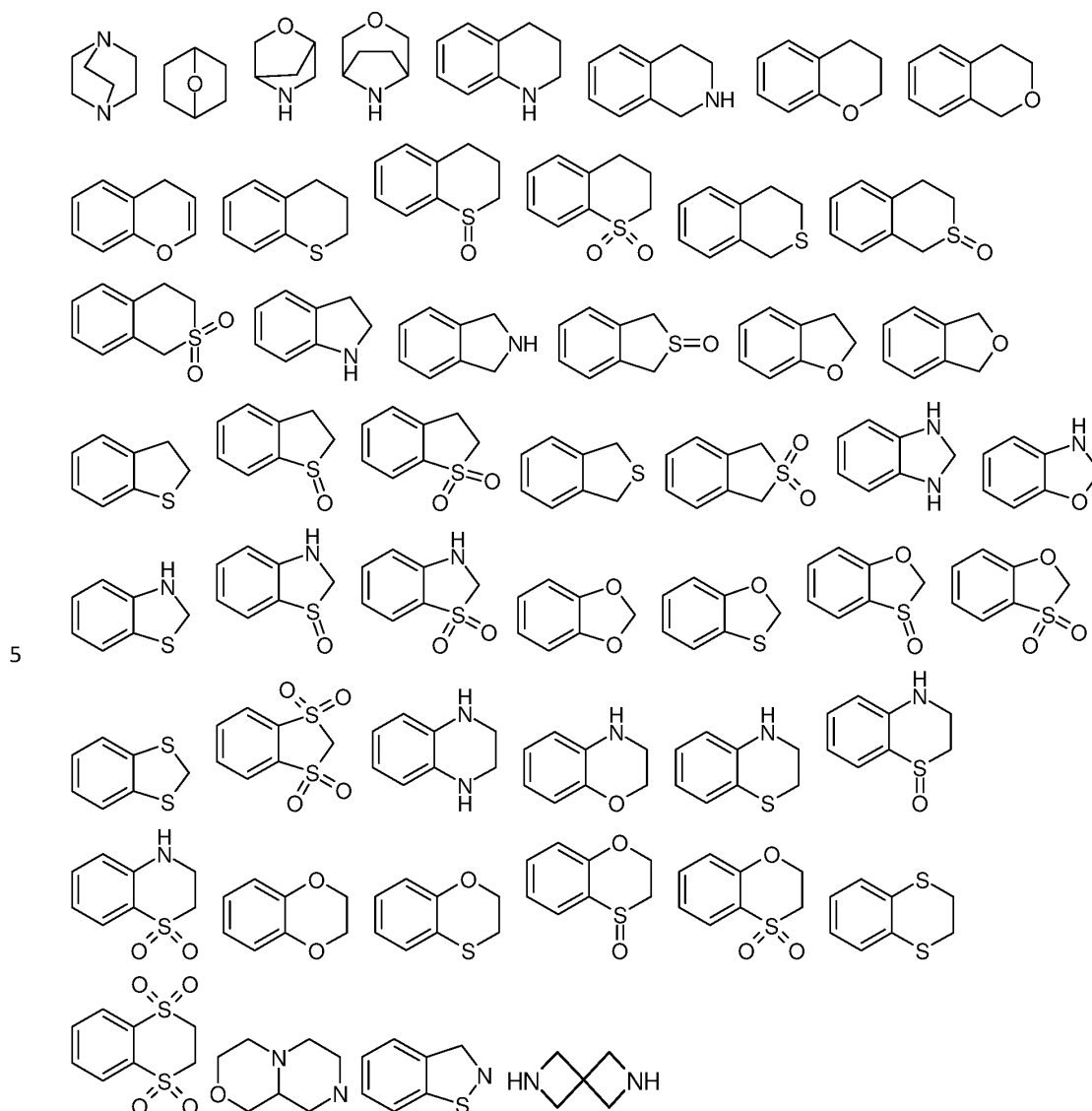


5 The term “aryl”, either alone or in combination with another radical, denotes a carbocyclic aromatic monocyclic group containing 6 carbon atoms, which is optionally further fused to a second five- or six-membered, carbocyclic group which is aromatic, fully saturated or partially saturated. The term “aryl” includes, but is not limited to, phenyl, indanyl, indenyl, naphthyl, anthracenyl, phenanthrenyl, tetrahydronaphthyl and dihydronaphthyl.

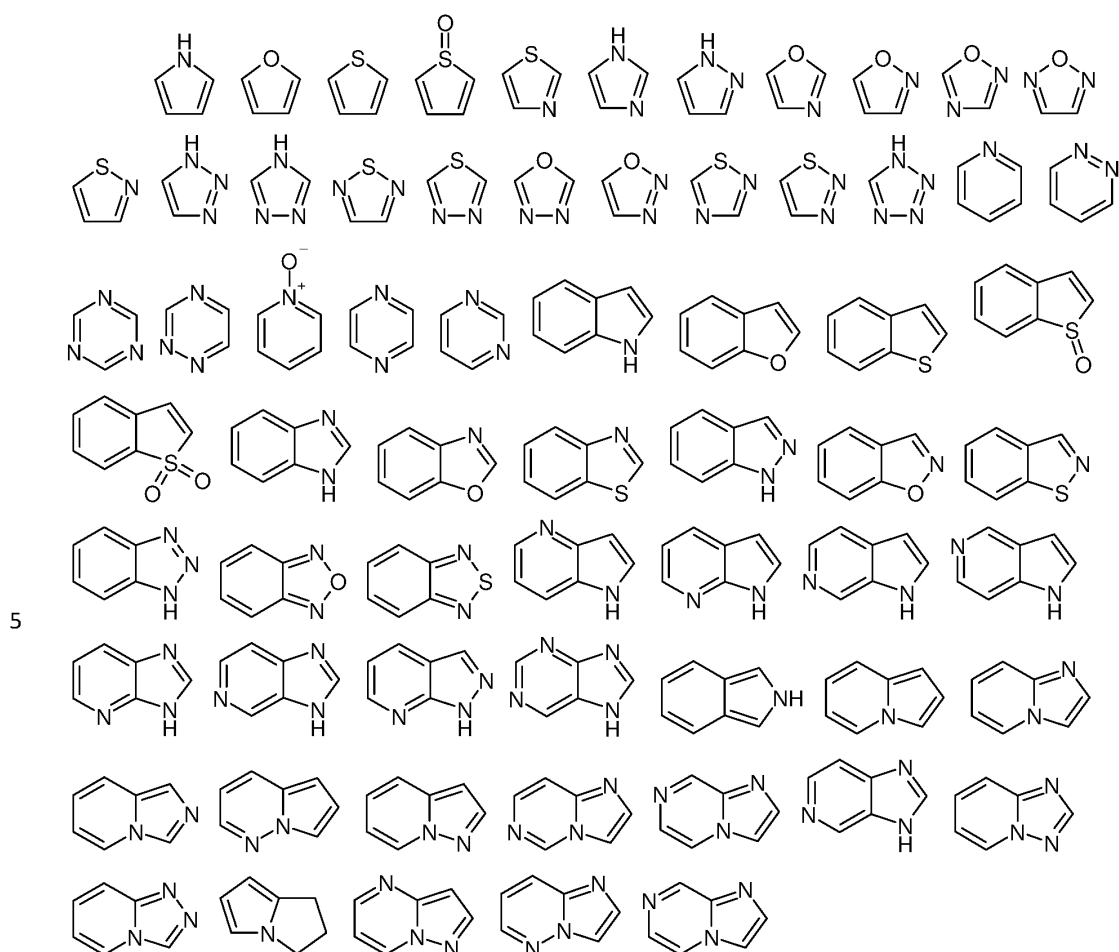
10 The term “aralkyl” refers to an aryl group that is bonded to the parent compound through a diradical alkylene bridge, $(-CH_2-)_n$, where n is 1-6 and where “aryl” is as defined herein.

15 The term “heterocyclyl” or “heterocycle” means a saturated or unsaturated mono- or polycyclic ring system optionally comprising aromatic rings, containing one or more heteroatoms selected from N, O, S, S(O) or S(O)₂ consisting of 3 to 14 ring atoms, wherein none of the heteroatoms is part of the aromatic ring. The term “heterocyclyl” or “heterocycle” is intended to include all possible isomeric forms. Thus, the term “heterocyclyl” or “heterocycle” includes the following exemplary structures (not depicted as radicals as each form is optionally attached through a covalent bond to any atom so long as appropriate valences are maintained):





The term “heteroaryl” means a mono- or polycyclic ring system, comprising at least one aromatic ring, containing one or more heteroatoms selected from N, O, S, S(O) or S(O)₂, consisting of 5 to 14 ring atoms, wherein at least one of the heteroatoms is part of an aromatic ring. The term “heteroaryl” is intended to include all the possible isomeric forms. Thus, the term “heteroaryl” includes the following exemplary structures (not depicted as radicals as each form is optionally attached through a covalent bond to any atom so long as appropriate valences are maintained):



Many of the terms given herein may be used repeatedly in the definition of a formula or group and in each case have one of the meanings given herein, independently of one another.

10

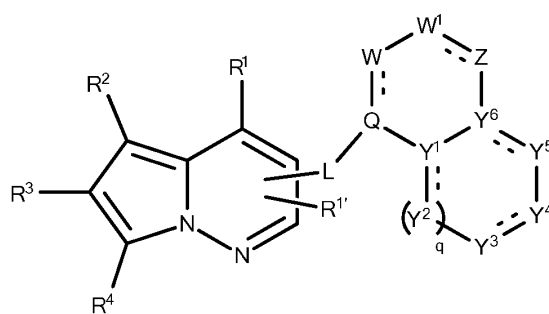
The term “bicyclic ring systems” means groups consisting of 2 joined cyclic substructures including spirocyclic, fused, and bridged ring systems.

The term “tricyclic ring systems” means groups consisting of 3 joined cyclic substructures including spirocyclic, fused, and bridged ring systems.

As used herein, the term “control” in connection with “parasitic infections and/or infestations in animals” means that the parasitic infection and/or infestation is ameliorated or improved, sustainedly reduced in incidence and/or prevented from worsening as regards the animal.

DETAILED DESCRIPTION:

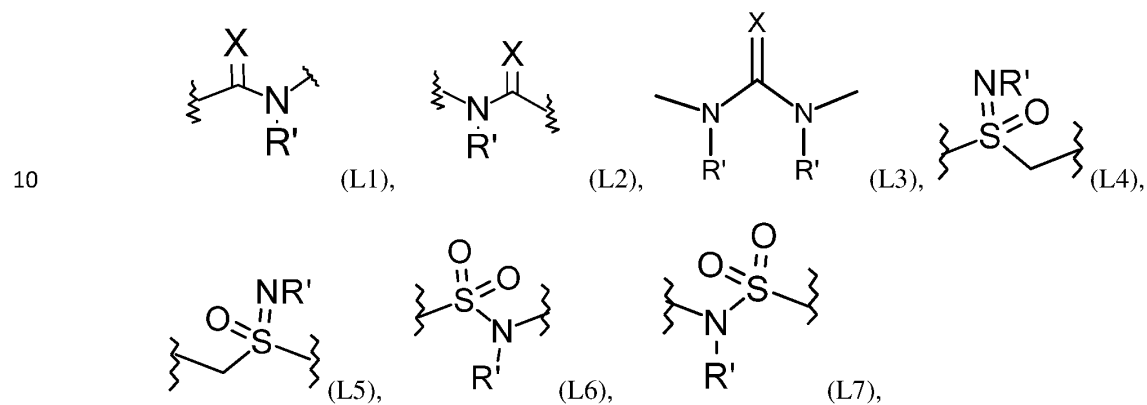
5 An embodiment of the present invention includes a compound of Formula (I):

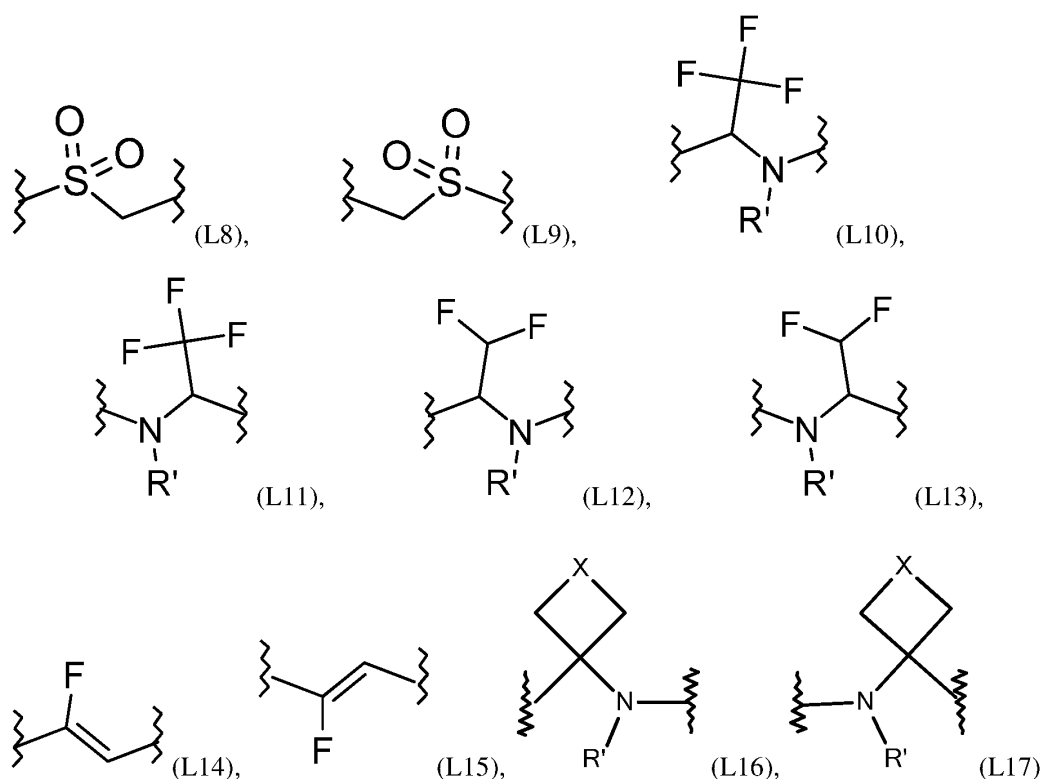


(I)

or a salt thereof, wherein:

L is L1, L2, L3, L4, L5, L6, L7, L8, L9, L10, L11, L12, L13, L14, L15, L16 or L17:





5 R' is hydrogen, optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, optionally substituted aralkyl, optionally substituted aryl, or two R' on the same L group together may form a 2- to 4-membered carbon chain to make a heterocycle;

10 R^1 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted

15

5 dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl), $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocycl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

$\text{R}^{1'}$ is hydrogen, halogen, alkyl or haloalkyl;

10 R^2 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl; optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocycl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, optionally substituted aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl), $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocycl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

20 R^3 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl; optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocycl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, optionally substituted aminocarbonyl, optionally substituted

alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl), $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to
 5 three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^4 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted
 10 dialkylaminocarbonyl, $-\text{S}(\text{O})_p$ (optionally substituted alkyl), $-\text{SF}_5$, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted 5- to 10-membered heteroaryl, a spirocyclic heterocyclyl-carbocyclyl group, a spirocyclic heterocyclyl-heterocyclyl group, a spirocyclic carbocyclyl-carbocyclyl group, a spirocyclic carbocyclyl-heterocyclyl group or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a
 15 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^5 and $\text{R}^{5'}$ are independently in each occurrence, hydrogen, halogen, cyano, nitro, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted
 20 dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkoxy, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, optionally substituted aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted di(alkyl)aminocarbonyl, optionally substituted alkylcarbonyloxy, optionally substituted alkylcarbonylamino, optionally substituted aryl, optionally substituted heteroaryl, $-\text{SF}_5$, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl); or R^5 together with $\text{R}^{5'}$
 25 together form a 2-6-membered chain optionally containing one or two heteroatoms selected

from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached; or $-NR^cR^d$, wherein R^c and R^d are independently H or optionally substituted alkyl; or R^c and R^d may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^6 and R^7 are independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkoxy, or optionally substituted cycloalkoxy, or R^6 together with R^7 form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;

R^8 is hydrogen or C_1 - C_4 -alkyl;

R^9 is hydrogen, halogen, alkyl, haloalkyl, cycloalkyl, alkenyl or alkynyl; Q is $C-R^9$ or N;

X is O, S or $N-R^1$;

Y^1 and Y^6 are each independently N, C, or $-CR^5-$;

Y^2 , Y^3 , Y^4 and Y^5 are each independently N, NR^1 , S, O, $-CR^5-$ or $CR^5R^{5'}$;

W is CR^6 , CR^6R^7 , O, SO_p , N or $N-R^8$, or W is absent;

W^1 is CR^6 , CR^6R^7 , O, SO_p , N or $N-R^8$;

Z is CR^7 , CR^6R^7 , O, SO_p , N or $N-R^8$, and

wherein at most three of Y^1 , Y^2 , Y^3 , Y^4 , Y^5 and Y^6 are heteroatoms;

q is 0 or 1;

p is independently in each occurrence is 0, 1, or 2; and

the dashed bonds (---) signifies a single or double bond;

or salt thereof;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with halogen, hydroxyl, oxo, alkyl, haloalkyl, cycloalkyl, cycloalkenyl, carboxyl, acyl, acyloxy, acetyl, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, haloalkylaminocarbonyl, dihaloalkylaminocarbonyl, amino, alkyl- or dialkylamino, amido, arylamino, alkoxy, haloalkoxy, alkylthio, haloalkylthio, aryloxy, nitro, cyano, azido, thiol, thioamido, imino, amidino, guanidino, carbonate, R₃Si- or R₃SiO- where R is alkyl, haloalkyl or aryl, SF₅, sulfate, alkylsulfonyl, haloalkylsulfonyl, alkoxysulfonyl, alkylsulfinyl, haloalkylsulfinyl, sulfamoyl, sulfoximine, sulfinimine, sulfonimidamide, sulfonediimine, phosphonyl, phosphinyl, phosphoryl, phosphine, phosphonamidate, phosphinamidate, phosphinate, phosphine oxide, thioester, anhydride, oxime, hydrazine, carbamate, phosphate, phosphonate, aryl, heteroaryl and heterocyclyl.

In another embodiment, the present invention includes a compound of Formula (I) as described above, or a salt thereof, wherein variables R¹, R², R³, R⁴, L, Q, W, W¹, Z, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶ and q have the same definitions as described above for Formula (I); the dashed bonds (----) signify a single or double bond; and

R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxycarbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, -SO_p(optionally substituted alkyl or haloalkyl), -SF₅, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4- or 5-membered-heterocyclyl group, which

may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (I) above.

In another embodiment, the present invention includes a compound of Formula (I) as described above, or a salt thereof, wherein variables R^1 , R^2 , R^3 , R^4 , L, Q, W, W^1 , Z, Y^1 , Y^2 , Y^3 , Y^4 , Y^5 , Y^6 and q have the same definitions as described above for Formula (I); the dashed bonds (----) signify a single or double bond; and

- 10 R^1 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted
- 15 aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted
- 20 trialkylsilyloxy, $-SO_p$ (optionally substituted alkyl or haloalkyl), $-SF_5$, or $-NR^aR^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7- or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 25 wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (I) above.

In another embodiment, the invention provides a compound of Formula (I), or a salt thereof,

wherein:

- R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, optionally substituted C₃-C₈-cycloalkyl, or optionally substituted phenyl;
- 5 R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl, -SF₅, tri-C₁-C₆-alkylsilyl, tri-C₁-C₆-alkylsilyloxy, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 10 R^{1'} is hydrogen, halogen, C₁-C₃-alkyl or C₁-C₃-haloalkyl;
- 25 R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl; optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to

- 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 10 R³ is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl; optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 25 R⁴ is C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl,
- 30

-SF₅, -S(O)_p(C₁-C₆-alkyl or C₁-C₆-haloalkyl), optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S; optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, a 5- to 11-membered spirocyclic heterocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic heterocyclyl-heterocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-heterocyclyl group, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, nitro, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted C₁-C₆-alkylcarbonyl, optionally substituted C₁-C₆-alkoxycarbonyl, aminocarbonyl, optionally substituted C₁-C₆-alkylaminocarbonyl, di(C₁-C₆-alkyl)aminocarbonyl, optionally substituted C₁-C₆-alkylcarbonyloxy, optionally substituted C₁-C₆-alkylcarbonylamino, optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, -SF₅, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl); or R⁵ together with R^{5'} together form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached; or -NR^cR^d, wherein R^c and R^d are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^c and R^d may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R⁹ is hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₃-C₈-cycloalkyl, C₂-C₆-alkenyl or C₂-C₆-alkynyl; and

L, Q, X, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, W, W¹, Z, R⁶, R⁷, R⁸, q, p and the dashed bonds (---) are as defined above for the compound of Formula (I);

wherein the term “optionally substituted” indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3- to 8-
 5 membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-haloalkylamino, C₁-C₆-dialkylamino, C₁-C₆-dihaloalkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, nitro, SF₅, C₁-C₆-trialkylsilyl, C₁-C₆-trialkylsiloxy, acyl, acyloxy, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl, C₁-C₆-haloalkylsulfonyl, phenyl, 5- or 6-membered heteroaryl or 5- or 6-membered heterocyclyl.

In another embodiment, the invention provides a compound of Formula (I), or a salt thereof, wherein:

- R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, optionally substituted C₃-
 15 C₈-cycloalkyl, or optionally substituted phenyl;
- R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl, -SF₅, tri-C₁-C₆-alkylsilyl, tri-C₁-C₆-alkylsilyloxy, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-

haloalkyl), or $-NR^aR^b$, wherein R^a and R^b are independently H or optionally substituted C_1 - C_6 -alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4- or 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

5 $R^{1'}$ is hydrogen, halogen, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl;

R^2 is hydrogen, cyano, halogen, hydroxyl, optionally substituted C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -haloalkoxy, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -haloalkoxy- C_1 - C_6 -alkyl, optionally substituted phenyl; optionally substituted phenyloxy, optionally substituted 5- or 6-
10 membered heteroaryl, optionally substituted C_3 - C_8 -cycloalkyl, optionally substituted C_3 - C_8 -cycloalkenyl, optionally substituted C_3 - C_8 -cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S, C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -haloalkylcarbonyl, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -haloalkoxycarbonyl, aminocarbonyl, C_1 - C_6 -alkylaminocarbonyl, C_1 - C_6 -haloalkylaminocarbonyl, di- C_1 - C_6 -alkylaminocarbonyl, di- C_1 - C_6 -
15 haloalkylaminocarbonyl, $-SO_p$ (optionally substituted C_1 - C_6 -alkyl or C_1 - C_6 -haloalkyl), SF_5 , or $-NR^aR^b$, wherein R^a and R^b are independently H, C_1 - C_6 -alkyl or C_1 - C_6 -haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
20

R^3 is hydrogen, cyano, halogen, hydroxyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -haloalkoxy, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -haloalkoxy- C_1 - C_6 -alkyl, optionally substituted phenyl; optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C_3 - C_8 -cycloalkyl, optionally substituted C_3 - C_8 -cycloalkenyl, optionally substituted C_3 - C_8 -cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S, C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -haloalkylcarbonyl, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -haloalkoxycarbonyl, aminocarbonyl, C_1 - C_6 -alkylaminocarbonyl, C_1 - C_6 -
25

haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocycl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R⁴ is C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SF₅, -S(O)_p(C₁-C₆-alkyl or C₁-C₆-haloalkyl), optionally substituted 3- to 7-membered heterocycl containing from one to three heteroatoms selected from the group consisting of N, O and S; optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, a 5- to 11-membered spirocyclic heterocycl-carbocycl group, a 5- to 11-membered spirocyclic heterocycl-heterocycl group, a 5- to 11-membered spirocyclic carbocycl-carbocycl group, a 5- to 11-membered spirocyclic carbocycl-heterocycl group, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocycl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, nitro, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted C₁-C₆-alkylcarbonyl, optionally substituted C₁-C₆-alkoxycarbonyl, aminocarbonyl, optionally substituted C₁-C₆-alkylaminocarbonyl, di(C₁-C₆-alkyl)aminocarbonyl, optionally substituted C₁-C₆-alkylcarbonyloxy, optionally substituted C₁-C₆-alkylcarbonylamino, optionally substituted phenyl, optionally

substituted 5- or 6-membered heteroaryl, -SF₅, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl); or R⁵ together with R^{5'} together form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached; or -NR^cR^d, wherein R^c and R^d are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^c and R^d may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

10 R⁹ is hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₃-C₈-cycloalkyl, C₂-C₆-alkenyl or C₂-C₆-alkynyl; and

L, Q, X, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, W, W¹, Z, R⁶, R⁷, R⁸, q, p and the dashed bonds (---) are as defined above for the compound of Formula (I);

wherein the term “optionally substituted” indicates that the group recited is optionally substituted
 15 by one or more halogen (chloro, fluoro, bromo, iodo), C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3- to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-haloalkylamino, C₁-C₆-dialkylamino, C₁-C₆-dihaloalkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, nitro, C₁-C₆-trialkylsilyl, C₁-C₆-trialkylsiloxyl, SF₅, acyl, acyloxy, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl, C₁-C₆-haloalkylsulfonyl, phenyl, 5- or 6-membered heteroaryl or 5- or 6-membered heterocyclyl.

In yet another embodiment, the invention provides a compound of Formula (I), or a salt thereof, wherein:

25 R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, optionally substituted C₃-C₈-cycloalkyl, or optionally substituted phenyl;

R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-

- haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl, -SF₅, tri-C₁-C₆-alkylsilyl, tri-C₁-C₆-alkylsilyloxy, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^{1'} is hydrogen, halogen, C₁-C₃-alkyl or C₁-C₃-haloalkyl;
- R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl; optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-

membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

- R^3 is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl; optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^4 is C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SF₅, -S(O)_p(C₁-C₆-alkyl or C₁-C₆-haloalkyl), optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S; optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, a 5- to 11-membered spirocyclic heterocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic heterocyclyl-heterocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-heterocyclyl group, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl;

or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, nitro, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted C₁-C₆-alkylcarbonyl, optionally substituted C₁-C₆-alkoxycarbonyl, aminocarbonyl, optionally substituted C₁-C₆-alkylaminocarbonyl, di(C₁-C₆-alkyl)aminocarbonyl, optionally substituted C₁-C₆-alkylcarbonyloxy, optionally substituted C₁-C₆-alkylcarbonylamino, optionally substituted phenyl, optionally substituted 5- or 6-membered heteroaryl, -SF₅, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl); or R⁵ together with R^{5'} together form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached; or -NR^cR^d, wherein R^c and R^d are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^c and R^d may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R⁹ is hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₃-C₈-cycloalkyl, C₂-C₆-alkenyl or C₂-C₆-alkynyl; and

L, Q, X, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, W, W¹, Z, R⁶, R⁷, R⁸, q, p and the dashed bonds (----) are as defined above for the compound of Formula (I);

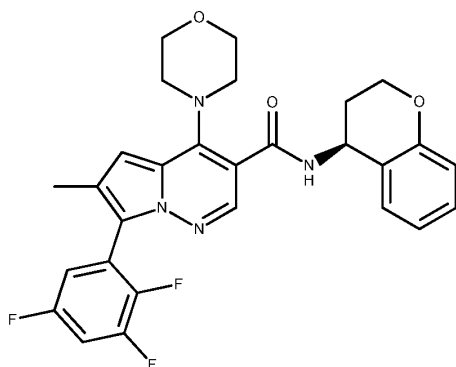
wherein the term “optionally substituted” indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3- to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-haloalkylamino, C₁-C₆-dialkylamino, C₁-C₆-dihaloalkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, nitro, C₁-C₆-trialkylsilyl, C₁-C₆-trialkylsiloxy, SF₅, acyl, acyloxy, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-

C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl, C₁-C₆-haloalkylsulfonyl, phenyl, 5- or 6-membered heteroaryl or 5- or 6-membered heterocyclyl.

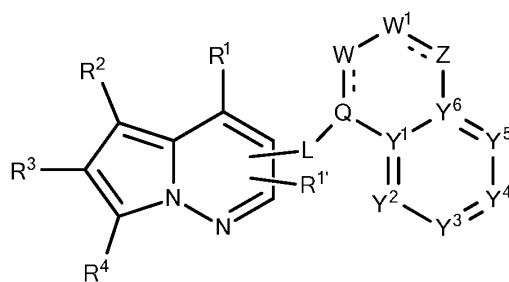
5 In another embodiment, the present invention includes a compound of Formula (I) as described above, or a salt thereof, wherein variables R¹, R², R³, R⁴, L, Q, W, W¹, Z, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶ and q have the same definitions as described above for Formula (I); the dashed bonds (----) signify a single or double bond; and

10 R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxycarbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, -SO_p(optionally substituted alkyl or haloalkyl), -SF₅, or -NR^aR^b, wherein
15
20 R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7- or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

25 wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (I) above; and with the proviso that the compound below is excluded:



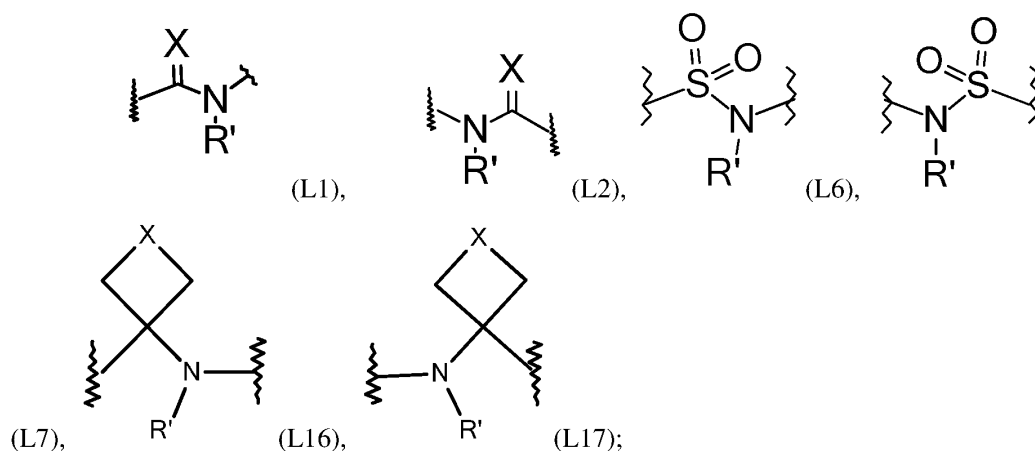
An embodiment of the present invention includes a compound of Formula (IA):



(IA)

5 or a salt thereof, wherein:

L is L1, L2, L6, L7, L16 or L17:



R' is hydrogen, optionally substituted alkyl, optionally substituted haloalkyl or optionally substituted aralkyl;

- 5 R^1 is hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl or $-NR^aR^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 10
- 15 $R^{1'}$ is hydrogen, halogen, optionally substituted alkyl or haloalkyl;
- R^2 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl or optionally substituted alkynyl;

- R^3 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl or optionally substituted alkynyl;
- 5 R^4 is optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted spirocyclic heterocyclyl-carbocyclyl group, optionally substituted spirocyclic heterocyclyl-heterocyclyl group, optionally substituted spirocyclic carbocyclyl-carbocyclyl group, optionally substituted spirocyclic carbocyclyl-heterocyclyl group, optionally substituted phenyl, optionally substituted 5- or 6-membered
- 10 heteroaryl, or $-NR^aR^b$, wherein R^a and R^b are independently H, alkyl or haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^5 and $R^{5'}$ are independently in each occurrence, hydrogen, halogen, cyano, optionally substituted
- 15 alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy;
- R^9 is hydrogen, halogen, alkyl or haloalkyl;
- R^6 and R^7 are independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, or R^6 together with
- 20 R^7 form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;
- Q is $C-R^9$ or N;
- 25 X is O, S or $N-R'$;
- Y^1 and Y^6 are independently C or N;
- Y^2 , Y^3 , Y^4 and Y^5 are each independently N or $-CR^5$;

W is CR⁶, CR⁶R⁷ or W is absent;

W¹ is CR⁶ or CR⁶R⁷;

Z is CR⁶, CR⁶R⁷ or O;

wherein at most three of Y¹, Y², Y³, Y⁴, Y⁵ and Y⁶ are N; and

5 the dashed bonds ($\overline{\text{---}}$) signifies a single or double bond;

a stereoisomer, tautomer, N-oxide, hydrate, solvate, or salt thereof;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with halogen, hydroxyl, alkyl, haloalkyl, cycloalkyl, carboxyl, acyl, acyloxy, acetyl, alkylcarbonyl, haloalkylcarbonyl, alkoxy carbonyl, haloalkoxy carbonyl, aminocarbonyl, alkylaminocarbonyl, 10 dialkylaminocarbonyl, haloalkylaminocarbonyl, dihaloalkylaminocarbonyl, amino, alkyl- or dialkylamino, amido, alkoxy, haloalkoxy, alkylthio, haloalkylthio, cyano, thiol, thioamido, aryl, heteroaryl, aryloxy, arylamino, heterocyclyl, SF₅, trialkylsilyl, trialkylsiloxy, alkylsulfonyl, alkoxy sulfonyl or alkylsulfinyl.

In another embodiment, the present invention includes a compound of Formula (IA), or a 15 salt thereof, as described above, wherein variables R¹, R², R³, R⁴, L, Q, W, W¹, Z, Y¹, Y², Y³, Y⁴, Y⁵ and Y⁶ have the same definitions as for Formula (IA); the dashed bonds ($\overline{\text{---}}$) signify a single or double bond; and

R¹ is hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted 20 alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen 25 to which they are attached, a 3-, 4-, 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with same substituents defined for “optionally substituted” for the broadest embodiment of the compound of Formula (IA) described above.

In still another embodiment, the present invention includes a compound of Formula (IA) as described above, or a salt thereof, wherein variables R^1 , R^2 , R^3 , R^4 , L, Q, W, W^1 , Z, Y^1 , Y^2 , Y^3 , Y^4 , Y^5 and Y^6 have the same definitions as for Formula (IA); the dashed bonds (-----) signify a single or double bond; and

R^1 is hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl or $-NR^aR^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7-, 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups as defined “optionally substituted” for the broadest embodiment of Formula (IA) described above.

In another embodiment, the invention provides a compound of Formula (IA), or a salt thereof,

wherein:

R' is hydrogen, optionally substituted C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, or optionally substituted benzyl;

R^1 is hydrogen, halogen, optionally substituted C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, hydroxy- C_1 - C_6 -alkyl, hydroxy- C_1 - C_6 -haloalkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -haloalkoxy- C_1 - C_6 -alkyl, amino- C_1 - C_6 -alkyl, C_1 - C_6 -alkylamino- C_1 - C_6 -alkyl, C_1 - C_6 -haloalkylamino- C_1 - C_6 -alkyl, di-

- 5 C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 10 R^{1'} hydrogen, halogen, optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl;
- R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- 15 R³ is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- 20 R⁴ is optionally substituted C₃-C₈- cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S; optionally substituted phenyl or optionally substituted 5- or 6-membered heteroaryl, a 5- to 11-membered spirocyclic heterocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic heterocyclyl-heterocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-heterocyclyl group, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 25

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy;

5 R⁶ and R⁷ are independently hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, or R⁶ together with R⁷ form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;

10 R⁹ is hydrogen, halogen, C₁-C₆-alkyl or C₁-C₆-haloalkyl; and

L, Q, X, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, W, W¹, Z and the dashed bonds (---) are as defined above for the compound of Formula (IA);

wherein the term “optionally substituted” indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3-
 15 to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, SF₅, C₁-C₆-trialkylsilyl, C₁-C₆-trialkylsiloxy, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-
 20 haloalkylthio, C₁-C₆-haloalkylsulfinyl or C₁-C₆-haloalkylsulfonyl.

In another embodiment, the invention provides a compound of Formula (IA), or a salt thereof, wherein:

R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, or optionally substituted benzyl;

25 R¹ is hydrogen, halogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-

- 5 C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^{1'} hydrogen, halogen, optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl;
- 10 R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- R³ is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- 15 R⁴ is optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S; optionally substituted phenyl or optionally substituted 5- or 6-membered heteroaryl, a 5- to 11-membered spirocyclic heterocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic heterocyclyl-heterocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-heterocyclyl group, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 20
- 25

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy;

5 R⁶ and R⁷ are independently hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, or R⁶ together with R⁷ form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;

10 R⁹ is hydrogen, halogen, C₁-C₆-alkyl or C₁-C₆-haloalkyl; and

L, Q, X, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, W, W¹, Z and the dashed bonds (---) are as defined above for the compound of Formula (IA);

wherein the term “optionally substituted” indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3-
 15 to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, SF₅, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl
 20 or C₁-C₆-haloalkylsulfonyl.

In another embodiment, the invention provides a compound of Formula (IA), or a salt thereof, wherein:

R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, or optionally substituted benzyl;

25 R¹ is hydrogen, halogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-

- 5 C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^{1'} hydrogen, halogen, optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl;
- 10 R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- R³ is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- 15 R⁴ is optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O and S; optionally substituted phenyl or optionally substituted 5- or 6-membered heteroaryl, a 5- to 11-membered spirocyclic heterocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic heterocyclyl-heterocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-carbocyclyl group, a 5- to 11-membered spirocyclic carbocyclyl-heterocyclyl group, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 20
- 25

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy;

5 R⁶ and R⁷ are independently hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, or R⁶ together with R⁷ form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;

10 R⁹ is hydrogen, halogen, C₁-C₆-alkyl or C₁-C₆-haloalkyl; and

L, Q, X, Y¹, Y², Y³, Y⁴, Y⁵, Y⁶, W, W¹, Z and the dashed bonds (---) are as defined above for the compound of Formula (IA);

wherein the term "optionally substituted" indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3-
 15 to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, SF₅, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl
 20 or C₁-C₆-haloalkylsulfonyl.

In some embodiments of Formula (IA):

R¹ is optionally substituted C₁-C₄-alkyl, optionally substituted C₁-C₄-alkoxy, optionally substituted C₂-C₄-alkenyl, optionally substituted C₂-C₄-alkynyl, optionally substituted, saturated or partially unsaturated 5-, 6-, or 7-membered heterocycle group, optionally substituted heteroaryl,
 25 or -NR^aR^b, wherein R^a and R^b are independently optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocycl group, which may include one to three additional heteroatoms selected from the group consisting of N, O and S and may be optionally substituted;

R^{1'} is hydrogen;

R' is hydrogen or C₁-C₄-alkyl;

R² is hydrogen, halogen, optionally substituted C₁-C₄-alkyl or optionally substituted C₁-C₄-alkoxy;

5 R³ is hydrogen, halogen, optionally substituted C₁-C₄-alkyl or optionally substituted C₁-C₄-alkoxy;

R⁴ is phenyl which may be optionally substituted with 1, 2, or 3 substituents; and

R⁵ and R^{5'} are independently hydrogen, halogen, cyano, C₁-C₄-alkyl or C₁-C₄haloalkyl, wherein "optionally substituted" indicates that the group recited may be optionally substituted with
10 the same groups as defined "optionally substituted" for the broadest embodiment of Formula (IA) described above.

In some embodiments of Formula (IA):

R¹ is optionally substituted C₁-C₄-alkyl, optionally substituted C₁-C₄-alkoxy, optionally substituted C₂-C₄-alkenyl, optionally substituted C₂-C₄-alkynyl, optionally substituted, saturated
15 or partially unsaturated 5-, 6-, or 7-membered heterocycle group, optionally substituted heteroaryl, or -NR^aR^b, wherein R^a and R^b are independently optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4- 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O and S and may be optionally substituted;

20 R^{1'} is hydrogen;

R' is hydrogen or C₁-C₄-alkyl;

R² is hydrogen, halogen, optionally substituted C₁-C₄-alkyl or optionally substituted C₁-C₄-alkoxy;

R³ is hydrogen, halogen, optionally substituted C₁-C₄-alkyl or optionally substituted C₁-
25 C₄-alkoxy;

R⁴ is phenyl which may be optionally substituted with 1, 2, or 3 substituents; and

R⁵ and R^{5'} are independently hydrogen, halogen, cyano, C₁-C₄-alkyl or C₁-C₄haloalkyl, wherein "optionally substituted" indicates that the group recited may be optionally substituted with the same groups as defined "optionally substituted" for the broadest embodiment of Formula (IA) described above.

In another embodiment of Formula (IA):

R¹ is optionally substituted C₁-C₄-alkyl, optionally substituted C₁-C₄-alkoxy, optionally substituted C₂-C₄-alkenyl, optionally substituted C₂-C₄-alkynyl, optionally substituted, saturated or partially unsaturated 5-, 6-, or 7-membered heterocycle group, optionally substituted heteroaryl, or -NR^aR^b, wherein R^a and R^b are independently optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O and S and may be optionally substituted;

R^{1'} is hydrogen;

R² is hydrogen or C₁-C₄-alkyl;

R² is hydrogen, halogen, optionally substituted C₁-C₄-alkyl or optionally substituted C₁-C₄-alkoxy;

R³ is hydrogen, halogen, optionally substituted C₁-C₄-alkyl or optionally substituted C₁-C₄-alkoxy;

R⁴ is phenyl which may be optionally substituted with 1, 2, or 3 substituents; and

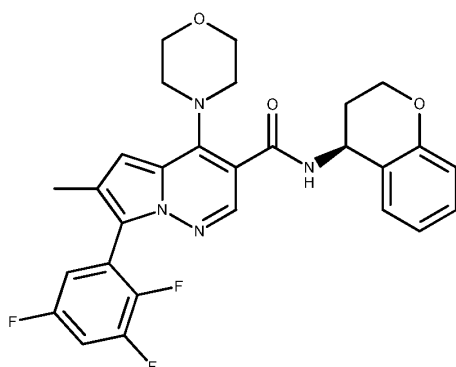
R⁵ and R^{5'} are independently hydrogen, halogen, cyano, C₁-C₄-alkyl or C₁-C₄haloalkyl, wherein "optionally substituted" indicates that the group recited may be optionally substituted with the same groups as defined "optionally substituted" for the broadest embodiment of Formula (IA) described above.

In still another embodiment, the present invention includes a compound of Formula (IA) as described above, or a salt thereof, wherein variables R^{1'}, R², R³, R⁴, L, Q, W, W¹, Z, Y¹, Y²,

Y^3 , Y^4 , Y^5 and Y^6 have the same definitions as for Formula (IA); the dashed bonds (-----) signify a single or double bond; and

R^1 is hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl or $-NR^aR^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7-, 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups as defined “optionally substituted” for the broadest embodiment of Formula (IA) described above; and with the proviso that the compound below is excluded:



In one embodiment, L is L1. In another embodiment, L is L2. In another embodiment, L is L3. In another embodiment, L is L4. In another embodiment, L is L5. In another embodiment, L is L6. In another embodiment, L is L7. In another embodiment, L is L8. In another embodiment, L is L9. In another embodiment, L is L10. In another embodiment, L is L11. In another embodiment, L is L12. In another embodiment, L is L13. In another embodiment, L is L14. In another embodiment, L is L15. In another embodiment, L is L16. In another embodiment, L is L17.

In some embodiments of Formula (I) or Formula (IA), R¹ is hydrogen.

In some embodiments, R¹ is C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₁-C₄-haloalkyl, amino, C₁-C₄-alkylamino, or di-(C₁-C₄-alkyl) amino.

In some embodiments, R¹ is dimethylamino.

5 In some embodiments, R¹ is C₁-C₄-alkyl or C₁-C₄-haloalkyl.

In another embodiment, R¹ is halogen.

In another embodiment, R¹ is chloro or fluoro.

In another embodiment, R¹ is C₁-C₄-alkyl-SO_p-, C₁-C₄-haloalkyl-SO_p- or -SF₅.

10 In other embodiments, R¹ is hydroxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-haloalkoxy-C₁-C₄-alkyl or C₁-C₄-haloalkoxy-C₁-C₄-haloalkyl.

In another embodiment, R¹ is hydroxy-C₁-C₃-alkyl.

In another embodiment, R¹ is -C(CH₃)₂OH.

In another embodiment, R¹ is methyl, ethyl, propyl, butyl, pentyl, isopropyl (*i*-Pr), *tert*-butyl (*t*-butyl), prop-1-en-2-yl, 2-fluoroprop-2-yl, 1,1-difluoroethyl or 2-hydroxyprop-2-yl.

15 In some embodiments, R¹ is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl or *tert*-butyl.

In other embodiments, R¹ is isopropyl or *tert*-butyl.

In one embodiment, R¹ is *tert*-butyl.

In another embodiment, R¹ is C₁-C₃-alkoxy or C₁-C₃-haloalkoxy.

20 In another embodiment, R¹ is OCH₃ or OCH₂CH₃.

In another embodiment, R¹ is OCF₃ or SCF₃.

In another embodiment, R¹ is CF₃, -CH₂CF₃, -CHF₂CF₃ or -CF₂CF₃.

In some embodiments, R¹ is C₂-C₄-alkenyl or C₂-C₄-haloalkenyl.

25 In some embodiments, R¹ is optionally substituted cyclopentyl or optionally substituted cyclohexyl.

In other embodiments, R¹ is optionally substituted cyclopropyl or optionally substituted cyclobutyl.

In another embodiment, R¹ is optionally substituted cyclopropyl.

30 In one embodiment, R¹ is cyclopropyl substituted by one or more C₁-C₆-alkyl or C₁-C₆-haloalkyl groups.

In another embodiment, R¹ is cyclopropyl substituted by one or more methyl or CF₃ groups.

In some embodiments, R¹ is an optionally substituted, saturated or unsaturated 6-membered heterocyclyl group.

In one embodiment, R¹ is -NR^aR^b, wherein R^a and R^b are independently hydrogen or C₁-C₆ alkyl. In another embodiment R¹ is -NR^aR^b, wherein R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O and S and may be optionally substituted.

In another embodiment R¹ is -NR^aR^b, wherein R^a and R^b may form, with the nitrogen to which they are attached, a 3- or 4-membered heterocyclyl group, which may be optionally substituted by one or more C₁-C₄-alkyl, C₁-C₄-haloalkyl or halogen.

In another embodiment, R¹ is -NR^aR^b, wherein R^a and R^b may form, with the nitrogen to which they are attached, a 4-membered azetidiny group, which may be optionally substituted by one or more halogen.

In another embodiment R¹ is -NR^aR^b, wherein R^a and R^b may form, with the nitrogen to which they are attached, a 4-membered heterocyclyl group, which is substituted by one or two halogen atoms. In another embodiment, R¹ is -NR^aR^b, wherein R^a and R^b may form, with the nitrogen to which they are attached, a 4-membered heterocyclyl group, which is substituted by one or two fluoro atoms.

In another embodiment, R¹ is C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl.

In some embodiments, R¹ is optionally substituted tetrahydrofuryl, dihydrofuryl, morpholino, pyranly, dihydropyranly, piperidiny, dihydropiperidiny, dihydrothiophene, or tetrahydrothiophene.

In some embodiments, R¹ is optionally substituted phenyl.

In some embodiments, R¹ is aziridiny, azetidiny, oxetany, pyrrolidiny, pyrroly, pyrazoly, oxetany, pyrazoliny, imidazolyl, imidazoliny, imidazolidiny, oxazolyl, oxazolidiny, isoxazoliny, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidiny, isothiazolyl, isothiazolidiny, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidiny, piperaziny, 2-oxopiperaziny, 2-oxopiperidiny, 2-oxopyrrolodiny, 2-oxoazepiny, azepiny, 4-piperidony, pyridiny, pyraziny, pyrimidiny,

pyridazinyl, pyranyl, dihydropyranyl, tetrahydropyranyl, thiopyranyl, dihydrothiopyranyl, tetrahydrothiopyranyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl, triazolyl or triazinyl.

In some embodiments, R^1 is aziridinyl, azetidiny, oxetanyl, pyrrolidinyl or pyrrolyl, all of which are optionally substituted by one or more C₁-C₄-alkyl, C₁-C₄-haloalkyl or halogen.

In some embodiments, R^1 is morpholinyl, piperidinyl or piperazinyl, each of which are optionally substituted by one or more C₁-C₄-alkyl, C₁-C₄-haloalkyl or halogen.

In some embodiments, R^1 is aziridinyl or azetidiny, optionally substituted by one or more C₁-C₄-alkyl, C₁-C₄-haloalkyl or halogen.

In other embodiments, R^1 is aziridinyl or azetidiny, optionally substituted by one or more C₁-C₃-alkyl, C₁-C₃-haloalkyl, chloro or fluoro.

In other embodiments, R^1 is aziridinyl or azetidiny, optionally substituted by one or more methyl, ethyl, trifluoromethyl, -CH₂CF₃, -CF₂CF₃, chloro or fluoro.

In other embodiments, R^1 is aziridinyl or azetidiny, optionally substituted by one or more methyl or fluoro.

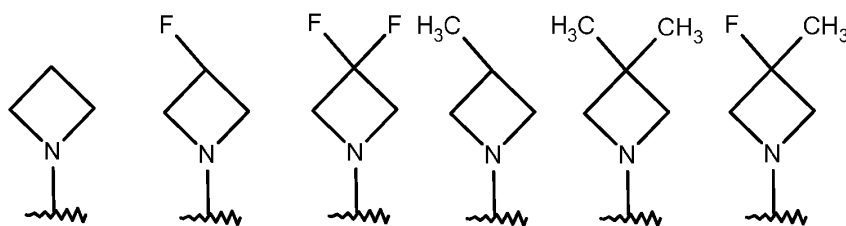
In another embodiment, R^1 is azetidiny substituted by one or more fluoro.

In yet another embodiment, R^1 is azetidiny substituted by two fluoro.

In another embodiment, R^1 is azetidiny substituted by one or more methyl groups.

In another embodiment, R^1 is azetidiny substituted by one or more fluoro and one or more methyl groups.

In yet another embodiment, R^1 is an azetidiny selected from the following groups:



In some embodiments, R^1 is pyrrolidinyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl each optionally substituted by one or more C₁-C₄-alkyl, C₁-C₄-haloalkyl or halogen.

In other embodiments, R¹ is morpholinyl, piperidinyl or piperazinyl, optionally substituted with one or more C₁-C₄-alkyl, C₁-C₄-haloalkyl or halogen.

In other embodiments, R¹ is morpholinyl, piperidinyl or piperazinyl, optionally substituted with one or more C₁-C₃-alkyl, C₁-C₃-haloalkyl, chloro or fluoro.

5 In other embodiments, R¹ is morpholinyl, piperidinyl or piperazinyl, optionally substituted with one or more methyl, ethyl, trifluoromethyl, -CH₂CF₃, -CF₂CF₃, chloro or fluoro.

In another embodiment, R¹ is morpholinyl.

In one embodiment, R¹ is hydrogen.

In another embodiment, R¹ is C₁-C₃-alkyl.

10 In another embodiment, R¹ is methyl.

In another embodiment, R¹ is C₁-C₃-haloalkyl.

In another embodiment, R¹ is CF₃.

In another embodiment, R¹ is halogen.

15 In some embodiments, R² is hydrogen, C₁-C₄-alkyl, C₁-C₄-haloalkyl, amino, C₁-C₄-alkylamino, or di-(C₁-C₄alkyl) amino.

In some embodiments, R² is methyl.

In another embodiment, R² is hydrogen, methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl or *tert*-butyl.

In another embodiment, R² is hydrogen, CF₃, -CH₂CF₃, -CHF₂CF₃ or -CF₂CF₃.

20 In one embodiment, R² is CF₃.

In some embodiments, R² is hydrogen.

In some embodiments, R² is halogen.

In another embodiment, R² is fluoro, bromo or chloro.

In another embodiment, R² is hydrogen, halogen, C₁-C₄alkyl or C₁-C₄haloalkyl;

25 In another embodiment, R² is hydrogen, chloro, fluoro, bromo, methyl or CF₃.

In another embodiment, R² is hydrogen, C₁-C₄-alkoxy, C₁-C₄-haloalkoxy or S(O)_p(C₁-C₄-alkyl or C₁-C₄-haloalkyl) where p is 0, 1 or 2.

In another embodiment, R² is methoxy, ethoxy, propoxy or butoxy.

In another embodiment, R² is methylthio, ethylthio, propylthio or butylthio.

30 In another embodiment, R² is -OCF₃ or -SCF₃.

In some embodiments, R² is C₂-C₄-alkenyl or C₂-C₄-haloalkenyl.

In some embodiments, R^2 is optionally substituted cyclopentyl or optionally substituted cyclohexyl.

In some embodiments, R^2 is an optionally substituted, saturated or unsaturated 6-membered heterocyclyl group.

5 In some embodiments, R^2 is optionally substituted tetrahydrofuryl, dihydrofuryl, morpholino, pyranyl, dihydropyranyl, piperidiny, dihydropiperidiny, dihydrothiophene, or tetrahydrothiophene.

In some embodiments, R^2 is optionally substituted phenyl.

10 In other embodiments, R^2 is phenyl substituted with 1, 2, or 3 substituents, which are independently halo, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkoxy, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

15 In another embodiment, R^2 is a 5- or 6-membered heteroaryl with 1 or 2 substituents, which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In one embodiment, R^2 is pyridinyl optionally substituted with halogen, cyano, nitro, C_1 - C_3 -alkyl, C_1 - C_3 -haloalkyl, C_1 - C_3 -alkoxy, C_1 - C_3 -haloalkoxy or (C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl) $S(O)_p$.

20 In some embodiments, R^2 is optionally substituted aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl, imidazolinyl, imidazolidinyl, oxazolyl, oxazolidinyl, isoxazoliny, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodiny, 2-oxoazepiny, azepiny, 4-piperidonyl, 25 pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, tetrahydropyranyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl, triazolyl or triazinyl.

In some embodiments, R^2 is aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, or morpholinyl, all of which are optionally substituted by one or more halogen.

30 In some embodiments, R^3 is hydrogen, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl, amino, C_1 - C_4 -alkylamino, or di-(C_1 - C_4 alkyl) amino.

In another embodiment, R³ is hydrogen, methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl or *tert*-butyl.

In a particular embodiment, R³ is methyl

In another embodiment, R³ is hydrogen, CF₃, -CH₂CF₃, -CHF₂CF₃ or -CF₂CF₃.

5 In some embodiments, R³ is hydrogen.

In some embodiments, R³ is halogen.

In another embodiment, R³ is fluoro, bromo or chloro.

In a particular embodiment, R³ is chloro.

In another embodiment, R³ is hydrogen, halogen, C₁-C₄alkyl or C₁-C₄haloalkyl;

10 In another embodiment, R³ is hydrogen, chloro, fluoro, bromo, methyl or CF₃.

In another embodiment, R³ is hydrogen, C₁-C₄-alkoxy, C₁-C₄-haloalkoxy or S(O)_p(C₁-C₄-alkyl or C₁-C₄-haloalkyl) where p is 0, 1 or 2.

In another embodiment, R³ is methoxy, ethoxy, propoxy or butoxy.

In another embodiment, R³ is methylthio, ethylthio, propylthio or butylthio.

15 In another embodiment, R³ is -OCF₃ or -SCF₃.

In some embodiments, R³ is C₁-C₄-alkenyl or C₁-C₄-haloalkenyl.

In some embodiments, R³ is optionally substituted cyclopentyl or optionally substituted cyclohexyl.

20 In some embodiments, R³ is an optionally substituted, saturated or unsaturated 6-membered heterocyclyl group.

In some embodiments, R³ is optionally substituted tetrahydrofuryl, dihydrofuryl, morpholino, pyranil, dihydropyranil, piperidiny, dihydropiperidiny, dihydrothiophene, or tetrahydrothiophene.

In some embodiments, R³ is optionally substituted phenyl.

25 In other embodiments, R³ is phenyl substituted with 1, 2, or 3 substituents, which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkoxy, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

30 In another embodiment, R³ is a 5- or 6-membered heteroaryl with 1 or 2 substituents, which are independently halo, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl,

cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In one embodiment, R³ is pyridinyl optionally substituted with halo, cyano, nitro, C₁-C₃-alkyl, C₁-C₃-haloalkyl, C₁-C₃-alkoxy, C₁-C₃-haloalkoxy or (C₁-C₃-alkyl or C₁-C₃-haloalkyl)S(O)_p.

5 In some embodiments, R³ is optionally substituted aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl, imidazolinyl, imidazolidinyl, oxazolyl, oxazolidinyl, isoxazolyl, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, 10 pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, tetrahydropyranyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl, triazolyl or triazinyl.

In some embodiments, R³ is aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, or morpholinyl, all of which are optionally substituted by one or more halogen.

15 In some embodiments, R⁴ is 6- to 10-membered aryl optionally substituted with 1, 2, 3, 4 or 5 substituents.

In some embodiments, R⁴ is C₁-C₄-alkyl or C₁-C₄-haloalkyl.

In some embodiments, R⁴ is methyl, ethyl, *n*-propyl, *n*-butyl, *iso*-propyl, *tert*-butyl, *sec*-butyl or *iso*-butyl.

20 In other embodiments, R⁴ is CF₃, -CH₂CF₃, -CHF₂CF₃ or -CF₂CF₃.

In some embodiments, R⁴ is optionally substituted C₃-C₈-cycloalkyl. In yet other embodiments, R⁴ is optionally substituted C₃-C₆-cycloalkyl. In yet other embodiments, R⁴ is optionally substituted C₃-C₈-cycloalkenyl or C₃-C₆-cycloalkenyl. In some embodiments, R⁴ is optionally substituted cyclopentyl or cyclohexyl. In other embodiments, R⁴ is optionally 25 substituted cyclopropyl or cyclobutyl.

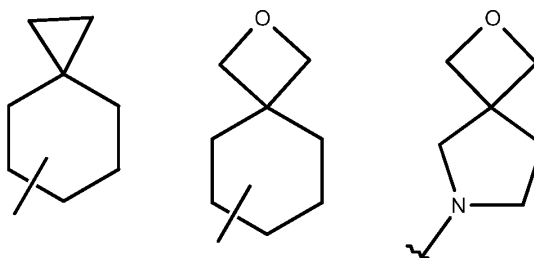
In one embodiment, R⁴ is cyclohexyl optionally substituted by one or more halo, C₁-C₃-alkyl or C₁-C₃-haloalkyl. In another embodiment, R⁴ is cyclohexyl substituted by 1 or 2 fluoro, chloro or CF₃.

In some embodiments, R⁴ is optionally substituted piperidinyl, morpholinyl, 30 tetrahydrofuranyl or dihydrofuranyl. In some embodiments, R⁴ is piperidinyl, morpholinyl, tetrahydrofuranyl or dihydrofuranyl substituted with one or more halogen, C₁-C₆-alkyl or C₁-C₆-

haloalkyl. In another embodiment, R^4 is piperidinyl, morpholinyl, tetrahydrofuranyl or dihydrofuranyl substituted with one or more methyl, chloro or fluoro.

In some embodiments, R^4 is 5- to 10-membered heteroaryl optionally substituted with 1, 2, 3, 4 or 5 substituents. In one embodiment, the 5- to 10-membered heteroaryl is pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, pyrrolyl, indolyl, quinoliny, isoquinoliny, quinazolinyl, quinoxalinyl, furanyl, thiophenyl, furyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyrazolyl benzofuranyl, benzothiophenyl, imidazopyridyl, imidazopyrimidyl or pyrrolopyrimidyl.

In other embodiments, R^4 is an optionally substituted spirocyclic heterocyclyl-carbocyclyl group, an optionally substituted spirocyclic heterocyclyl-heterocyclyl group, an optionally substituted spirocyclic carbocyclyl-carbocyclyl group or an optionally substituted spirocyclic carbocyclyl-heterocyclyl group. In other embodiments, R^4 is a 5- to 11-membered optionally substituted spirocyclic heterocyclyl-carbocyclyl group, a 5- to 11-membered optionally substituted spirocyclic heterocyclyl-heterocyclyl group, a 5- to 11-membered optionally substituted spirocyclic carbocyclyl-carbocyclyl group or a 5- to 11-membered optionally substituted spirocyclic carbocyclyl-heterocyclyl group. Non-limiting examples of spirocyclic carbocyclyl-carbocyclyl, spirocyclic carbocyclyl-heterocyclyl and spirocyclic heterocyclyl-heterocyclyl groups are shown below for illustration.



However, it will be apparent to persons skilled in the art that the second ring of the spirocyclic group may be joined at any available carbon of the first ring. It will also be understood that the first ring of the spirocyclic group may be bonded to the molecule at any available atom. Thus, the present invention includes 3-, 4-, 5-, 6- and 7-membered carbocyclic or heterocyclic rings as defined herein joined to a second 3-, 4-, 5-, 6- and 7-membered carbocyclic or heterocyclic ring at any available carbon atom of the first ring.

In some embodiments, R^4 is phenyl substituted with 1 to 4 substituents. In another embodiment, R^4 is phenyl substituted by 1 to 3 substituents. In yet another embodiment, R^4 is

phenyl substituted by 1 or 2 substituents. In some embodiments, R⁴ is phenyl substituted by 1, 2, 3 or 4 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, phenyl, substituted phenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In some embodiments, R⁴ is para-substituted phenyl.

In some embodiments, R⁴ is meta-substituted phenyl.

In some embodiments, R⁴ is ortho-substituted phenyl.

In some embodiments, R⁴ is halophenyl.

10 In some embodiments, R⁴ is haloalkylphenyl.

In some embodiments, R⁴ is haloalkoxyphenyl.

In some embodiments, R⁴ is phenyl substituted with 2 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In some embodiments, R⁴ is 2,3-disubstituted phenyl.

In some embodiments, R⁴ is 2,4-disubstituted phenyl.

In some embodiments, R⁴ is 2,5-disubstituted phenyl.

In some embodiments, R⁴ is a 2,6-disubstituted phenyl.

20 In some embodiments, R⁴ is a 3,5-disubstituted phenyl.

In other embodiments, R⁴ is a 3,4-disubstituted phenyl.

In other embodiments, R⁴ is a 3,6-disubstituted phenyl.

In some embodiments, R⁴ is dihalophenyl, e.g., dichlorophenyl; difluorophenyl; or chlorophenyl, fluorophenyl.

25 In some embodiments, R⁴ is 2,3-dihalophenyl.

In other embodiments, R⁴ is 2,3-dichlorophenyl or 2,3-difluorophenyl.

In another embodiment, R⁴ is 3,5-dichlorophenyl or 2,3-difluorophenyl.

In some embodiments, R⁴ is chlorophenyl. In another embodiment, R⁴ is fluorophenyl. In another embodiment, R⁴ is dichlorophenyl. In another embodiment, R⁴ is difluorophenyl. In yet another embodiment, R⁴ is 3,5-dichlorophenyl. In another embodiment, R⁴ is 3,5-difluorophenyl. In another embodiment, R⁴ is 2,6-dichlorophenyl. In another embodiment, R⁴ is 2,6-difluorophenyl.

In some embodiments, R^4 is phenyl substituted with 3 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

5 In some embodiments, R^4 is trihalophenyl, e.g., trichlorophenyl; trifluorophenyl; or chloro-, chloro-, fluorophenyl, or fluoro-, fluoro-, chlorophenyl.

In another embodiment, R^4 is 2,3,5-trihalophenyl. In another embodiment, R^4 is 2,4,6-trihalophenyl. In one embodiment, R^4 is 2,5-dichloro-4-fluorophenyl. In one embodiment, R^4 is 2,4,6-trifluorophenyl. In another embodiment, R^4 is 2,4,6-trichlorophenyl. In one embodiment, R^4 is 2,6-dichloro-4-fluorophenyl. In another embodiment, R^4 is 2,3,5-trifluorophenyl. In another embodiment, R^4 is 2,3,5-trichlorophenyl. In another embodiment, R^4 is 2,3-difluoro-5-chlorophenyl. In another embodiment, R^4 is 2,3-dichloro-5-fluorophenyl.

In some embodiments, R^4 is phenyl substituted with halogen and haloalkyl.

In some embodiments, R^4 is phenyl substituted with halogen and haloalkoxy.

15 In some embodiments, R^4 is phenyl substituted with haloalkyl and haloalkoxy.

In some embodiments, R^4 is phenyl substituted with 2 halogen and haloalkyl.

In some embodiments, R^4 is phenyl substituted with 2 halogen and haloalkoxy.

In some embodiments, R^4 is phenyl substituted with 1 haloalkyl, 1 halogen, and 1 haloalkoxy.

20 In some embodiments, R^4 is phenyl substituted with 1 halogen and 2 haloalkyl.

In some embodiments, R^4 is 5-membered heteroaryl optionally substituted with 1 or 2 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

25 In some embodiments, R^4 is 6-membered heteroaryl optionally substituted with 1 or 2 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In some embodiments, R^4 is 2-pyridyl optionally substituted with 1 or 2 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl,

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cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In some embodiments, R⁴ is 3-pyridyl optionally substituted with 1 or 2 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In some embodiments, R⁴ is 4-pyridyl optionally substituted with 1 or 2 substituents which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In another embodiment, R⁴ is 4-pyridyl which is unsubstituted or substituted with 1 or 2 chloro or fluoro. In yet another embodiment R⁴ is 3-pyridyl which is unsubstituted or substituted with 1 or 2 chloro or fluoro.

In other embodiments, R⁴ is an optionally substituted 3- to 7-membered heterocycle. In some embodiments, R⁴ is optionally substituted aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl, imidazoliny, imidazolidinyl, oxazolyl, oxazolidinyl, isoxazoliny, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, azepinyl, 4-piperidonyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, tetrahydropyranyl, morpholinyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl, triazolyl or triazinyl.

In another embodiment, R⁴ may be a heterocyclic, bridged bicyclic group, which may be optionally substituted.

In some embodiments, R⁵ and/or R^{5'} are hydrogen.

In some embodiments, each R⁵ and/or R^{5'} are independently hydrogen, C₁-C₄-alkyl, C₁-C₄-haloalkyl, amino, C₁-C₄-alkylamino, or di-(C₁-C₄alkyl) amino.

In another embodiment, each R⁵ and/or R^{5'} are independently hydrogen, methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl or *tert*-butyl.

In another embodiment, R⁵ and/or R^{5'} are independently hydrogen, CF₃, -CH₂CF₃, -CHF₂CF₃ or -CF₂CF₃.

In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen or halogen.

In another embodiment, R^5 and/or $R^{5'}$ are independently hydrogen, fluoro or chloro.

In another embodiment, R^5 and/or $R^{5'}$ are independently hydrogen, C₁-C₄-alkoxy, C₁-C₄-haloalkoxy or S(O)_p(C₁-C₄-alkyl or C₁-C₄-haloalkyl), where p is 0, 1 or 2.

5 In another embodiment, R^5 and/or $R^{5'}$ are independently hydrogen, methoxy, ethoxy, propoxy or butoxy.

In another embodiment, R^5 and/or $R^{5'}$ are independently hydrogen, methylthio, ethylthio, propylthio or butylthio.

In another embodiment, R^5 and/or $R^{5'}$ are independently hydrogen, -OCF₃ or -SCF₃.

10 In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, C₁-C₄-alkenyl or C₁-C₄-haloalkenyl.

In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, C₁-C₄-alkylcarbonyl or C₁-C₄-alkoxycarbonyl.

15 In other embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, C₁-C₄-alkylcarbonylamino.

In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, optionally substituted cyclopentyl or optionally substituted cyclohexyl.

20 In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, optionally substituted tetrahydrofuryl, dihydrofuryl, morpholino, pyranyl, dihydropyranyl, piperidinyl, dihydropiperidinyl, dihydrothiophene, or tetrahydrothiophene.

In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, optionally substituted phenyl.

25 In other embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, phenyl substituted with 1, 2, or 3 substituents, which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkoxy, cycloalkenyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

30 In other embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, a 5- or 6-membered heteroaryl with 1 or 2 substituents, which are independently halogen, cyano, nitro, alkylsulfonyl, haloalkylsulfonyl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, haloalkyl, haloalkenyl,

haloalkynyl, halocycloalkyl, halocycloalkenyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy or haloalkenyloxy.

In some embodiments, R^5 and/or $R^{5'}$ are independently hydrogen, optionally substituted aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, pyrazolyl, oxetanyl, pyrazolinyl, imidazolyl, imidazoliny, imidazolidinyl, oxazolyl, oxazolidinyl, isoxazoliny, isoxazolyl, thiazolyl, thiadiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, furyl, tetrahydrofuryl, thienyl, oxadiazolyl, piperidinyl, piperaziny, 2-oxopiperaziny, 2-oxopiperidinyl, 2-oxopyrrolodiny, 2-oxoazepiny, azepiny, 4-piperidonyl, pyridiny, pyraziny, pyrimidinyl, pyridaziny, tetrahydropyrany, morpholiny, thiamorpholiny, thiamorpholiny sulfoxide, thiamorpholiny sulfone, 1,3-dioxolane and tetrahydro-1,1-dioxothienyl, triazolyl or triaziny.

In some embodiments, R^5 and $R^{5'}$ are independently hydrogen, aziridinyl, azetidiny, oxetanyl, pyrrolidinyl, pyrrolyl, or morpholiny, all of which are optionally substituted by one or more halogen.

In some embodiments, R^6 and R^7 are independently in each occurrence hydrogen, halogen, C_1 - C_4 -alkyl, C_1 - C_4 -haloalkyl. In another embodiment, R^6 and R^7 are independently hydrogen, halogen or C_1 - C_4 -alkyl. In another embodiment, R^6 and R^7 are each hydrogen. In one embodiment, R^6 and R^7 together with the carbon to which they are attached for a carbonyl group ($C=O$). In another embodiment, R^6 and R^7 together with the carbon to which they are attached for a thiocarbonyl group ($C=S$). In yet another embodiment, R^6 and R^7 together with the carbon to which they are attached for an imino group ($C=NR'$).

In one embodiment, R^9 is H. In another embodiment, R^9 is C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl.

In some embodiments, Q is N.

In other embodiments, Q is $C-R^9$.

In some embodiments, X is O.

In some embodiments, X is S.

In some embodiments, X is NR' .

In some embodiments, W is CH_2 .

In another embodiment, W is CH, $C-C_1-C_3$ -alkyl or $C-C_1-C_3$ -haloalkyl. In other embodiments, W is CH_2 , $C(C_1-C_3-alkyl)_2$ or $C(C_1-C_3-haloalkyl)_2$.

In other embodiments, W is CH_2 , $C(CH_3)_2$, $C(C_2H_5)_2$ or $C(CF_3)_2$.

In some embodiments, W is absent.

In some embodiments, W^1 is CH_2 .

In another embodiment, W^1 is CH , $C-C_1-C_3$ -alkyl or $C-C_1-C_3$ -haloalkyl.

In other embodiments, W^1 is CH_2 , $C(C_1-C_3\text{-alkyl})_2$ or $C(C_1-C_3\text{-haloalkyl})_2$.

In other embodiments, W^1 is CH_2 , $C(CH_3)_2$, $C(C_2H_5)_2$ or $C(CF_3)_2$.

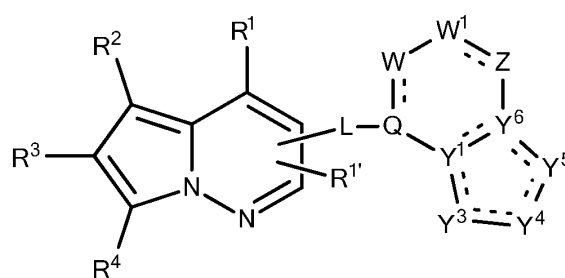
5 In some embodiments, Z is CH_2 .

In another embodiment, Z is CH , $C-C_1-C_3$ -alkyl or $C-C_1-C_3$ -haloalkyl.

In other embodiments, Z is $C(C_1-C_3\text{-alkyl})_2$ or $C(C_1-C_3\text{-haloalkyl})_2$.

In some embodiments, Z is O .

10 In some embodiments, the compound of Formula (I), or a salt thereof, is the compound of Formula (I-1):



(I-1)

15 wherein variables L , R^1 , $R^{1'}$, R^2 , R^3 , R^4 , Y^1 , Y^3 , Y^4 , Y^5 , Y^6 , Q , W , W^1 and Z are as defined for any of the embodiments of Formula (I) described above; and the dashed bonds (---) signify a single or double bond.

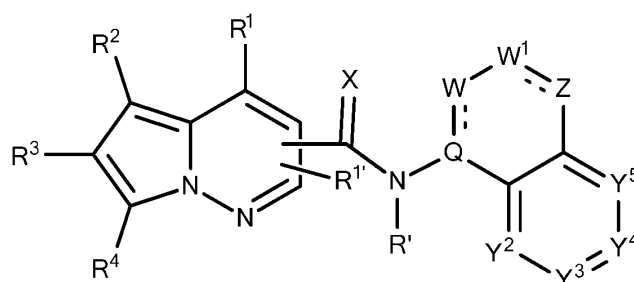
In another embodiment, a compound of Formula (I-1) is provided wherein variables L , R^1 , $R^{1'}$, R^2 , R^3 , R^4 , Y^1 , Y^3 , Y^4 , Y^5 , Y^6 , Q , W , W^1 and Z are as defined for any of the embodiments of
20 Formula (I) described above; and the dashed bonds (---) signify a single or double bond.

In one embodiment of Formula (I-1), Z is O . In one embodiment of Formula (I-1), W is CH_2 and Z is O . In one embodiment, W is absent. In another embodiment, W is absent and Z is CH_2 . In one embodiment, Q is N . In another embodiment, Q is $C-R^9$. In another embodiment of Formula (I-1), Q is CH . In another embodiment of Formula (I-1), W is CH_2 , W^1 is CH_2 and Z is
25 CH_2 . In another embodiment of Formula (I-1), W and W^1 are independently CR^6R^7 wherein R^6

and R^7 are H, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl and Z is O. In another embodiment, W and W^1 are each CH_2 and Z is O.

In one embodiment of Formula (I-1), Y^3 is S. In another embodiment of Formula (I-1), Y^5 is S. In another embodiment, Y^3 is N. In another embodiment Y^5 is N. In another embodiment of
 5 Formula (I-1), Y^5 is N and Y^3 is S. In yet another embodiment of Formula (I-1), Y^5 is S and Y^3 is N. In another embodiment of Formula (I-1), Y^6 and Y^3 are each N. In another embodiment of Formula (I-1), Y^6 is N and Y^4 is N. In another embodiment, Y^1 is N and Y^5 is N. In another embodiment, Y^3 is N and Y^5 is N. In another embodiment, Y^3 is N and Y^4 is N. In another embodiment, Y^3 is NR' and Y^4 is N. In another embodiment, Y^3 is NR' where R' is hydrogen or
 10 C_1 - C_3 -alkyl and Y^4 is N.

In some embodiments, the compound of Formula (I), or a salt thereof, is the compound of formula (I-2):



(I-2)

15 wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R' , Y^2 , Y^3 , Y^4 , Y^5 , X, Q, W, W^1 and Z are as defined for any of the embodiments of Formula (I) described above; and the dashed bonds (---) signify a single or double bond.

In another embodiment, a compound of Formula (I-2) is provided wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R' , Y^2 , Y^3 , Y^4 , Y^5 , X, Q, W, W^1 and Z are as defined for any of the embodiments
 20 of Formula (IA) described above.

In one embodiment of Formula (I-2), Q is $C-R^9$. In another embodiment of Formula (I-2), Q is CH . In another embodiment of Formula (I-2), Q is N.

In one embodiment of Formula (I-2), Z is O. In one embodiment of Formula (I-2), W is CH_2 and Z is O. In one embodiment, W is absent. In another embodiment, W is absent and Z is CH_2 . In another embodiment, W is absent, Z is CH_2 and one of Y^2 , Y^3 , Y^4 and Y^5 is N. In another
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embodiment, W is absent, Z is CH₂ and two of Y², Y³, Y⁴ and Y⁵ are N. In another embodiment, W is absent, Z is CH₂ and Y² is N. In another embodiment, W is absent, Z is CH₂ and Y⁴ is N. In another embodiment, W is absent, Z is CH₂ and Y⁵ is N. In another embodiment, W is absent and Z is O.

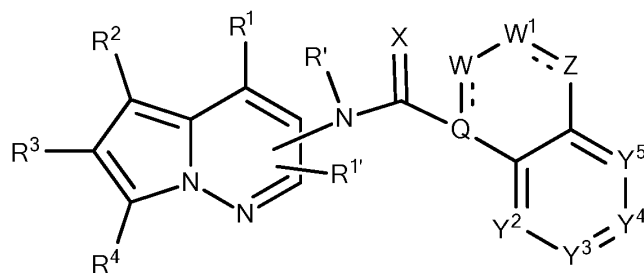
5 In another embodiment of Formula (I-2), W is CH₂, W¹ is CH₂ and Z is CH₂. In another embodiment of Formula (I-2), W and W¹ are independently CR⁶R⁷ wherein R⁶ and R⁷ are H, C₁-C₃-alkyl or C₁-C₃-haloalkyl and Z is O. In an embodiment, W and W¹ are independently CR⁶R⁷ wherein R⁶ and R⁷ are H or methyl, and Z is O. In another embodiment, W and W¹ are each CH₂ and Z is O.

10 In one embodiment of Formula (I-2), each of Y², Y³, Y⁴ and Y⁵ are independently CR⁵. In one embodiment, each of Y², Y³, Y⁴ and Y⁵ are independently CH.

In another embodiment, Z is O and W is CR⁶R⁷, wherein R⁶ and R⁷ together with the carbon atom to which they are attached form C=O.

In another embodiment of Formula (I-2), W¹ is CR⁶R⁷, wherein R⁶ and R⁷ together form a
15 2 to 5-membered chain, optionally containing one or two N, O, Si or S atoms, to form a carbocyclic or heterocyclic ring. In another embodiment, W¹ is CR⁶R⁷, wherein R⁶ and R⁷ together form a 3, 4 or 5-membered chain to form a cyclobutyl, cyclopentyl or cyclohexyl ring.

In other embodiments, the compound of Formula (I), or a salt thereof, is the compound of Formula (I-3) below:



(I-3)

wherein variables R¹, R^{1'}, R², R³, R⁴, R', Y², Y³, Y⁴, Y⁵, X, Q, W, W¹ and Z are as defined for any of the embodiments of Formula (I) described above; and the dashed bonds (---) signify a single or double bond.

In another embodiment, a compound of Formula (I-3) is provided wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R^5 , Y^2 , Y^3 , Y^4 , Y^5 , X , Q , W , W^1 and Z are as defined for any of the embodiments of Formula (IA) described above.

In one embodiment of Formula (I-3), Q is $C-R^9$. In another embodiment of Formula (I-3),
5 Q is CH . In another embodiment of Formula (I-3), Q is N .

In one embodiment of Formula (I-3), Z is O . In one embodiment of Formula (I-3), W is CH_2 and Z is O . In one embodiment, W is absent. In another embodiment, W is absent and Z is CH_2 . In another embodiment, W is absent, Z is CH_2 and one of Y^2 , Y^3 , Y^4 and Y^5 is N . In another embodiment, W is absent, Z is CH_2 and two of Y^2 , Y^3 , Y^4 and Y^5 are N . In another embodiment,
10 W is absent, Z is CH_2 and Y^2 is N . In another embodiment, W is absent, Z is CH_2 and Y^4 is N . In another embodiment, W is absent, Z is CH_2 and Y^5 is N . In another embodiment, W is absent and Z is O .

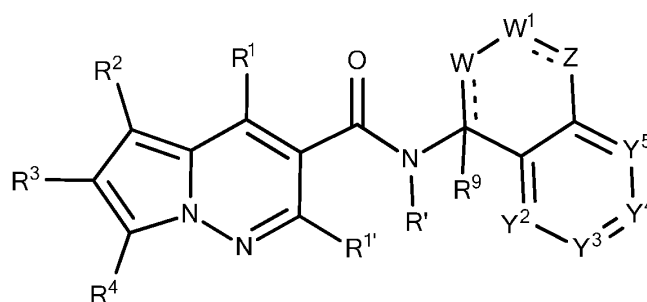
In another embodiment of Formula (I-3), W is CH_2 , W^1 is CH_2 and Z is CH_2 . In another embodiment of Formula (I-3), W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H , C_1 -
15 C_3 -alkyl or C_1 - C_3 -haloalkyl and Z is O . In an embodiment, W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H or methyl and Z is O . In another embodiment, W and W^1 are each CH_2 and Z is O .

In one embodiment of Formula (I-3), each of Y^2 , Y^3 , Y^4 and Y^5 are independently CR^5 . In one embodiment, each of Y^2 , Y^3 , Y^4 and Y^5 are independently CH .

20 In another embodiment, Z is O and W is CR^6R^7 , wherein R^6 and R^7 together with the carbon atom to which they are attached form $C=O$.

In another embodiment of Formula (I-3), W^1 is CR^6R^7 , wherein R^6 and R^7 together form a 2 to 5-membered chain, optionally containing one or two N , O , Si or S atoms, to form a carbocyclic or heterocyclic ring. In another embodiment, W^1 is CR^6R^7 , wherein R^6 and R^7 together form a 3,
25 4 or 5-membered chain to form a cyclobutyl, cyclopentyl or cyclohexyl ring.

In some embodiments, the compound of formula (I), or a salt thereof, is the compound of Formula (Ia):



(Ia)

wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R' , R^9 , W , W^1 , Z , Y^2 , Y^3 , Y^4 and Y^5 are as defined for any of the embodiments of Formula (I) described above; and the dashed bonds (---) signify a single or double bond.

In another embodiment, a compound of Formula (Ia) is provided wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R' , R^9 , W , W^1 , Z , Y^2 , Y^3 , Y^4 and Y^5 are as defined for any of the embodiments of Formula (Ia) described above; and the dashed bonds (---) signify a single or double bond.

In one embodiment of Formula (Ia), R^9 is CH. In another embodiment of Formula (Ia), R' is H. In another embodiment, W and W^1 are CH_2 . In another embodiment, $R^{1'}$ is H.

In one embodiment of Formula (Ia), Z is O. In one embodiment of Formula (Ia), W is CH_2 and Z is O. In one embodiment, W is absent. In another embodiment, W is absent and Z is CH_2 . In another embodiment, W is absent, Z is CH_2 and one of Y^2 , Y^3 , Y^4 and Y^5 is N. In another embodiment, W is absent, Z is CH_2 and two of Y^2 , Y^3 , Y^4 and Y^5 are N. In another embodiment, W is absent, Z is CH_2 and Y^2 is N. In another embodiment, W is absent, Z is CH_2 and Y^4 is N. In another embodiment, W is absent, Z is CH_2 and Y^5 is N. In another embodiment, W is absent and Z is O.

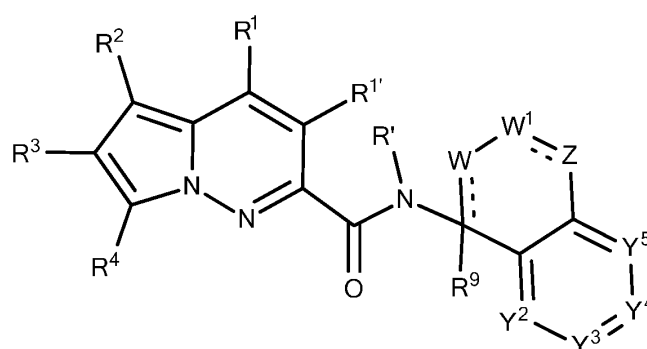
In another embodiment of Formula (Ia), W is CH_2 , W^1 is CH_2 and Z is CH_2 . In another embodiment of Formula (Ia), W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl and Z is O. In an embodiment, W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H or methyl and Z is O. In another embodiment, W and W^1 are each CH_2 and Z is O.

In one embodiment of Formula (Ia), each of Y^2 , Y^3 , Y^4 and Y^5 are independently CR^5 . In one embodiment, each of Y^2 , Y^3 , Y^4 and Y^5 are independently CH.

In another embodiment, Z is O and W is CR⁶R⁷, wherein R⁶ and R⁷ together with the carbon atom to which they are attached form C=O.

In another embodiment of Formula (Ia), W¹ is CR⁶R⁷, wherein R⁶ and R⁷ together form a 2 to 5-membered chain, optionally containing one or two N, O, Si or S atoms, to form a carbocyclic or heterocyclic ring. In another embodiment, W¹ is CR⁶R⁷, wherein R⁶ and R⁷ together form a 3, 4 or 5-membered chain to form a cyclobutyl, cyclopentyl or cyclohexyl ring.

In some embodiments, the compound of formula (I), or a salt thereof, is the compound of Formula (Ib):



(Ib)

wherein variables R¹, R^{1'}, R², R³, R⁴, R', R⁹, Y², Y³, Y⁴, Y⁵, W, W¹ and Z are as defined for any of the embodiments of Formula (I) described above; and the dashed bonds (---) signify a single or double bond.

In another embodiment, a compound of Formula (Ib) is provided wherein variables R¹, R^{1'}, R², R³, R⁴, R', R⁹, W, W¹, Z, Y², Y³, Y⁴ and Y⁵ are as defined for any of the embodiments of Formula (IA) described above; and the dashed bonds (---) signify a single or double bond.

In one embodiment of Formula (Ib), R⁹ is CH. In another embodiment of Formula (Ib), R' is H. In another embodiment W and W¹ are each CH₂. In another embodiment, R^{1'} is H.

In one embodiment of Formula (Ib), Z is O. In one embodiment of Formula (Ib), W is CH₂ and Z is O. In one embodiment, W is absent. In another embodiment, W is absent and Z is CH₂. In another embodiment, W is absent, Z is CH₂ and one of Y², Y³, Y⁴ and Y⁵ is N. In another embodiment, W is absent, Z is CH₂ and two of Y², Y³, Y⁴ and Y⁵ are N. In another embodiment, W is absent, Z is CH₂ and Y² is N. In another embodiment, W is absent, Z is CH₂ and Y⁴ is N. In

another embodiment, W is absent, Z is CH₂ and Y⁵ is N. In another embodiment, W is absent and Z is O.

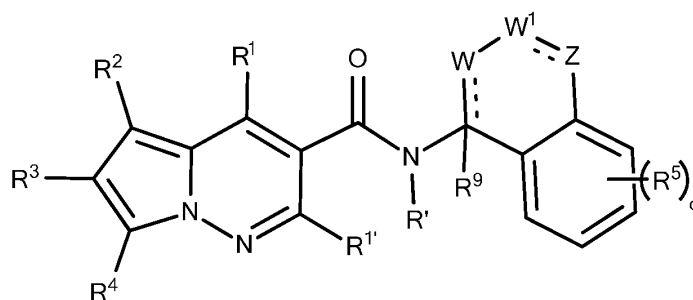
In another embodiment of Formula (Ib), W is CH₂, W¹ is CH₂ and Z is CH₂. In another embodiment of Formula (Ib), W and W¹ are independently CR⁶R⁷ wherein R⁶ and R⁷ are H, C₁-C₃-alkyl or C₁-C₃-haloalkyl and Z is O. In an embodiment, W and W¹ are independently CR⁶R⁷ wherein R⁶ and R⁷ are H or methyl and Z is O. In another embodiment, W and W¹ are each CH₂ and Z is O.

In one embodiment of Formula (Ib), each of Y², Y³, Y⁴ and Y⁵ are independently CR⁵. In one embodiment, each of Y², Y³, Y⁴ and Y⁵ are independently CH.

In another embodiment, Z is O and W is CR⁶R⁷, wherein R⁶ and R⁷ together with the carbon atom to which they are attached form C=O.

In another embodiment of Formula (Ib), W¹ is CR⁶R⁷, wherein R⁶ and R⁷ together form a 2 to 5-membered chain, optionally containing one or two N, O, Si or S atoms, to form a carbocyclic or heterocyclic ring. In another embodiment, W¹ is CR⁶R⁷, wherein R⁶ and R⁷ together form a 3, 4 or 5-membered chain to form a cyclobutyl, cyclopentyl or cyclohexyl ring.

In some embodiments, the compound of formula (I), or a salt thereof, is the compound of Formula (Ic):



(Ic)

wherein variables R¹, R^{1'}, R², R³, R⁴, R', R⁹, R⁵, W, W¹ and Z are as defined for any of the embodiments of Formula (I) described above; o is 0, 1, 2, 3 or 4; and the dashed bonds (---) signify a single or double bond.

In another embodiment, a compound of Formula (Ic) is provided wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R' , R^9 , R^5 , W , W^1 and Z are as defined for any of the embodiments of Formula (IA) described above; o is 0, 1, 2, 3 or 4; and the dashed bonds (-----) signify a single or double bond.

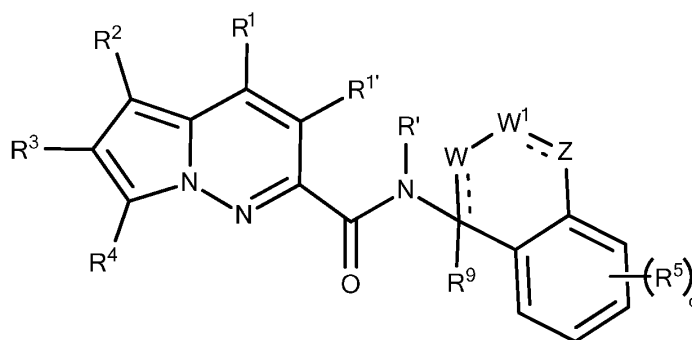
In one embodiment of Formula (Ic), R^9 is CH . In another embodiment of Formula (Ic), R' is H. In another embodiment, W and W^1 are each CH_2 . In another embodiment, $R^{1'}$ is H.

In one embodiment of Formula (Ic), Z is O. In one embodiment of Formula (Ic), W is CH_2 and Z is O. In one embodiment, W is absent. In another embodiment, W is absent and Z is CH_2 . In another embodiment, W is absent and Z is O.

In another embodiment of Formula (Ic), W is CH_2 , W^1 is CH_2 and Z is CH_2 . In another embodiment of Formula (Ic), W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl and Z is O. In an embodiment, W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H or methyl and Z is O. In another embodiment, W and W^1 are each CH_2 and Z is O.

In one embodiment of Formula (Ic), o is 1. In another embodiment, o is 2. In still another embodiment, o is 3. In one embodiment, R^5 is halogen. In another embodiment, R^5 is chloro or fluoro. In another embodiment, o is 1 or 2 and R^5 is chloro or fluoro.

In other embodiments, the compound of Formula (I), or a salt thereof, is the compound of formula (Id):



(Id)

wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R' , R^9 , R^5 , W , W^1 and Z are as defined for any of the embodiments of Formula (I) described above; o is 0, 1, 2, 3 or 4; and the dashed bonds (-----) signify a single or double bond.

In another embodiment, a compound of Formula (Id) is provided wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R^5 , R^9 , R^5 , W , W^1 and Z are as defined for any of the embodiments of Formula (IA) described above; o is 0, 1, 2, 3 or 4; and the dashed bonds (---) signify a single or double bond.

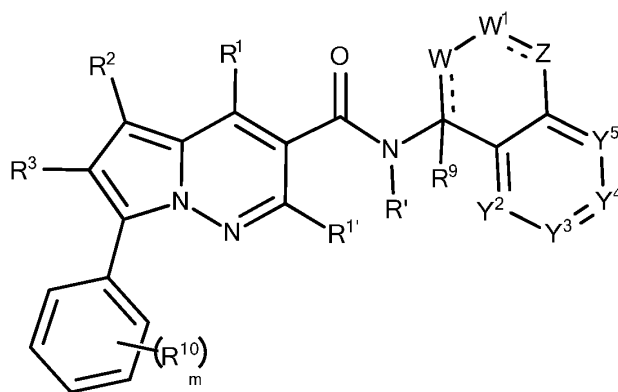
In one embodiment of Formula (Id), R^9 is CH . In another embodiment of Formula (Id), $R^{1'}$ is H. In another embodiment, W and W^1 are each CH_2 . In another embodiment, $R^{1'}$ is H.

In one embodiment of Formula (Id), Z is O. In one embodiment of Formula (Id), W is CH_2 and Z is O. In one embodiment, W is absent. In another embodiment, W is absent and Z is CH_2 . In another embodiment, W is absent and Z is O.

In another embodiment of Formula (Id), W is CH_2 , W^1 is CH_2 and Z is CH_2 . In another embodiment of Formula (Id), W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl and Z is O. In an embodiment, W and W^1 are independently CR^6R^7 wherein R^6 and R^7 are H or methyl and Z is O. In another embodiment, W and W^1 are each CH_2 and Z is O.

In one embodiment of Formula (Id), o is 1. In another embodiment, o is 2. In still another embodiment, o is 3. In one embodiment, R^5 is halogen. In another embodiment, R^5 is chloro or fluoro. In another embodiment, o is 1 or 2 and R^5 is chloro or fluoro.

In another embodiment, the compound of formula (I), or a salt thereof, is the compound of formula (Ie):



20

(Ie)

wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^5 , R^9 , Y^2 , Y^3 , Y^4 , Y^5 , W , W^1 and Z are as defined for Formula (I); m is 0, 1, 2, 3, 4 or 5; and each R^{10} is cyano, halogen, hydroxyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -haloalkoxy, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 -

C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl), where p is 0, 1 or 2, SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted, wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (I) above.

In another embodiment, the present invention includes a compound of Formula (Ie) as described above, or a salt thereof, wherein variables R¹, R², R³, R⁴, R⁹, Y², Y³, Y⁴, Y⁵, W, W¹ and Z are as defined for Formula (I); m is 0, 1, 2, 3, 4 or 5; each R¹⁰ is cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl) where p is 0, 1 or 2; SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted; and

R^1 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, $-SO_p$ (optionally substituted alkyl or haloalkyl) where p is 0, 1 or 2; $-SF_5$, or $-NR^aR^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4- or 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (I) above.

In another embodiment, the present invention includes a compound of Formula (Ie) as described above, or a salt thereof, wherein variables R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , Y^2 , Y^3 , Y^4 , Y^5 , W, W^1 and Z are as defined for Formula (I); m is 0, 1, 2, 3, 4 or 5; each R^{10} is cyano, halogen, hydroxyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -haloalkoxy, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -haloalkoxy- C_1 - C_6 -alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C_3 - C_8 -cycloalkyl, optionally substituted C_3 - C_8 -cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -haloalkylcarbonyl, C_1 - C_6 -alkoxy carbonyl, C_1 - C_6 -haloalkoxy carbonyl, aminocarbonyl, C_1 - C_6 -alkylaminocarbonyl, C_1 - C_6 -haloalkylaminocarbonyl, di- C_1 - C_6 -alkylaminocarbonyl, di- C_1 - C_6 -haloalkylaminocarbonyl, $-SO_p$ (optionally substituted C_1 - C_6 -alkyl or C_1 - C_6 -haloalkyl) where p is 0, 1 or 2; SF_5 , or $-NR^aR^b$, wherein R^a and R^b are independently H, C_1 - C_6 -alkyl or C_1 - C_6 -haloalkyl;

or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7- or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted; and

R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, -SO_p(optionally substituted alkyl or haloalkyl) where p is 0, 1 or 2; -SF₅, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7- or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (I) described above.

In another embodiment, a compound of Formula (Ie) is provided wherein variables R¹, R^{1'}, R², R³, R', R⁹, W, W¹, Z, Y², Y³, Y⁴ and Y⁵ are as defined for Formula (IA); m is 0, 1, 2, 3, 4 or 5; and each R¹⁰ is cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxy carbonyl, C₁-C₆-haloalkoxy carbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-

C₆-alkyl or C₁-C₆-haloalkyl), where p is 0, 1 or 2, SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted, wherein "optionally substituted" indicates that the group recited may be optionally substituted with the same groups defined for "optionally substituted" for the broadest embodiment of Formula (IA) above.

In another embodiment, the present invention includes a compound of Formula (Ie) as described above, or a salt thereof, wherein variables R^{1'}, R², R³, R', R⁹, Y², Y³, Y⁴, Y⁵, W, W¹ and Z are as defined for Formula (IA); m is 0, 1, 2, 3, 4 or 5; each R¹⁰ is cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl) where p is 0, 1 or 2; SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted; and

R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxycarbonyl, aminocarbonyl, optionally substituted

alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, $-\text{SO}_p(\text{optionally substituted alkyl or haloalkyl})$ where p is 0, 1 or 2; $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4- or 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (IA) described above.

10 In another embodiment, the present invention includes a compound of Formula (Ie) as described above, or a salt thereof, wherein variables R^1 , R^2 , R^3 , R^4 , R^5 , Y^1 , Y^2 , Y^3 , Y^4 , Y^5 , W, W^1 and Z are as defined for Formula (IA); m is 0, 1, 2, 3, 4 or 5; each R^{10} is cyano, halogen, hydroxyl, C_1 - C_6 -alkyl, C_1 - C_6 -haloalkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -haloalkoxy, C_2 - C_6 -alkenyl, C_2 - C_6 -haloalkenyl, C_2 - C_6 -alkynyl, C_2 - C_6 -haloalkynyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -haloalkoxy- C_1 - C_6 -alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C_3 - C_8 -cycloalkyl, optionally substituted C_3 - C_8 -cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C_1 - C_6 -alkylcarbonyl, C_1 - C_6 -haloalkylcarbonyl, C_1 - C_6 -alkoxycarbonyl, C_1 - C_6 -haloalkoxycarbonyl, aminocarbonyl, C_1 - C_6 -alkylaminocarbonyl, C_1 - C_6 -haloalkylaminocarbonyl, di- C_1 - C_6 -alkylaminocarbonyl, di- C_1 - C_6 -haloalkylaminocarbonyl, $-\text{SO}_p(\text{optionally substituted } \text{C}_1\text{-C}_6\text{-alkyl or } \text{C}_1\text{-C}_6\text{-haloalkyl})$ where p is 0, 1 or 2; SF_5 , or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H, C_1 - C_6 -alkyl or C_1 - C_6 -haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted; and

25 R^1 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally

- substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, -SO_p(optionally substituted alkyl or haloalkyl) where p is 0, 1 or 2; -SF₅, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7- or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (IA) above.

In another embodiment, the invention provides a compound of Formula (Ie) described above wherein:

- R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, or optionally substituted benzyl;
- R¹ is optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₂-C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^{1'} hydrogen, halogen, optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl;

- R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- 5 R³ is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- each R⁵ is independently in each occurrence, hydrogen, halogen, cyano, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy;
- 10 R⁶ and R⁷ are independently hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, or R⁶ together with R⁷ form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be
- 15 optionally substituted;
- R⁹ is hydrogen, halogen, C₁-C₆-alkyl or C₁-C₆-haloalkyl;
- each R¹⁰ is cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl,
- 20 optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl,
- 25 C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl) where p is 0, 1 or 2; SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they

are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

m is 0, 1, 2, 3, 4 or 5; and

- 5 Y², Y³, Y⁴, Y⁵, W, W¹, Z, X and the dashed bonds (-----) are as defined above for the compound of Formula (IA);

wherein the term “optionally substituted” indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3- to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, SF₅, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl or C₁-C₆-haloalkylsulfonyl.

- 15 In another embodiment, the invention provides a compound of Formula (Ie) described above wherein:

R' is hydrogen, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, or optionally substituted benzyl;

- 20 R¹ is optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, hydroxy-C₁-C₆-alkyl, hydroxy-C₁-C₆-haloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, amino-C₁-C₆-alkyl, C₁-C₆-alkylamino-C₁-C₆-alkyl, C₁-C₆-haloalkylamino-C₁-C₆-alkyl, di-C₁-C₆-alkylamino-C₁-C₆-alkyl, di-C₁-C₆-haloalkylamino-C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₂-C₆-alkenyloxy, C₂-C₆-haloalkenyloxy, C₂-C₆-alkynyloxy, C₂-C₆-haloalkynyloxy, C₁-C₆-haloalkoxy, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkenyl, optionally substituted 3- to 7-membered heterocyclyl, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₆-alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7-, 8-membered-heterocyclyl group, which may

include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

- R^{1'} hydrogen, halogen, optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl;
- 5 R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- R³ is hydrogen, cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl or C₁-C₆-haloalkoxy-C₁-C₆-alkyl;
- 10 each R⁵ is independently in each occurrence, hydrogen, halogen, cyano, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy;
- R⁶ and R⁷ are independently hydrogen, halogen, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₂-C₆-alkenyl, C₂-C₆-alkynyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, or R⁶ together with R⁷ form a 2-6-membered
- 15 chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;
- R⁹ is hydrogen, halogen, C₁-C₆-alkyl or C₁-C₆-haloalkyl;
- 20 each R¹⁰ is cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy,
- 25 optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl,

di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl) where p is 0, 1 or 2; SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

m is 0, 1, 2, 3, 4 or 5; and

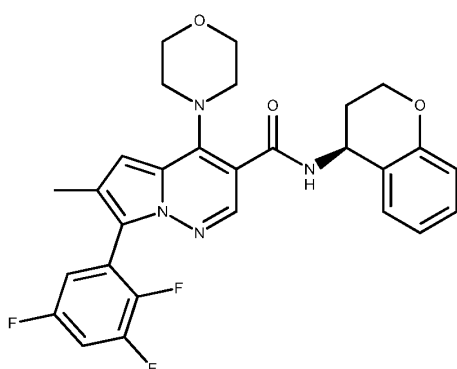
Y², Y³, Y⁴, Y⁵, W, W¹, Z, X and the dashed bonds (---) are as defined above for the compound of Formula (IA);

wherein the term “optionally substituted” indicates that the group recited is optionally substituted by one or more halogen (chloro, fluoro, bromo, iodo), hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, 3- to 8-membered cycloalkyl, amino, C₁-C₆-alkylamino, C₁-C₆-dialkylamino, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, cyano, SF₅, acetyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-dialkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, C₁-C₆-dihaloalkylaminocarbonyl, C₁-C₆-alkylthio, C₁-C₆-alkylsulfinyl, C₁-C₆-alkylsulfonyl, C₁-C₆-haloalkylthio, C₁-C₆-haloalkylsulfinyl or C₁-C₆-haloalkylsulfonyl.

In another embodiment, the present invention includes a compound of Formula (Ie) as described above, or a salt thereof, wherein variables R^{1'}, R², R³, R⁴, R⁹, Y², Y³, Y⁴, Y⁵, W, W¹ and Z are as defined for Formula (IA); m is 0, 1, 2, 3, 4 or 5; each R¹⁰ is cyano, halogen, hydroxyl, C₁-C₆-alkyl, C₁-C₆-haloalkyl, C₁-C₆-alkoxy, C₁-C₆-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl) where p is

0, 1 or 2; SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted; and

- 5 R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, -SO_p(optionally substituted alkyl or haloalkyl)
- 10 where p is 0, 1 or 2; -SF₅, or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 6-, 7- or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- 15 wherein “optionally substituted” indicates that the group recited may be optionally substituted with the same groups defined for “optionally substituted” for the broadest embodiment of Formula (IA) above; and with the proviso that the compound below is excluded:
- 20



In one embodiment of formula (Ie), R¹⁰ is halogen. In another embodiment, R¹⁰ is chloro. In yet another embodiment, R¹⁰ is fluoro. In another embodiment, R¹⁰ is chloro or fluoro and m is 1, 2 or 3. In yet another embodiment, R¹⁰ is fluoro and m is 2. In another embodiment, R¹⁰ is chloro and m is 2. In another embodiment, R¹⁰ is fluoro or chloro, m is 2 and the fluoro or chloro are substituted are the 3- and 5-positions of the phenyl ring. In another embodiment, R¹⁰ is fluoro or chloro, m is 2 and the fluoro or chloro are substituted at the 2- and 6-positions.

In another embodiment of formula (Ie), R¹⁰ is fluoro or chloro and m is 3. In another embodiment, R¹⁰ is fluoro or chloro, m is 3 and the fluoro or chloro are substituted at the 2-, 3- and 5-positions of the phenyl ring. In another embodiment of formula (Ie), R¹⁰ is fluoro or chloro, m is 3, wherein chloro is substituted at the 2- and 3-positions and fluoro is substituted at the 5-position of the phenyl ring. In another embodiment, R¹⁰ is fluoro, m is 3 and the fluoro is substituted at the 2-, 3- and 5-positions of the phenyl ring. In yet another embodiment, R¹⁰ is chloro, m is 3 and the fluoro is substituted at the 2-, 3- and 5-positions of the phenyl ring.

In one embodiment of Formula (Ie), R⁹ is H. In another embodiment of Formula (Ie), R' is H. In another embodiment, R^{1'} is H. In another embodiment, W and W¹ are each CH₂.

In another embodiment of Formula (Ie), W is CH₂, W¹ is CH₂ and Z is CH₂. In another embodiment of Formula (Ie), W and W¹ are independently CR⁶R⁷ wherein R⁶ and R⁷ are H, C₁-C₃-alkyl or C₁-C₃-haloalkyl and Z is O. In another embodiment, W and W¹ are each CH₂ and Z is O.

In one embodiment of Formula (Ie), R¹ is optionally substituted C₁-C₆-alkyl, optionally substituted C₃-C₆-cycloalkyl, -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₃-alkyl, or wherein R^a and R^b together with the nitrogen form an optionally-substituted 3-, 4-, 5- or 6-membered heterocycle, which may include one additional heteroatom selected from O or N; R² is hydrogen or optionally substituted C₁-C₃-alkyl; R³ is hydrogen, optionally substituted C₁-C₃-alkyl or halogen; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is halogen and m is 2 or 3; W is CH₂ or is absent; W¹ is CH₂; Z is CH₂ or O and Y², Y³, Y⁴ and Y⁵ are each independently N, CH or C-halogen; wherein the optional substituents are one or more halogen, hydroxy, cyano, C₁-C₃-alkyl, C₁-C₃-haloalkyl, 3- to 8-membered cycloalkyl, amino, C₁-C₃-alkylamino, C₁-C₃-dialkylamino, C₁-C₃-alkoxy and C₁-C₃-haloalkoxy.

In another embodiment of Formula (Ie), R¹ is C₁-C₄-alkyl, -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₃-alkyl, or wherein R^a and R^b together with the

nitrogen form an optionally substituted 3- or 4-membered heterocycle; R² is hydrogen; R³ is hydrogen, optionally substituted C₁-C₃-alkyl, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen; R⁹ is hydrogen; R¹⁰ is chloro or fluoro and m is 2 or 3; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each independently CH or C-halogen; wherein the optional substituents are one or
 5 more halogen, hydroxy, C₁-C₃-alkyl, C₁-C₃-haloalkyl, C₁-C₃-alkoxy or C₁-C₃-haloalkoxy.

In another embodiment of Formula (Ie), R¹ is methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *sec*-butyl, *tert*-butyl, -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₃-alkyl, or wherein R^a and R^b together with the nitrogen form an aziridine, azetidine or pyrrolidinyl ring, each of which is optionally substituted by one or more fluoro or
 10 methyl; R² is hydrogen; R³ is hydrogen, optionally substituted C₁-C₃-alkyl, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro or fluoro and m is 2 or 3; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each independently CH or C-halogen; wherein the optional substituents are one or more chloro, fluoro, hydroxy, C₁-C₃-alkyl or C₁-C₃-haloalkyl.

In another embodiment of Formula (Ie), R¹ is *iso*-propyl, *tert*-butyl, -N(CH₃)₂, azetidiny optionally substituted by one or more fluoro or methyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro or fluoro and m is 2 or 3; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.
 15

In another embodiment of Formula (Ie), R¹ is *iso*-propyl, *tert*-butyl, -N(CH₃)₂, azetidiny optionally substituted by one or more fluoro or methyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro or fluoro and m is 3, wherein the chloro or fluoro substituents are located at the 2, 3 and 5 positions of the phenyl ring; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and
 20 Y⁵ are each CH.

In another embodiment of Formula (Ie), R¹ is *iso*-propyl, *tert*-butyl, -N(CH₃)₂, azetidiny optionally substituted by one or more fluoro or methyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro and m is 3, wherein the chloro substituents are substituted at the 2, 3 and
 25 5 positions of the phenyl ring; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.

In another embodiment of Formula (Ie), R¹ is *iso*-propyl, *tert*-butyl, -N(CH₃)₂, azetidinyloptionally substituted by one or more fluoro or methyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is fluoro and m is 3, wherein the fluoro substituents are substituted at the 2, 3 and 5 positions of the phenyl ring; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.

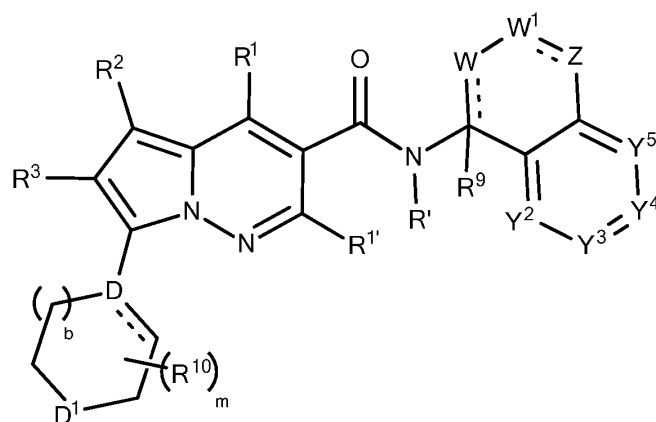
In another embodiment of Formula (Ie), R¹ is morpholinyl, piperidinyl or piperazinyl optionally substituted by one or more fluoro or methyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro or fluoro and m is 2 or 3; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.

In another embodiment of Formula (Ie), R¹ is morpholinyl, piperidinyl or piperazinyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro or fluoro and m is 3, wherein the chloro or fluoro substituents are located at the 2, 3 and 5 positions of the phenyl ring; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.

In another embodiment of Formula (Ie), R¹ is morpholinyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is chloro and m is 3, wherein the chloro substituents are substituted at the 2, 3 and 5 positions of the phenyl ring; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.

In another embodiment of Formula (Ie), R¹ is morpholinyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; R¹⁰ is fluoro and m is 3, wherein the fluoro substituents are substituted at the 2, 3 and 5 positions of the phenyl ring; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH.

In other embodiments, the compound of Formula (I) is the compound of Formula (If):



(If)

wherein variables R¹, R^{1'}, R², R³, R', R⁹, Y², Y³, Y⁴, Y⁵, W, W¹ and Z are as defined for any of the embodiments of Formula (I); R¹⁰ and m are as defined for formula (Ie) above; b is 0 or 1; the dashed bond ($\overline{\text{---}}$) signifies a single or double bond; D is N, SiR¹¹ where R¹¹ is C₁-C₆alkyl or C₁-C₆haloalkyl, C or C-R⁵; D¹ is N-R', O, SiR¹¹R¹², where R¹¹ and R¹² are independently C₁-C₆alkyl or C₁-C₆haloalkyl, -CR⁵R^{5'}, S(O)_p, where p is 0, 1 or 2, or D¹ is CR⁵R^{5'}, wherein R⁵ and R^{5'} together form a 2- to 5-membered chain optionally substituted with one heteroatom in the chain to form a spirocyclic group.

In another embodiment, a compound of Formula (If) is provided wherein variables R¹, R^{1'}, R², R³, R', R⁹, W, W¹, Z, Y², Y³, Y⁴ and Y⁵ are as defined for any of the embodiments of Formula (IA) described above; R¹⁰ and m are as defined for formula (Ie); b is 0 or 1; the dashed bond (----) signifies a single or double bond; D is N, SiR¹¹ where R¹¹ is C₁-C₆alkyl or C₁-C₆haloalkyl, C or C-R⁵; D¹ is N-R', O, SiR¹¹R¹² where R¹¹ and R¹² are independently C₁-C₆alkyl or C₁-C₆haloalkyl, -CR⁵R^{5'}, S(O)_p, where p is 0, 1 or 2, or D¹ is CR⁵R^{5'}, wherein R⁵ and R^{5'} together form a 2- to 5-membered chain optionally substituted with one heteroatom in the chain to form a spirocyclic group.

In one embodiment of Formula (If), R⁹ is CH. In another embodiment of Formula (If), R⁹ is CH. In another embodiment, R¹¹ is H. In another embodiment, W and W¹ are each CH₂.

20 In one embodiment of Formula (If), R¹ is optionally substituted C₁-C₆-alkyl, optionally substituted C₃-C₆-cycloalkyl, -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₃-alkyl, or wherein R^a and R^b together with the nitrogen form an optionally-substituted 3-, 4-, 5- or 6-membered heterocycle, which may include one additional heteroatom

selected from O or N; R² is hydrogen or optionally substituted C₁-C₃-alkyl; R³ is hydrogen, optionally substituted C₁-C₃-alkyl or halogen; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; D is N or CH; D¹ is CH₂, CF₂, N or O; R¹⁰ is halogen or C₁-C₃-alkyl and m is 1 or 2; W is CH₂ or is absent; W¹ is CH₂; Z is CH₂ or O and Y², Y³, Y⁴ and Y⁵ are each independently N,
5 CH or C-halogen; wherein the optional substituents are one or more halogen, hydroxy, cyano, C₁-C₃-alkyl, C₁-C₃-haloalkyl, 3- to 8-membered cycloalkyl, amino, C₁-C₃-alkylamino, C₁-C₃-dialkylamino, C₁-C₃-alkoxy and C₁-C₃-haloalkoxy.

In another embodiment of Formula (If), R¹ is C₁-C₄-alkyl, -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted C₁-C₃-alkyl, or wherein R^a and R^b together with the
10 nitrogen form an optionally substituted 3- or 4-membered heterocycle; R² is hydrogen; R³ is hydrogen, optionally substituted C₁-C₃-alkyl, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen; R⁹ is hydrogen; D is N; D¹ is CH₂, CF₂ or O; R¹⁰ is fluoro or methyl and m is 1 or 2; W and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each independently CH or C-halogen; wherein the optional substituents are one or more halogen, hydroxy, C₁-C₃-alkyl, C₁-C₃-haloalkyl, C₁-C₃-alkoxy or C₁-C₃-haloalkoxy.
15

In another embodiment of Formula (If), R¹ is *iso*-propyl, *tert*-butyl, -N(CH₃)₂, azetidinyloptionally substituted by one or more fluoro or methyl, or morpholinyl; R² is hydrogen; R³ is hydrogen, methyl, -CF₃, -CH₂F, -CHF₂, chloro or fluoro; R^{1'} is hydrogen; R' is hydrogen or C₁-C₃-alkyl; R⁹ is hydrogen; D is N; D¹ is CH₂, CF₂ or O; R¹⁰ is fluoro or methyl and m is 1 or 2; W
20 and W¹ are each CH₂; Z is O and Y², Y³, Y⁴ and Y⁵ are each CH. In another embodiment of Formula (If), W is CH₂, W¹ is CH₂ and Z is CH₂. In another embodiment of Formula (If), W and W¹ are independently CR⁶R⁷ wherein R⁶ and R⁷ are H, C₁-C₃-alkyl or C₁-C₃-haloalkyl and Z is O. In another embodiment, W and W¹ are each CH₂ and Z is O.

In some embodiments, the present invention provides compounds of formula (If), wherein
25 the dashed bond is a single bond.

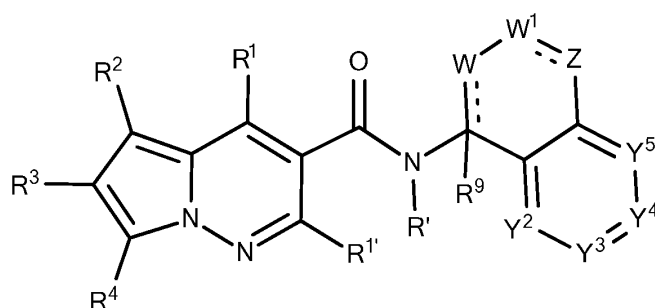
In some embodiments, the present invention provides compounds of formula (If), wherein the dashed bond is a double bond.

It will be appreciated by persons of skill in the art that in Formulae (Ic) and (Id) above, where variable R⁵ is indicated to be present as substituents on the aromatic rings (e.g. (R⁵)_o groups,
30 where o is 0, 1, 2, 3 or 4), they will represent non-hydrogen substituents since in embodiments

where o is 0, R⁵ will not be present. The same principle applies to variable R¹¹ in the compounds of formula (Ie) and (If).

In other embodiments, the invention provides compounds of Formula (Ia), wherein variables R¹, R^{1'}, R², R³, R⁴, R', R⁵, R⁹, W, W¹ and Z are as defined for Formula (I) above, and Y², Y³, Y⁴ and Y⁵ are as shown in Table 1:

In other embodiments, the invention provides compounds of Formula (Ia), wherein variables R¹, R^{1'}, R², R³, R⁴, R', R⁵, R⁹, W, W¹ and Z are as defined for any of the embodiments of Formula (IA) described above, and Y², Y³, Y⁴ and Y⁵ are as shown in Table 1:

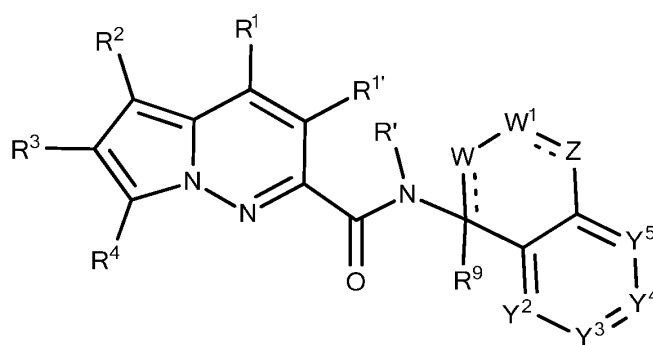


(Ia)

Table 1

Formula	Y ²	Y ³	Y ⁴	Y ⁵
Ia-1	CR ⁵	CR ⁵	CR ⁵	CR ⁵
Ia-2	N	CR ⁵	CR ⁵	CR ⁵
Ia-3	CR ⁵	N	CR ⁵	CR ⁵
Ia-4	CR ⁵	CR ⁵	N	CR ⁵
Ia-5	CR ⁵	CR ⁵	CR ⁵	N
Ia-6	N	N	CR ⁵	CR ⁵
Ia-7	CR ⁵	N	N	CR ⁵
Ia-8	CR ⁵	CR ⁵	N	N
Ia-9	N	CR ⁵	N	CR ⁵
Ia-10	CR ⁵	N	CR ⁵	N
Ia-11	N	CR ⁵	CR ⁵	N

In other embodiments, the invention provides compounds of Formula (Ib), wherein variables R^1 , $R^{1'}$, R^2 , R^3 , R^4 , R^5 , R' , R^9 , W , W^1 and Z are as defined for any of the embodiments of Formula (IA) described above, and Y^2 , Y^3 , Y^4 and Y^5 are as shown in Table 2:

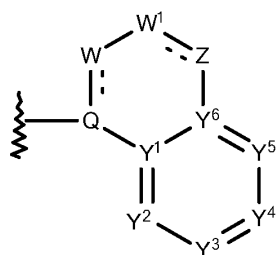


(Ib)

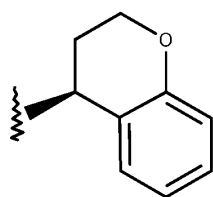
Table 2

Formula	Y^2	Y^3	Y^4	Y^5
Ib-1	CR^5	CR^5	CR^5	CR^5
Ib-2	N	CR^5	CR^5	CR^5
Ib-3	CR^5	N	CR^5	CR^5
Ib-4	CR^5	CR^5	N	CR^5
Ib-5	CR^5	CR^5	CR^5	N
Ib-6	N	N	CR^5	CR^5
Ib-7	CR^5	N	N	CR^5
Ib-8	CR^5	CR^5	N	N
Ib-9	N	CR^5	N	CR^5
Ib-10	CR^5	N	CR^5	N
Ib-11	N	CR^5	CR^5	N

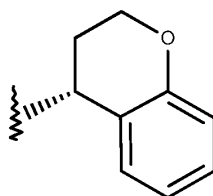
In other embodiments, the present invention provides compounds of formulae (IA-1) shown in Table 3 below, wherein L , R^1 , $R^{1'}$, R^2 , R^3 and R^4 are defined in the table; $L1$, $L2$ and $L3$ are as defined for Formula (I); X is O unless otherwise noted in the table, R' is hydrogen unless otherwise noted in the table, and wherein the group



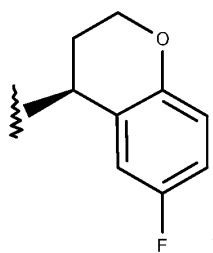
is one of the following Ring Systems:



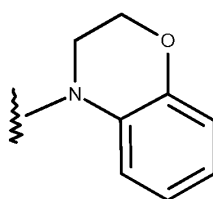
Ring System A;



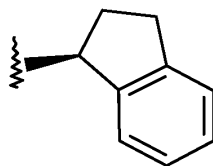
Ring System B;



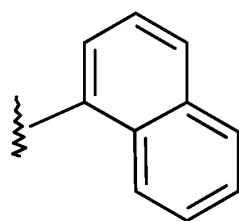
Ring System C;



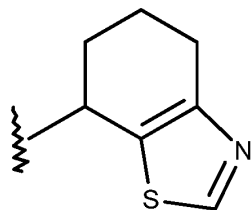
Ring System D;



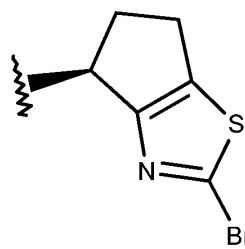
Ring System E;



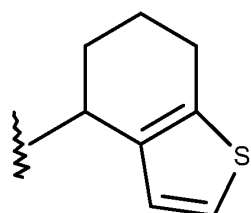
Ring System F;



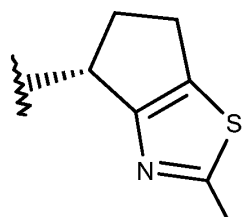
Ring System G;



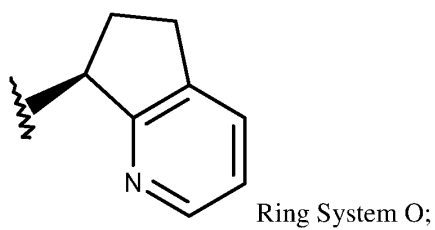
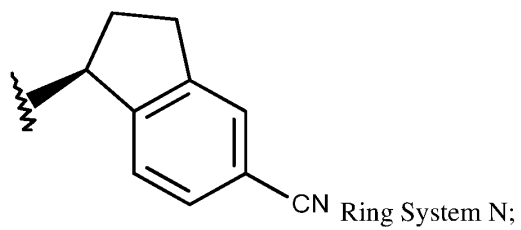
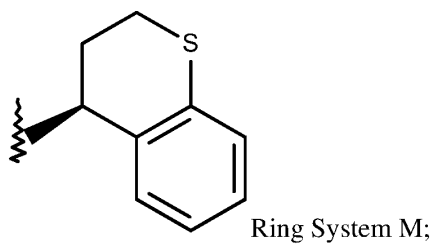
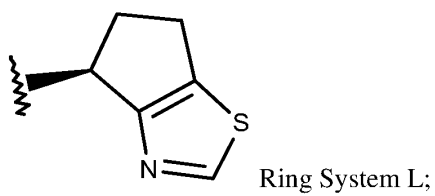
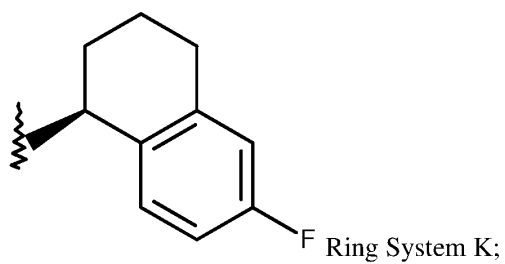
Br Ring System H;

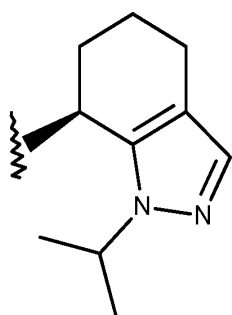


Ring System I;

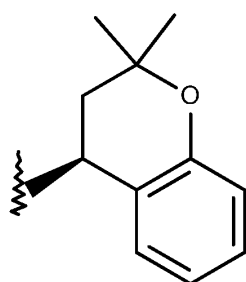


Br Ring System J;

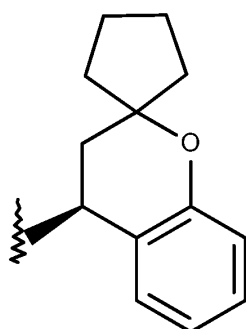




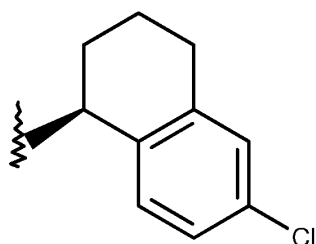
Ring System Q;



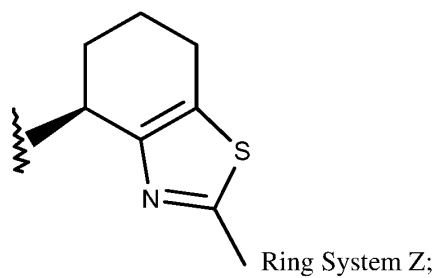
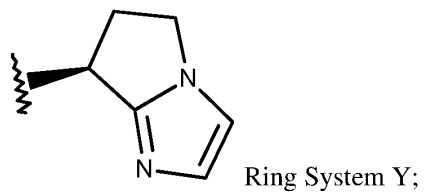
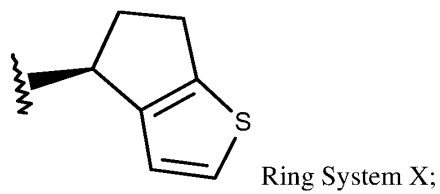
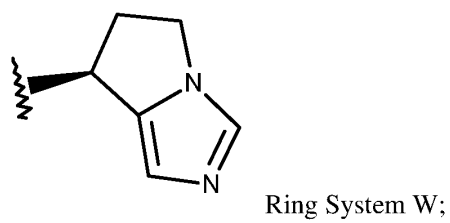
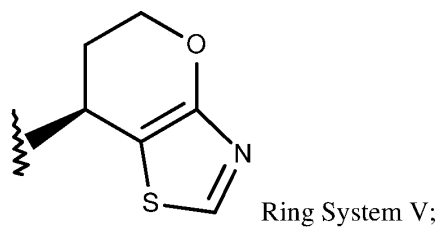
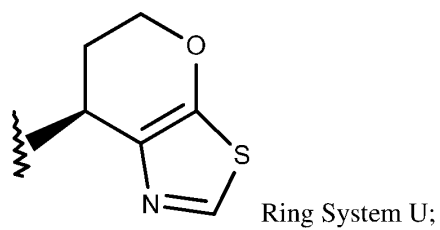
Ring System R;

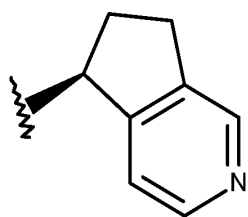


Ring System S;

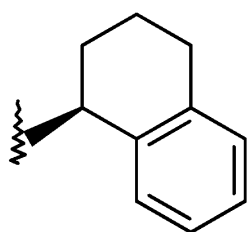


Ring System T;

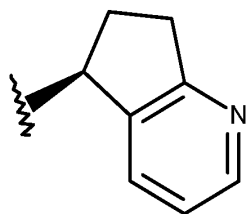




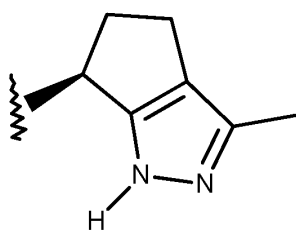
Ring System AA;



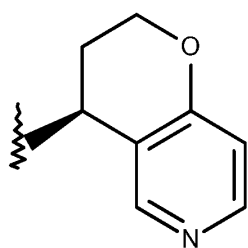
Ring System AB;



Ring System AC;



Ring System AD;

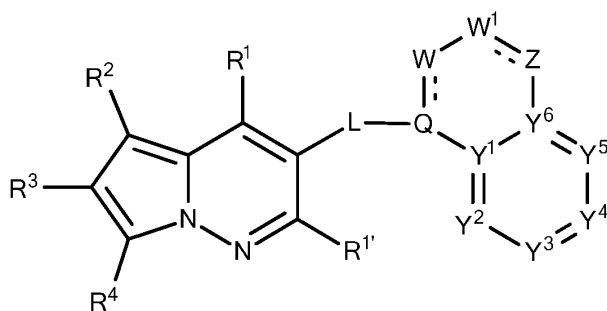


Ring System AE.

5

In Table 3, “Me” represents methyl, “*i*-Pr” means isopropyl, “*t*-Bu” means *tert*-butyl; the expression “3,5-di-Cl-Ph” represents the 3,5-dichlorophenyl group; “2,6-di-Cl-4-F-Ph” means 2,6-dichloro-4-fluorophenyl; “2,4,6-tri-F-Ph” means 2,4,6-trifluorophenyl; “2,3,5-tri-F-Ph”

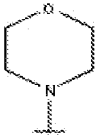
represents 2,3,5-trifluorophenyl; “2,3,5-tri-Cl-Ph means 2,3,5-trichlorophenyl; and “2,3-di-Cl-5-F-Ph” means 2,3-dichloro-5-fluorophenyl, and so on.

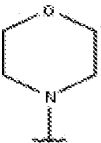
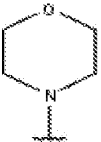


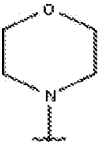
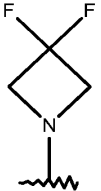
Formula (IA-1)

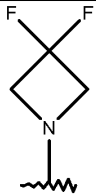
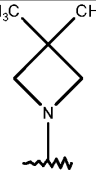
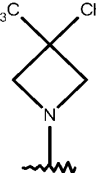
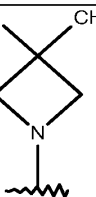
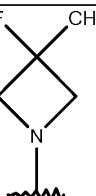
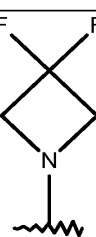
5 Table 3

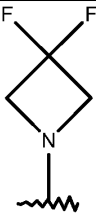
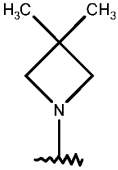
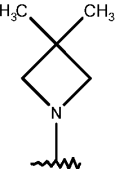
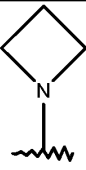
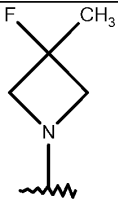
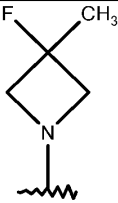
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A461	L2	<i>i</i> -Pr	H	H	Me	3,5-di-Cl-Ph	B	494 [M+H] ⁺
A462	L2	<i>i</i> -Pr	H	H	Me	3,5-di-Cl-Ph	A	494 [M+H] ⁺
A463	L1	<i>i</i> -Pr	H	H	Cl	3,5-di-Cl-Ph	A	514 [M+H] ⁺
A464	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl-Ph	A	508 [M+H] ⁺
A465	L1	<i>i</i> -Pr	H	H	Me	3,5-di-Cl-Ph	A	495 [M+H] ⁺
A466	L1	<i>i</i> -Pr	H	H	F	3,5-di-Cl-Ph	A	498 [M+H] ⁺
A467	L1	<i>i</i> -Pr	H	Cl	H	3,5-di-Cl-Ph	A	514 [M+H] ⁺
A468	L1	<i>i</i> -Pr	H	CF ₃	H	3,5-di-Cl-Ph	A	548 [M+H] ⁺
A469	L1	<i>i</i> -Pr	H	Me	H	3,5-di-Cl-	A	494

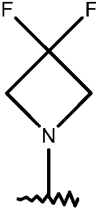
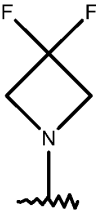
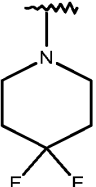
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
						Ph		[M+H] ⁺
A470	L1	<i>i</i> -Pr	H	H	H	3,5-di-Cl- Ph	A	480 [M+H] ⁺
A483	L1	<i>t</i> -Bu	H	H	CF ₃	3,5-di-Cl- Ph	A	562 [M+H] ⁺
A482	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	D	509 [M+H] ⁺
A484	L1	<i>t</i> -Bu	H	H	Cl	2,4,6-tri-F- Ph	A	514 [M+H] ⁺
A485	L1	<i>t</i> -Bu	H	H	Cl	2,6-di-Cl- 4-F-Ph	A	547 [M+H] ⁺
A486	L1	<i>t</i> -Bu	H	H	Cl	2,3,5-tri-F- Ph	A	514 [M+H] ⁺
A472	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri- Cl-Ph	A	544 [M+H] ⁺
A471	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-F- Ph	A	494 [M+H] ⁺
A476	L1	<i>t</i> -Bu	H	H	Me	2,4,6-tri-F- Ph	A	494 [M+H] ⁺
A487	L1	<i>t</i> -Bu	H	H	Me	2,6-di-Cl- 4-F-Ph	A	526 [M+H] ⁺
A499	L1		H	H	Me	3,5-di-Cl- Ph	A	537 [M+H] ⁺
A475	L1	-N(CH ₃) ₂	H	H	Cl	3,5-di-Cl- Ph	A	516 [M+H] ⁺
A473	L1	-N(CH ₃) ₂	H	H	Cl	2,3,5-tri- Cl-Ph	A	550 [M+H] ⁺

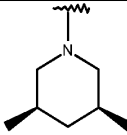
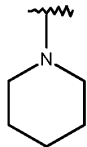
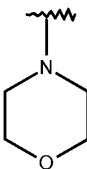
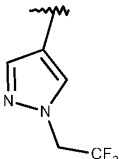
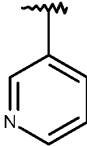
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A474	L1	-N(CH ₃) ₂	H	H	Cl	2,3,5-tri-F- Ph	A	551 [M+H] ⁺
A477	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	A	529 [M+H] ⁺
A478	L1	-N(CH ₃) ₂	H	H	Cl	2,3-di-Cl- 5-F-Ph	A	534 [M+H] ⁺
A490	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	555 [M+H] ⁺
A491	L1		H	H	Me	2,3,5-tri-F- Ph	A	523 [M+H] ⁺
A488	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	C	544 [M+H] ⁺
A479	L1	<i>i</i> -Pr	H	H	Cl	3,5-di-Cl- Ph	D	516 [M+H] ⁺
A489	L1	<i>i</i> -Pr	H	H	Me	2,3-di-Cl- 5-F-Ph	A	512 [M+H] ⁺
A480	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	E	492 [M+H] ⁺
A481	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	A	526 [M+H] ⁺
A502	L1	<i>t</i> -Bu	H	H	Cl	2,3-di-Cl- 5-F-Ph	A	547 [M+H] ⁺

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A492	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	E	513 [M+H] ⁺
A493	L1	-N(CH ₃) ₂	H	H	Me	2,3-di-Cl- 5-F-Ph	A	513 [M+H] ⁺
A516	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	D	530 [M+H] ⁺
A494	L1	<i>t</i> -Bu	H	H	Cl	2,3-di-Cl- 5-F-Ph	D	548 [M+H] ⁺
A482	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	D	509 [M+H] ⁺
A495	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	D	527 [M+H] ⁺
A496	L1	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl- 5-F-Ph	D	534 [M+H] ⁺
A497	L1	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	D	495 [M+H] ⁺
A498	L1	<i>i</i> -Pr	H	H	Me	2,3-di-Cl- 5-F-Ph	D	513 [M+H] ⁺
A501	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	572 [M+H] ⁺
A505	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	578 [M+H] ⁺

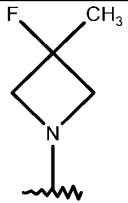
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A504	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	561 [M+H] ⁺
A511	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	570 [M+H] ⁺
A512	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	553 [M+H] ⁺
A508	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	574 [M+H] ⁺
A510	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	557 [M+H] ⁺
A506	L1		H	H	Cl	2,3,5-tri- Cl-Ph	A	598 [M+H] ⁺

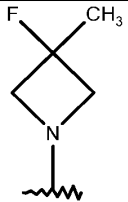
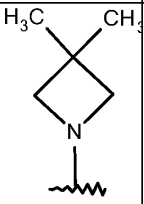
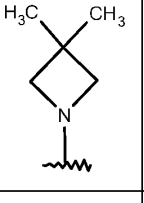
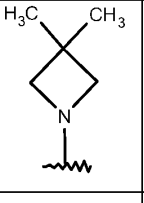
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A507	L1		H	H	Cl	2,3-di-Cl- 5-F-Ph	A	582 [M+H] ⁺
A515	L1		H	H	Cl	2,3,5-tri- Cl-Ph	A	590 [M+H] ⁺
A520	L1		H	H	Cl	2,3-di-Cl- 5-F-Ph	A	574 [M+H] ⁺
A503	L1		H	H	Cl	2,3-di-Cl- 5-F-Ph	A	546 [M+H] ⁺
A509	L1		H	H	Cl	2,3,5-tri- Cl-Ph	A	594 [M+H] ⁺
A514	L1		H	H	Cl	2,3-di-Cl- 5-F-Ph	A	578 [M+H] ⁺
A521	L1	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	F	488 [M+H] ⁺

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A513	L1	<i>i</i> -Pr	H	H	Me	2,3,5-tri-F- Ph	A	479 [M+H] ⁺
A517	L1	<i>i</i> -Pr	H	H	Me	2,3,5-tri- Cl-Ph	A	529 [M+H] ⁺
A518	L1	<i>t</i> -Bu	H	Br	Me	2,3-di-Cl- Ph	A	587 [M+H] ⁺
A519	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- Ph	A	508 [M+H] ⁺
A522	L1	<i>t</i> -Bu	H	H	Cl	2,3,5-tri- Cl-Ph	A	563 [M+H] ⁺
A523	L1	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl- 5-F-Ph	A	532 [M+H] ⁺
A500	L1	H	<i>i</i> -Pr	H	H	3,5-di-Cl- Ph	A	572 [M+H] ⁺
A525	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	578 [M+H] ⁺
A526	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	562 [M+H] ⁺
A527	L1	<i>t</i> -Bu	H	H	Me		A	483 [M+H] ⁺

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A528	L1	<i>t</i> -Bu	H	H	Me		A	475 [M+H] ⁺
A524	L1	<i>t</i> -Bu	H	H	Me		A	447 [M+H] ⁺
A529	L1	<i>t</i> -Bu	H	H	Me		A	449 [M+H] ⁺
A530	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri- Cl-Ph	A	543 [M+H] ⁺
A531	L1	<i>t</i> -Bu	H	H	Me		A	512 [M+H] ⁺
A532	L1	<i>t</i> -Bu	H	H	Me		A	440 [M+H] ⁺
A533	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	G	532 [M+H] ⁺
A534	L1	<i>t</i> -Bu	H	H	Cl	2,3-di-Cl- 5-F-Ph	A	547 [M+H] ⁺
A535	L3	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	G	547 [M+H] ⁺
A536a	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-	H	597

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
						5-F-Ph		[M+H] ⁺
A537	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	I	531 [M+H] ⁺
A536b	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	J	597 [M+H] ⁺
A538	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	K	543 [M+H] ⁺
A539	L1; X=S	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl- 5-F-Ph	A	548 [M+H] ⁺
A540	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	L	518 [M+H] ⁺
A541	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	M	543 [M+H] ⁺
A542	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	N	536 [M+H] ⁺
A543	L1; R'=Me	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	A	541 [M+H] ⁺
A544	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	O	512 [M+H] ⁺
A545	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	P	513 [M+H] ⁺
A546	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	Q	557 [M+H] ⁺
A547	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	R	555 [M+H] ⁺
A548	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	S	582 [M+H] ⁺
A549	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-	T	559

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
						5-F-Ph		[M+H] ⁺
A550	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	U	534 [M+H] ⁺
A551	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	V	534 [M+H] ⁺
A552	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	W	501 [M+H] ⁺
A553	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	X	517 [M+H] ⁺
A554	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	Y	501 [M+H] ⁺
A555	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	Z	546 [M+H] ⁺
A556	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	AA	512 [M+H] ⁺
A557	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	AB	525 [M+H] ⁺
A558	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	E	511 [M+H] ⁺
A559	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	AC	512 [M+H] ⁺
A560	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	AD	515 [M+H] ⁺
A561	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	575 [M+H] ⁺

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.	ESI-MS
A562	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	558 [M+H] ⁺
A563	L1		H	H	Me	2,3,5-tri- Cl-Ph	A	571 [M+H] ⁺
A564	L1		H	H	Me	2,3-di-Cl- 5-F-Ph	A	554 [M+H] ⁺
A565	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	D	531 [M+H] ⁺
A566	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-F- Ph	A	495 [M+H] ⁺
A567	L1		H	H	Cl	2,3-di-Cl- 5-F-Ph	A	575 [M+H] ⁺
A568	L1	-N(CH ₃) ₂	H	H	Me	2,3,5-tri- Cl-Ph	A	531 [M+H] ⁺
A569	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- 5-F-Ph	AE	528 [M+H] ⁺

For avoidance of doubt, each of the compounds presented in Table 3 has been prepared and characterized.

Veterinary compositions

5 The compositions of the invention which comprise effective amounts of compounds of the invention or salts thereof, including those of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) and (IA-1), in combination with an acceptable carrier or diluent.

 In another embodiment, the invention comprises an effective amount of a compound of the invention, or a pharmaceutically acceptable salt thereof, in combination with one or more
10 additional active agents and an acceptable carrier or diluent.

 The compositions may be in a variety of solid and liquid forms which are suitable for various methods of application or administration to an animal. For example, the veterinary compositions comprising the compound may be in compositions suitable for oral administration, injectable administration, including subcutaneous and parenteral administration, and topical
15 administration (*e.g.* spot-on or pour-on), dermal or subdermal administration. The compositions are intended to be administered to an animal including, but not limited to, mammals, birds and fish. Examples of mammals include but are not limited to humans, cattle, sheep, goats, llamas, alpacas, pigs, horses, donkeys, dogs, cats and other livestock or domestic mammals. Examples of birds include turkeys, chickens, ostriches and other livestock or domestic birds. The use of the
20 compound to protect companion animals such as dogs and cats from endoparasites is particularly useful.

 In some embodiments, the compositions of the invention may be in a form suitable for oral use. Suitable dosage forms for oral administration include dietary supplements, troches, lozenges, chewables, tablets, hard or soft capsules, bolus, emulsions, aqueous or oily suspensions, aqueous
25 or oily solutions, oral drench compositions, dispersible powders or granules, premixes, syrups or elixirs, enteric compositions or pastes. Compositions intended for oral use may be prepared according to any method known in the art for the manufacture of pharmaceutical compositions.

 Suitable tablets may be obtained, for example, by mixing one or more compounds of formula (I) with known excipients, for example inert diluents, carriers, disintegrants, adjuvants,
30 surfactants, binders and/or lubricants.

In one embodiment of the invention, a soft chewable veterinary composition is provided comprising an effective amount of at least one compound of formula (I), optionally in combination with an effective amount of at least one second active agent in a pharmaceutically acceptable carrier.

5 In another embodiment, the compositions for oral administration include a tablet or capsule. In yet another embodiment, the compositions for oral administration include a chewable tablet.

Methods of Treatment

10 As discussed above, the compounds of the invention are effective against endoparasites and may be used to treat, control and/or prevent parasitic infections in animals. In one embodiment, the present invention provides a method of treating, controlling and/or preventing an endoparasite infection in an animal (*e.g.* a mammal or bird) comprising administering an effective amount of a compound of the invention, including the compounds of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia),
15 (Ib), (Ic), (Id), (Ie), (If) or (IA-1), or pharmaceutically acceptable salts thereof, or a composition comprising the compound, to the animal. In some embodiments, the animals which can be treated are mammals that include, but are not limited to, humans, cats, dogs, cattle, chickens, cows, bison, deer, goats, horses, llamas, camels, pigs, sheep and yaks. In one embodiment of the invention, the mammals treated are humans, cats or dogs. In another embodiment, the invention provides a
20 method of treating or preventing endoparasite infections in horses. In another embodiment, the mammals treated are livestock animals such as cattle or sheep. In another embodiment, the compound of the invention may be used to treat fish.

The present invention also provides a use of the compound of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) or (IA-1) in the preparation of a medicament for the treatment,
25 control and/or prevention of parasitic infections in animals. The present invention also provides the compounds of the invention for use in the treatment, control and/or prevention of a parasitic infection in animals.

In another embodiment, the compound of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) or (IA-1) may be combined with at least a second active agent that is active
30 against ectoparasites (*e.g.* fleas and ticks) for use in the treatment, control and/or prevention of an endoparasitic infection and an ectoparasitic infestation in and on an animal. In another

embodiment, the invention provides methods for the treatment, control and/or prevention of an endoparasitic infection and an ectoparasitic infestation in and on an animal comprising administering to the animal an effective amount of the compound of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) or (IA-1) in combination with at least one additional active agent that is active against ectoparasites. In addition, the present invention provides the use of a compound of the invention in combination with at least a second active agent for the preparation of a medicament for the treatment, control and/or prevention of an endoparasitic infection and an ectoparasitic infestation is provided.

In still another embodiment of the invention, a method is provided for the treatment, control and/or prevention of a parasitic infestation at a locus, which comprises administering or applying an effective amount of a compound of Formula (I), Formula (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) or (IA-1), or pharmaceutically acceptable salts thereof, to the locus. With respect to animal health applications, "locus" is intended to mean a habitat, breeding ground, area, material or environment in which a parasite is growing or may grow, excluding in or on an animal.

In one embodiment of the invention, the compounds of Formula (I), Formula (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) or (IA-1) have been found to have superior efficacy against endoparasites, and in particular against endoparasites that are resistant to active agents of the macrocyclic lactone class. In one embodiment, the invention provides method for the treatment and/or prevention of parasitic infections of endoparasites that are resistant to treatment with macrocyclic lactones.

In another embodiment, the invention provides a method for the treatment, control and/or prevention of a parasitic infestation and/or infection in an animal, comprising administering an effective amount of an anthelmintic compound of the invention in combination with an effective amount of another antiparasitic active agent to the animal in need thereof.

In one embodiment, the compounds and compositions of the invention may be used for treating, controlling and/or preventing an endoparasitic infection of the following parasite genera: *Anaplocephala* (*Anoplocephala*), *Ancylostoma*, *Necator*, *Ascaris*, *Brugia*, *Bunostomum*, *Capillaria*, *Chabertia*, *Cooperia*, *Cyathostomum*, *Cylicocyclus*, *Cylicodontophorus*, *Cylicostephanus*, *Craterostomum*, *Dictyocaulus*, *Dipetalonema*, *Dipylidium*, *Dirofilaria*, *Dracunculus*, *Echinococcus*, *Enterobius*, *Fasciola*, *Filaroides*, *Habronema*, *Haemonchus*, *Metastrongylus*, *Moniezia*, *Necator*, *Nematodirus*, *Nippostrongylus*, *Oesophagostomum*,

Onchocerca, *Ostertagia*, *Oxyuris*, *Parascaris*, *Schistosoma*, *Strongylus*, *Taenia*, *Toxocara*, *Strongyloides*, *Toxascaris*, *Trichinella*, *Trichuris*, *Trichostrongylus*, *Triodontophorus*, *Uncinaria*, *Wuchereria*, and combinations thereof.

In a particularly preferred embodiment of the invention, the compounds and compositions
5 of the invention are used to treat, control and/or prevent an infection by *Dirofilaria immitis*. The compounds have been found to be highly effective against *D. immitis* microfilaria and L4 larvae, including isolates of *D. immitis* that are resistant to macrocyclic lactone therapy. Thus, the compounds may be used to protect animals from developing heartworm disease by killing the immature stages of *D. immitis* before they can develop into adult worms, including those that are
10 resistant to macrocyclic lactones and other active agents. In one embodiment, the compound and compositions comprising the compounds may be used to prevent the development of heartworm disease by killing immature stages of *D. immitis* that are resistant to macrocyclic lactones. In another embodiment the compounds and compositions of the invention are used to treat, control and/or prevent an infection by *Dirofilaria repens* or *Dirofilaria hongkongensis*.

15 In another embodiment, the compound of Formula (I), Formula (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) or (IA-1) may be used to treat, control and/or prevent a parasitic infection by a parasite selected from *Haemonchus contortus*, *Ostertagia circumcincta*, *Trichostrongylus axei*, *Trichostrongylus colubriformis*, *Cooperia curticei*, *Nematodirus battus* and combinations thereof.

20 In another embodiment for treatment against both endoparasites and ectoparasites when combined with ectoparasitocidal agents, the ectoparasite is one or more insect or arachnid including those of the genera *Ctenocephalides*, *Rhipicephalus*, *Dermacentor*, *Ixodes*, *Boophilus*, *Amblyomma*, *Haemaphysalis*, *Hyalomma*, *Sarcoptes*, *Psoroptes*, *Otodectes*, *Chorioptes*, *Hypoderma*, *Damalinia*, *Linognathus*, *Haematopinus*, *Solenoptes*, *Trichodectes*, and/or *Felicola*.

25 In another embodiment for the treatment against ectoparasites, the ectoparasite is from the genera *Ctenocephalides*, *Rhipicephalus*, *Dermacentor*, *Ixodes* and/or *Boophilus*. The ectoparasites treated include but are not limited to fleas, ticks, mites, mosquitoes, flies, lice, blowfly and combinations thereof. Specific examples include but are not limited to cat and dog fleas (*Ctenocephalides felis*, *Ctenocephalides* spp. And the like), ticks (*Rhipicephalus* spp., *Ixodes* spp.,
30 *Dermacentor* spp., *Amblyomma* spp. And the like), and mites (*Demodex* spp., *Sarcoptes* spp., *Otodectes* spp. And the like), lice (*Trichodectes* spp., *Cheyletiella* spp., *Linognathus* spp., and the

like), mosquitoes (*Aedes* spp., *Culex* spp., *Anopheles* spp., and the like) and flies (*Haematobia* spp., *Musca* spp., *Stomoxys* spp., *Dermatobia* spp., *Cochliomyia* spp., and the like). In yet another embodiment for the treatment against ectoparasites, the ectoparasite is a flea and/or tick.

Additional examples of ectoparasites include, but are not limited to the tick genus
5 *Boophilus*, especially those of the species *microplus* (cattle tick), *decoloratus* and *annulatus*; myiasis such as *Dermatobia hominis* (known as Berne in Brazil) and *Cochliomyia hominivorax* (greenbottle); sheep myiasis such as *Lucilia sericata*, *Lucilia cuprina* (known as blowfly strike in Australia, New Zealand and South Africa). Flies proper, namely those whose adult constitutes the parasite, such as *Haematobia irritans* (horn fly) and *Stomoxys calcitrans* (stable fly); lice such as
10 *Linognathus vitulorum*, etc.; and mites such as *Sarcoptes scabiei* and *Psoroptes ovis*. The above list is not exhaustive and other ectoparasites are well known in the art to be harmful to animals and humans. These include, for example migrating dipterous larvae.

In each aspect of the invention, the compounds and compositions of the invention can be applied against a single pest or combinations thereof.

15 Mixtures with other active agents

In another embodiment, the compositions comprising the compounds of the invention, including those of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) and (IA-1), may also include other veterinary pharmaceutical agents. Veterinary pharmaceutical agents that may be included in the compositions of the invention are well-known in the art (see *e.g.* *Plumb's*
20 *Veterinary Drug Handbook*, 5th Edition, ed. Donald C. Plumb, Blackwell Publishing, (2005) or *The Merck Veterinary Manual*, 9th Edition, (January 2005)).

In one embodiment of the invention, arylpyrazole compounds such as phenylpyrazoles, known in the art may be combined with the compounds of Formula (I) or Formula (IA) in the compositions of the invention.

25 In another embodiment of the invention, one or more macrocyclic lactones, which act as an acaricide, anthelmintic agent and/or insecticide, can be added to the compositions of the invention. Macrocyclic lactones include both avermectins and milbemycin active agents.

In another embodiment of the invention, a composition comprising a compound of the invention in combination with a class of acaricides or insecticides known as insect growth
30 regulators (IGRs) is provided. Compounds belonging to this group are well known to the

practitioner and represent a wide range of different chemical classes. These compounds all act by interfering with the development or growth of the insect pests.

In one embodiment the IGR is a compound that mimics juvenile hormone.

In another embodiment, the IGR compound is a chitin synthesis inhibitor.

5 In yet another embodiment of the invention, adulticide insecticides and acaricides can also be added to the composition of the invention. In some embodiments, the compositions of the invention may include one or more antinematodal agents.

In other embodiments, the compositions of the invention may include antitrepatodal agents.

10 Anticestodal compounds may also be advantageously used in the compositions of the invention.

In yet other embodiments, the compositions of the invention may include other active agents that are effective against arthropod parasites.

15 An antiparasitic agent that can be combined with the compound of the invention to form a composition can be a biologically active peptide or protein including, but not limited to, cyclic depsipeptides, which act at the neuromuscular junction by stimulating presynaptic receptors belonging to the secretin receptor family resulting in the paralysis and death of parasites.

20 In another embodiment, the compositions of the invention may comprise an active agent from the neonicotinoid class of pesticides. The neonicotinoids bind and inhibit insect specific nicotinic acetylcholine receptors.

In another embodiment, the compositions of the invention may advantageously include one or more isoxazoline active agents known in the art. Isoxazoline active agents are highly effective against ectoparasites such as fleas and ticks, among others.

25 In another embodiment of the invention, nodulisporic acid and its derivatives (a class of known acaricidal, anthelmintic, anti-parasitic and insecticidal agents) may be added to the compositions of the invention.

In another embodiment, anthelmintic compounds of the amino acetonitrile class (AAD) of compounds may be added to the compositions of the invention. In another embodiment, aryloazol-2-yl cyanoethylamino compounds may be included in compositions.

30 The compositions of the invention may also be combined with paraherquamide compounds and derivatives of these compounds. The paraherquamide family of compounds is a known class

of compounds that include a spirodioxepino indole core with activity against certain parasites. In addition, the structurally related marcfortine family of compounds are also known and may be combined with the formulations of the invention.

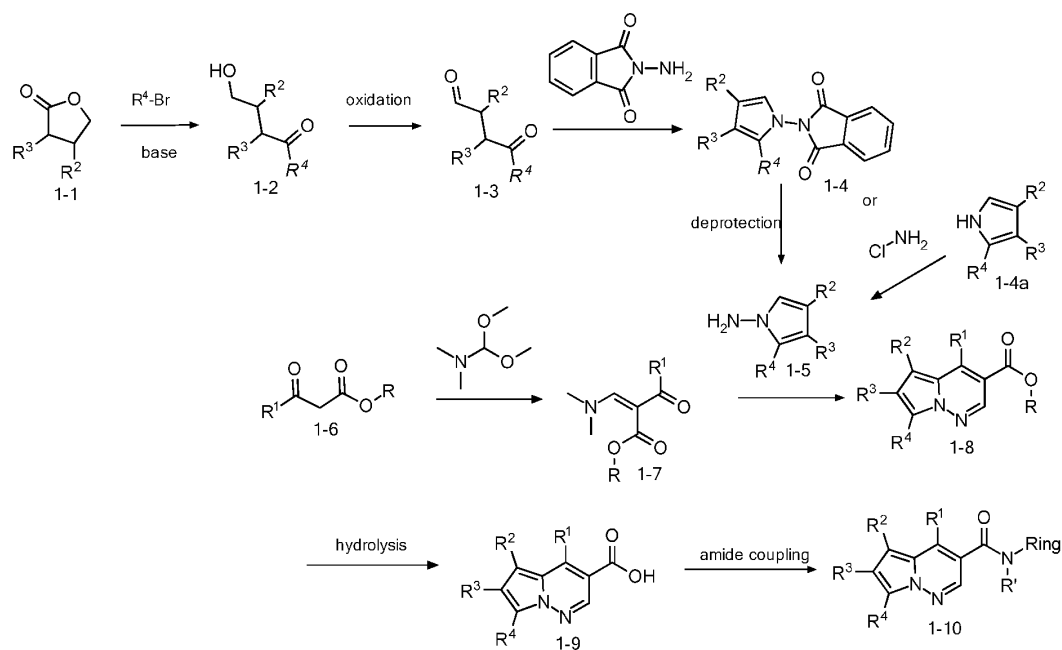
5 In another embodiment of the invention, the compositions may include a spinosyn active agent produced by the soil actinomycete *Saccharopolyspora spinosa* or a semi-synthetic spinosoid active agent. The spinosyns are typically referred to as factors or components A, B, C, D, E, F, G, H, J, K, L, M, N, O, P, Q, R, S, T, U, V, W, or Y, and any of these components, or a combination thereof, may be used in the compositions of the invention.

10 The invention will now be further described by way of the following non-limiting examples.

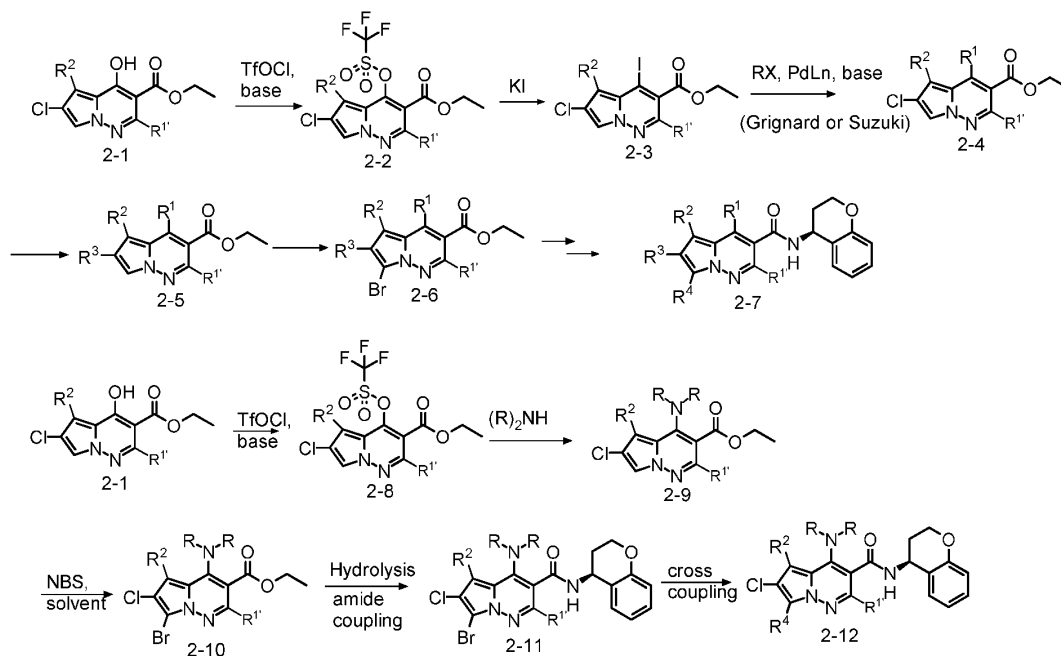
Methods of Synthesis

The compounds of the invention, including the compounds of Formula (I), Formula (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) and (IA-1), or salts thereof, described herein may be prepared according to the process described in schemes 1 and 2 shown below. A person of skill in the art
15 will be able to prepare a variety of compounds of the invention by adapting processes described below with alternate starting materials and/or reagents known in the art.

Scheme 1



Scheme 2



EXAMPLES:**Preparation Examples**

The Examples that follow are intended to only illustrate the present invention without restricting it. The compounds of the invention, including those of formulae (I), (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) and (IA-1), or salts thereof, may be prepared by adopting one of the following reaction schemes. The starting materials for their preparation may be commercially available or can be prepared by methods known by persons of skill in the art and as described in the literature or may be an intermediate in any other of the schemes described herein. It will be appreciated that the following procedures may be modified by persons of skill in the art to prepare additional compounds according to the invention. For example, a person of skill in the art will understand that replacement of certain starting materials or the use of different intermediates will enable the preparation of different compounds of Formula (I), Formula (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) and (IA-1).

The terms "ambient temperature" and "room temperature" are used interchangeably and designate a temperature of about 20 °C. Although the following subject matter is described in some detail by way of illustration and example for purposes of clarity of understanding, it will be understood by those skilled in the art that certain changes and modifications can be practiced within the scope of the Examples.

Abbreviations:

ACN	acetonitrile
Alox	aluminium oxide
Aq.	aqueous
Atm	atmosphere
°C	degree celsius
CyH/CH	cyclohexane

conc.	concentrated
DCC	<i>N,N'</i> -dicyclohexylmethanediimine
DCM	dichloromethane
1,2-DCE	1,2-dichloroethane
DEE/ Et ₂ O	diethyl ether
DIPE	diisopropyl ether
DIPEA	<i>N,N</i> -diisopropylethylamine
1,2-DME	1,2-dimethyl ether
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethyl sulfoxide
ESI-MS	electrospray ionisation mass spectrometry
EtOAc/EE/EA	ethyl acetate
ex	example
eq	equivalent
h	hour
HAc/HOAc	acetic acid
HATU	<i>N,N,N',N'</i> -tetramethyl- <i>O</i> -(7-azabenzotriazol-1-yl)uranium hexafluorophosphate
HCl	hydrochlorid acid
HNO ₃	nitric acid

HPLC	high performance liquid chromatography
iPrMgCl	isopropylmagnesium chloride
K ₃ PO ₄	tripotassium phosphate
LiHMDS	lithium- <i>bis</i> (trimethylsilyl)amide
LAH	lithium aluminum hydride
LiOH	lithium hydroxide
MeI	methyl iodide
MeOH	methanol
NaH	sodium hydride
NaHCO ₃	sodium bicarbonate
Na ₂ SO ₄	sodium sulfate
NBS	<i>N</i> -bromosuccinimide
NCIS/NCS	<i>N</i> -chlorosuccinimide
NH ₃	ammonia
NH ₄ Cl	ammonium chloride
NBS	<i>N</i> -bromosuccinimide
NIS	<i>N</i> -iodosuccinimide
NMP	<i>N</i> -methyl-2-pyrrolidone
min	minute
mL	milliliter

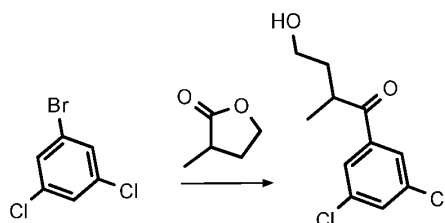
mmol	millimole
Pd/C	palladium on activated carbon
Pd(dppf)Cl ₂	[1,1'- <i>bis</i> (diphenylphosphino)ferrocene]dichloropalladium(II)
PE	petroleum ether
psi	pound per square inch
PtO ₂	platinum dioxide
RT	room temperature (about 20 °C)
R _t	retention time
sat.	saturated
TBAF	tetra-n-butylammonium fluoride
tBuOH	tert-butyl alcohol
tBuOK	potassium tert-butoxide
TEA	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin-layer chromatography on SiO ₂
TMSOK	potassium trimethylsilanolate

Some examples of Formula (I), Formula (IA), (I-1), (I-2), (I-3), (Ia), (Ib), (Ic), (Id), (Ie), (If) and (IA-1), or salts thereof, are derived after separation of racemic mixtures and obtained as enantiomerically pure products. The stereochemistry is in some cases arbitrarily assigned and the

5 respective compound characterized by analytical methods.

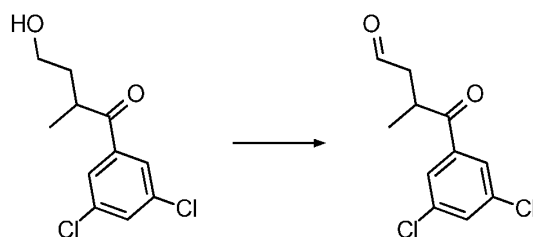
Preparation Example 1: Compound A465. Compound A465 was prepared according to general Scheme 1 shown above as described below. In addition, the following compounds of the invention can be prepared by adapting general Scheme 1 and the reactions described below for the synthesis of example A465 as well as by employing and modifying reactions known in the literature (see for example WO2021030379, WO2012125886 and WO2012125893): A461, A462, A463, A464, A469, A466, A467, A468, A470, A471, A473, A474, A475, A476, A483, A484, A486, A487, A488, A489, A492, A494, A495, A496, A497, A498, A500.

1. Synthesis of 1-(3,5-dichlorophenyl)-4-hydroxy-2-methylbutan-1-one



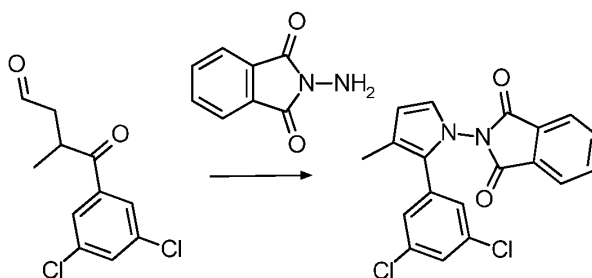
A mixture of 3.0 g (13.3 mmol) 1-bromo-3,5-dichlorobenzene in 50 mL THF anhydrous was cooled to -95 °C with a MeOH/nitrogen bath, 10.8 mL (17.3 mmol) tert-butyllithium was added dropwise, followed by 1.99 g (19.9 mmol) alpha-methyl-gamma-butyrolactone in 10 mL THF anhydrous. The reaction mixture was stirred at -85 °C for 1 h. The reaction mixture was quenched with sat. NH₄Cl solution at -90°C and the solution warmed to RT and extracted twice with EE. The organic layers are collected, dried, filtered and the filtrate is evaporated to obtain 3.6 g (27 %) of the crude product as yellow oil.

2. Synthesis of 4-(3,5-dichlorophenyl)-3-methyl-4-oxobutanal



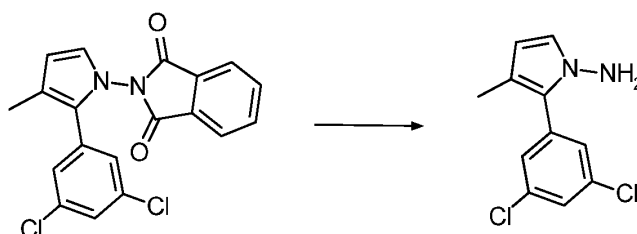
A mixture of 2.59 mL (26.42 mmol) DMSO in 25 mL DCM was cooled to -78 °C. 1.6 mL (18.9 mmol) oxalyl chloride was added dropwise and the solution was stirred for 15 min. 3.6 g (3.6 mmol) 1-(3,5-dichlorophenyl)-4-hydroxy-2-methylbutan-1-one in 8 mL DCM was added and the reaction mixture was stirred at -78 °C for 1 h. 11.67 mL (83.76 mmol) TEA was added and the solution warmed to RT and stirred at RT for 1.5 h. The reaction mixture was quenched with water and extracted with DCM. The organic layers were collected, dried, filtered and the filtrate was evaporated. The residue was purified by column chromatography (silica gel; PE/EtOAc) and the solvents were removed in vacuo to obtain 1.10 g (92.0 %) of the product as yellow oil.

3. Synthesis of 2-[2-(3,5-dichlorophenyl)-3-methyl-1H-pyrrol-1-yl]-2,3-dihydro-1H-isoindole-1,3-dione



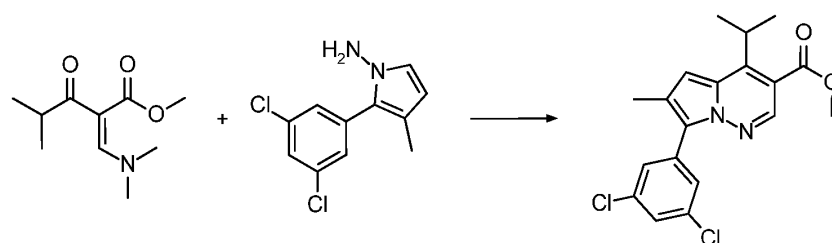
A mixture of 1.10 g (3.36 mmol) 4-(3,5-dichlorophenyl)-3-methyl-4-oxobutanal, 600 mg (3.7 mmol) N-amino phthalimide and 9.26 mL (37.0 mmol) was stirred at 100°C for 1 h. The reaction mixture was evaporated and the crude residue was crystallized with PE/EE to obtain 720 mg (57.0%) of 2-[2-(3,5-dichlorophenyl)-3-methyl-1H-pyrrol-1-yl]-2,3-dihydro-1H-isoindole-1,3-dione as a white solid.

4. Synthesis of 2-(3,5-dichlorophenyl)-3-methyl-1H-pyrrol-1-amine



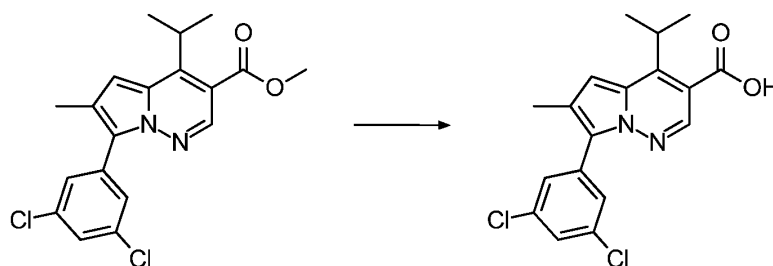
A mixture of 1.1 g (3.0 mmol) 2-[2-(3,5-dichlorophenyl)-3-methyl-1H-pyrrol-1-yl]-2,3-dihydro-1H-isoindole-1,3-dione and 0.2 mL (7.4 mmol) hydrazine monohydrate in 12 mL EtOH was stirred at reflux for 2 h. The reaction mixture was filtered and the filtrate was evaporated. The crude residue was purified by column chromatography (silica gel; PE/EtOAc) and the solvents were removed in vacuo to obtain 650 mg (91 %) of the product as white solid

5. Synthesis of methyl 7-(3,5-dichlorophenyl)-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxylate



To a mixture of 1.1 g (4.6 mmol) of 2-(3,5-dichlorophenyl)-3-methyl-1H-pyrrol-1-amine in 40 mL of methanol were added 820.0 mg (4.1 mmol) of methyl (2Z)-2-(dimethylamino)-methylidene-4-methyl-3-oxopentanoate and 1.2 mL of 4M HCl in dioxane and the mixture was stirred at 80°C for 3h. After evaporation of the solvents, the crude residue was purified by column chromatography (silica gel; cyclohexane/EtOAc) and the solvents were removed in vacuo to obtain 380 mg (24 %) of the product as a solid.

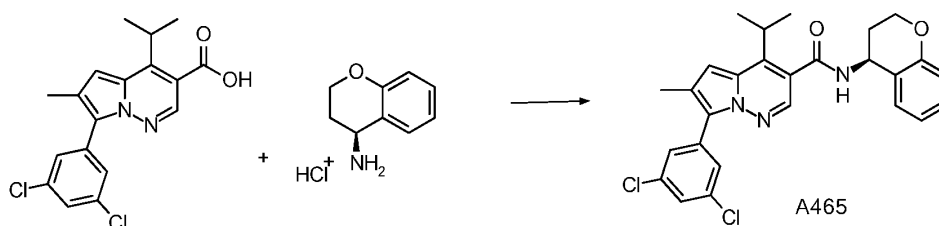
6. Synthesis of 7-(3,5-dichlorophenyl)-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxylic acid



To a mixture of 94.5 mg (0.2 mmol) of methyl 7-(3,5-dichlorophenyl)-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxylate and 1.5 mL solution of LiOH (1M) was added 1.5 mL

of THF. After stirring for 2h at 40°C the reaction mixture was heated to 60°C over night. Then, the solution was acidified with 4 M HCl at RT and the resulting residue was filtered off and washed with 2mL of H₂O. After drying of the residue, 84 mg (93.0%) of 7-(3,5-dichlorophenyl)-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxylic acid were obtained as a yellow solid.

5 **7. Synthesis of 7-(3,5-dichlorophenyl)-N-[(4S)-3,4-dihydro-2H-1-benzopyran-4-yl]-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxamide (A465)**

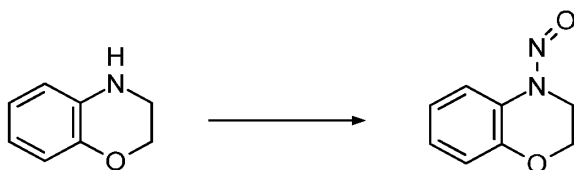


A solution of 350 mg (0.9 mmol) of 7-(3,5-dichlorophenyl)-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxylic acid in 8 mL of DMF was treated with 650 µl of DIPEA and 410 mg (1.7 mmol) of HATU and stirred for 10 min. After addition of 200 mg (1.1 mmol) of (S)-chroman-4-amine hydrochloride the mixture was stirred for 16h at room temperature. The solvents were removed in vacuo and the residue was purified by column chromatography (silica gel; PE/EtOAc). After removal of the solvents in vacuo 310 mg (65.0%) of 7-(3,5-dichlorophenyl)-N-[(4S)-3,4-dihydro-2H-1-benzopyran-4-yl]-6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxamide (**A465**) were obtained as white solid. (ESI, m/z): 495 [M+H]⁺

Preparation Example 2: Synthesis of 3,4 - dihydro - 2H - 1,4 - benzoxazin - 4 - amine

3,4 - dihydro - 2H - 1,4 - benzoxazin - 4 - amine, which is used in the synthesis of compounds of the invention containing Ring System D (see Table 3 above) such as compounds A479, A482, A494, A495, A496, A497, A498, A516 and A565, is prepared according to the process described below.

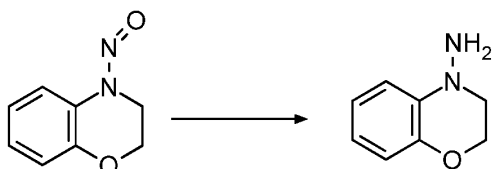
1. Synthesis of 4 - nitroso - 3,4 - dihydro - 2H - 1,4 - benzoxazine



Into a 500mL round-bottom flask. were added 3,4 - dihydro - 2H - 1,4 - benzoxazine (3.0 g, 22.2 mmol) and HCl (300 ml, 3M) and NaNO₂ (1.8 g, 26.1 mmol) was added in portions at 2 h at 0 °C under nitrogen atmosphere. The resulting mixture was concentrated under reduced pressure.

- 5 The residue was purified by silica gel column chromatography, eluted with PE / EA (10:1) to afford 4 - nitroso - 3,4 - dihydro - 2H - 1,4 - benzoxazine (2.7 g, 75 %) as a yellow oil.

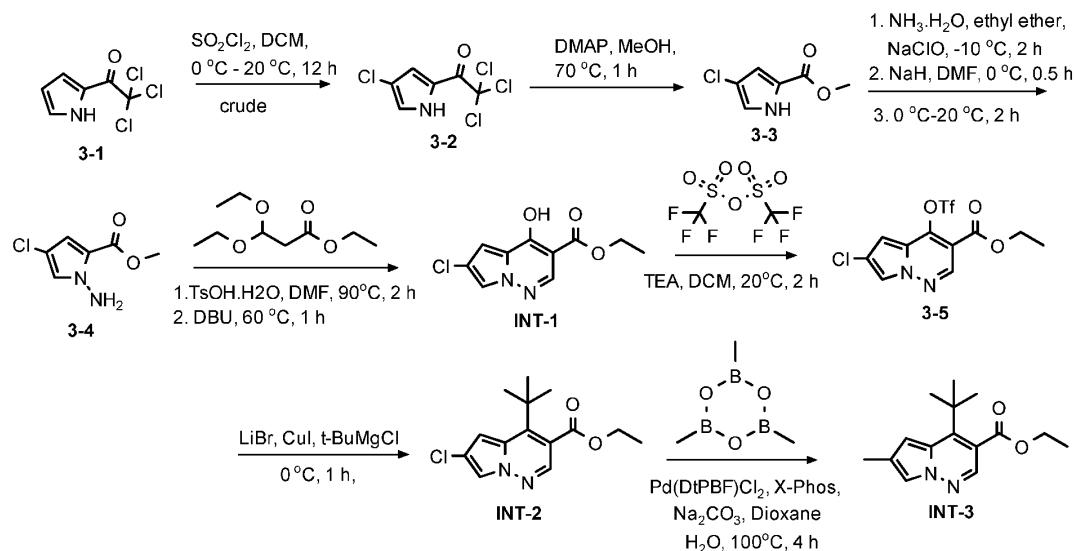
2. Synthesis of 3,4 - dihydro - 2H - 1,4 - benzoxazin - 4 - amine



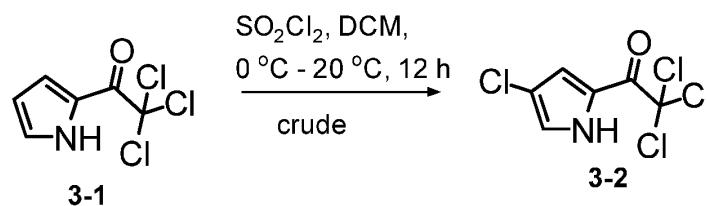
- 10 Into a 500mL round-bottom flask. were added 4 - nitroso - 3,4 - dihydro - 2H - 1,4 - benzoxazine (2.7 g, 19.2 mmol) and THF (300 ml) and LAH (1.35 g, 1.9 mmol) was added in portions at 2 h at 0 °C under nitrogen atmosphere. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE / EA (10:1) to afford 3,4 - dihydro - 2H - 1,4 - benzoxazin - 4 - amine (2.2 g, 45 %) as a yellow oil.

- 15 **Preparation Example 3:** Scheme 3 below describes the synthesis of intermediate compounds **INT-1**, **INT-2** and **INT-3**, which correspond respectively to compounds 2-1 wherein R^{1'} and R² are hydrogen; compound 2-4 wherein R¹ is *tert*-butyl, R² and R^{1'} are hydrogen and compound and R³ is chloro; and compound 2-5 wherein R¹ is *tert*-butyl, R² and R^{1'} are hydrogen and compound and R³ is methyl. These intermediates are used to prepare various compounds of the invention as depicted in Scheme 2 and described in detail below.
- 20

Scheme 3

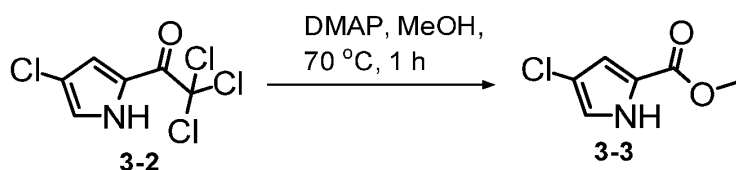


1. Synthesis of 2,2,2-trichloro-1-(4-chloro-1H-pyrrol-2-yl)ethanone (3-2)



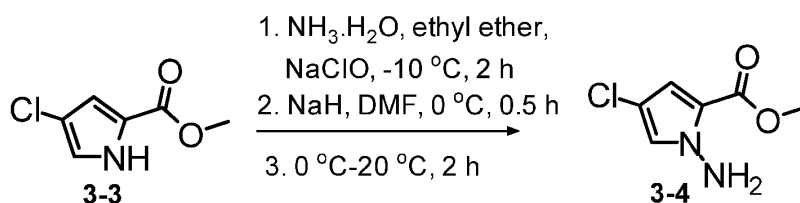
- 5 Into a 5.0 L 3-necked round-bottom flask, was placed 2,2,2-trichloro-1-(1H-pyrrol-2-yl)ethanone (3-1, 600 g, 2824.2 mmol) in DCM (4.0 L). To this was added SO_2Cl_2 (419.30 g, 3106.6 mmol) dropwise at 0°C . The reaction mixture was stirred for 12 h at 20°C . The resulting mixture was adjusted to pH 8 with aqueous Na_2CO_3 (2 M). The resulting mixture was extracted with DCM (2.0 L x 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford 2,2,2-trichloro-1-(4-chloro-1H-pyrrol-2-yl)ethanone (**3-2**, 730 g, crude) as a black solid which was used directly in the next step.

2. Synthesis of methyl 4-chloro-1H-pyrrole-2-carboxylate (3-3)



Into a 3.0 L 3-necked round-bottom flask, was placed 2,2,2-trichloro-1-(4-chloro-1H-pyrrol-2-yl)ethanone (**3-2**, 730 g, crude), MeOH (2.5 L) and DMAP (72.34 g, 592.1 mmol). The reaction mixture was stirred at 70 °C for 1 h. The mixture was allowed to cool down to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (10/1) to afford methyl 4-chloro-1H-pyrrole-2-carboxylate (**3-3**, 330 g, 73% 2 steps) as a white solid.

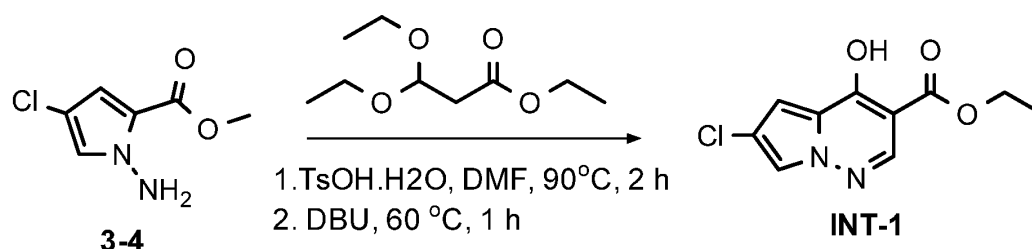
3. Synthesis of methyl 1-amino-4-chloropyrrole-2-carboxylate (**3-4**)



Into a 5 L 3-necked round-bottom flask, was placed NH_4Cl (80 g, 1495.6 mmol), ethyl ether (1.5 L) and $\text{NH}_3.\text{H}_2\text{O}$ (120 mL). To this was added NaClO (1.7 L) dropwise at -10 °C. The reaction mixture was stirred at -10 °C for 2 h. Then the aqueous phase was removed by separation funnel. The organic layer was washed with 1.0 L of cooled brine. The organic layer (1.5 L) was dried over anhydrous Na_2SO_4 and stored at -40 °C for 1 h. Into another 2.0 L 3-necked round-bottom flask was placed methyl 4-chloro-1H-pyrrole-2-carboxylate (**3-3**, 80 g, 501.3 mmol) in DMF (800 mL). This was followed by addition of NaH (30.08 g, 752.0 mmol, 60 %) in portion at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. Then the above organic layers (1.5 L) were added. The combined reaction mixture was stirred at 20 °C for 2 h. The reaction was then quenched by the addition of 600 mL of $\text{Na}_2\text{S}_2\text{O}_4$ Saturated aqueous solution and the reaction mixture was stirred for 15 min. The resulting mixture was extracted with EA (3 x 1.0 L). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction was repeated one more time and the combined residue was purified by silica gel column

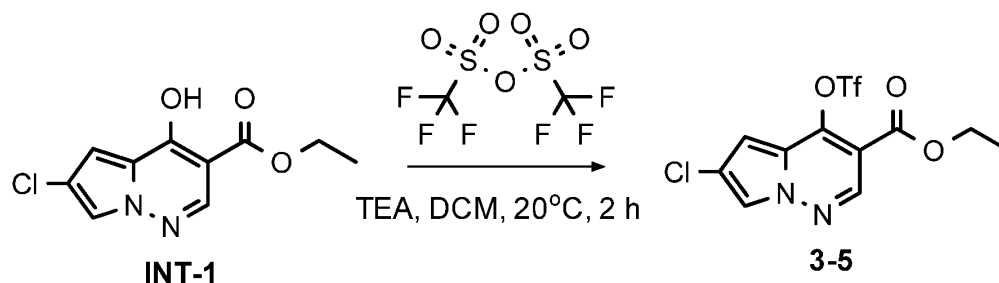
chromatography, eluted with PE/EA (20/1) to afford methyl 1-amino-4-chloropyrrole-2-carboxylate (**3-4**, 188 g, 71 %) as a white solid.

4. Synthesis of ethyl 6-chloro-4-hydroxypyrrolo[1,2-b]pyridazine-3-carboxylate (INT-1)



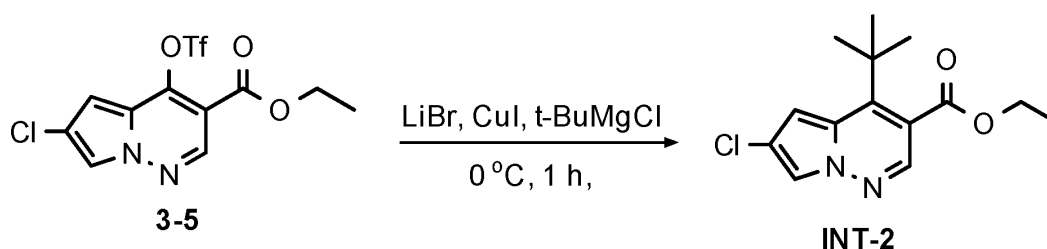
- 5 Into a 3.0 L round-bottom flask, was placed methyl 1-amino-4-chloropyrrole-2-carboxylate (**3-4**, 150 g, 859.2 mmol) in DMF (1.5 L) and ethyl 3,3-diethoxypropanoate (196.15 g, 1031.0 mmol) and PTSA (22.19 g, 128.9 mmol) were added. The reaction mixture was stirred at 90 °C for 2 h. The mixture was allowed to cool down to 60 °C. Then the DBU (261.61 g, 1718.4 mmol) was added at 60 °C. The reaction mixture was stirred at 60 °C for 1 h. The mixture was allowed to cool
- 10 down to room temperature. The resulting mixture was diluted with EA (4.0 L) and washed with 3 x 1.0 L of water. The resulting solution was dried Na₂SO₄ and concentrated under reduced pressure. The crude product was stirred as a slurry with EtOH/water (3/1) to afford ethyl 6-chloro-4-hydroxypyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-1**, 127 g, 61 %) as a white solid after filtration. (ES, m/z): 239 [M-H]⁻; ¹H NMR (300 MHz, CDCl₃, ppm): δ 12.28 (s, 1H), 8.30 (s, 1H),
- 15 7.69 (d, *J* = 2.0 Hz, 1H), 6.89 (d, *J* = 1.6 Hz, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H).

5. Synthesis of ethyl 6-chloro-4-(trifluoromethanesulfonyloxy)pyrrolo[1,2-b]pyridazine-3-carboxylate (3-5)



Into a 2.0 L round-bottom flask, was placed ethyl 6-chloro-4-hydroxypyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-1**, 82 g, 340.8 mmol), DCM (800 mL), TEA (103.44 g, 1022.3 mmol). To this was added triflic anhydride (153.82 g, 545.2 mmol) dropwise at 0 °C. The reaction mixture was stirred at 20 °C for 2 h. The resulting mixture was diluted with DCM (1.0 L) and washed with 3 x 500 mL of water. The organic phase was collected and dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (50/1) to afford ethyl 6-chloro-4-(trifluoromethanesulfonyloxy)pyrrolo[1,2-b]pyridazine-3-carboxylate (**3-5**, 90.5 g, 71 %) as a yellow solid.

6. Synthesis of ethyl 4-tert-butyl-6-chloropyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-2**)

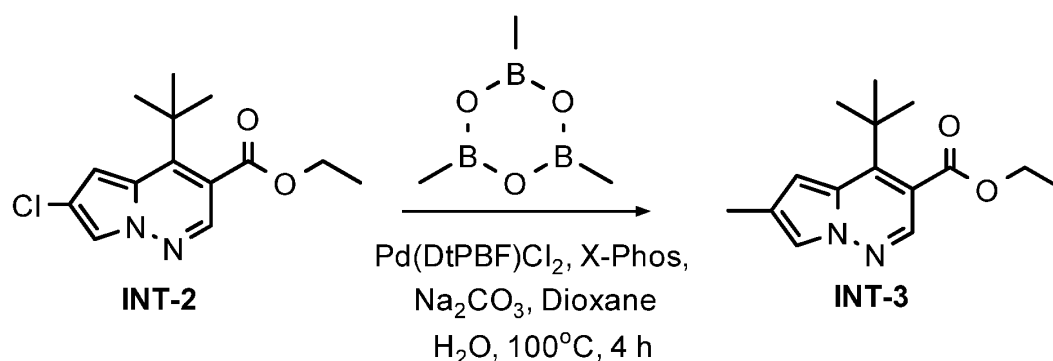


10

Into a 2.0 L three necks round-bottom flask, was placed ethyl 6-chloro-4-(trifluoromethanesulfonyloxy)pyrrolo[1,2-b]pyridazine-3-carboxylate (**3-5**, 62 g, 166.3 mmol), THF (1.2 L). To this was added LiBr (108.35 g, 1247.6 mmol) and CuI (237.62 g, 1247.6 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. This was followed addition of tert-butylmagnesium chloride (38.88 g, 332.7 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. The reaction was quenched by the addition of NH₄Cl (4 M in H₂O, 1.0 L) at 0 °C. The mixture was extracted with EA (3 x 500 mL). The organic phase was collected and dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (25/1) to afford ethyl 4-tert-butyl-6-chloropyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-2**, 42.5 g, 91 %) as a yellow oil.

20

7. Synthesis of ethyl 4-tert-butyl-6-methylpyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-3**)



Into a 1.0 L round bottom flask, was placed ethyl 4-tert-butyl-6-chloropyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-2**, 42 g, 149.6 mmol), dioxane (500 mL), H_2O (25 mL, 1387.7 mmol), Na_2CO_3 (39.64 g, 374.0 mmol), trimethylboroxine (65.73 g, 524.0 mmol), X-Phos (7.13 g, 14.7 mmol) and Pd(DtPBF)Cl_2 (9.75 g, 14.9 mmol) under nitrogen atmosphere. The reaction mixture was stirred at 100°C for 4 h. The mixture was allowed to cool down to room temperature. The resulting mixture was diluted with EA (1.5 L) and washed with 3 x 500 mL of water. The organic phase was collected and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography, eluted with PE/EA (20/1) to afford ethyl 4-tert-butyl-6-methylpyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-3**, 31 g, 79 %) as a yellow oil. (ES, m/z): 261 $[\text{M}+\text{H}]^+$; ^1H NMR (300 MHz, CDCl_3 , *ppm*): δ 7.75 (s, 1H), 7.54 (s, 1H), 6.68 (s, 1H), 4.36 (q, $J = 7.2$ Hz, 2H), 2.37 (s, 3H), 1.58 (s, 9H), 1.40 (t, $J = 7.2$ Hz, 3H).

Utilizing intermediates **INT-1**, **INT-2** and **INT-3** described above, the following compounds of the invention can be obtained by adapting the process shown in Scheme 2: A477, A478, A479, A480, A481, A482, A490, A491, A493, A499, A501, A502, A503, A504, A505, A506, A507, A508, A509, A510, A511, A512, A513, A514, A515, A516, A517, A518, A519, A520, A521, A522, A523, A524; A525, A526, A527, A528, A529, A530, A531, A532, A533, A534, A535, A536a, A536b, A538, A540, A541, A542, A544, A545, A546, A547, A548, A549, A550, A551, A552, A553, A554, A556, A557, A558, A559, A560, A561, A562, A563, A564, A565, A566, A567, A568.

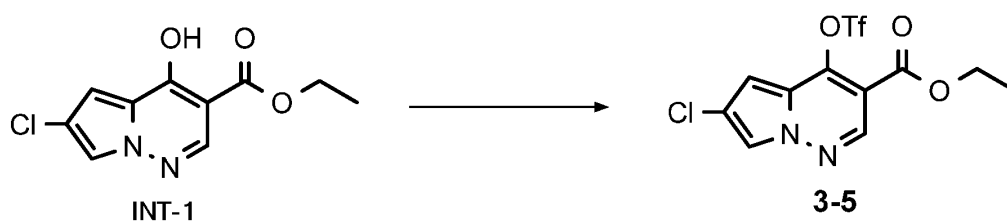
It is understood by persons of ordinary skill in the art that the order of reactions depicted in the chemical schemes described herein may be changed according to the reactivity of substituents. Furthermore, it will be understood that reactants known in the literature can be prepared according

to published procedures. In addition, it is understood that in case racemic mixtures are obtained by the chemical reactions described herein, desired enantiomers may be isolated in pure form by known purification methods known in the art, including but not limited to chiral HPLC methods.

5 **Preparation Example 4: 7 - (2,3 - dichloro - 5 - fluorophenyl) - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 4 - (dimethylamino) - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxamide (A493)**

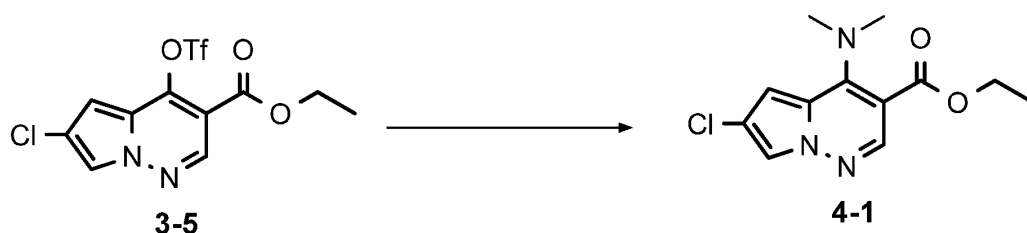
Compound A493 was prepared according to the general process described in Scheme 2. The specific synthesis details are provided below.

10 **1. Synthesis of ethyl 6 - chloro - 4 - (trifluoromethanesulfonyloxy)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (3-5)**



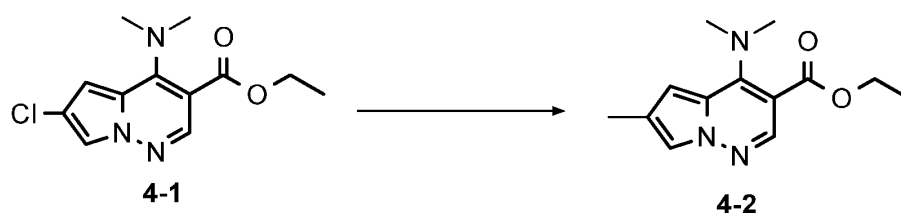
To a solution of 613.0 mg (2.5 mmol) of ethyl 6-chloro-4-hydroxypyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-1**) and 776 μ L (5.6 mmol) triethylamine in 5 mL of dichloromethane was added 471 μ L (2.8 mmol) trifluoromethane anhydride at 0 °C. The solution was stirred over night at RT. Afterwards, water was added and the layers separated by phase transfer cartridge. The organic layer was dried over Na₂SO₄ and the solvent was evaporated under reduced pressure to yield 1.2 g of crude product as a brown oil. (**3-5**, ESI, m/z): 373 [M+H]⁺.

20 **2. Synthesis of ethyl 6 - chloro - 4 - (dimethylamino)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (4-1)**



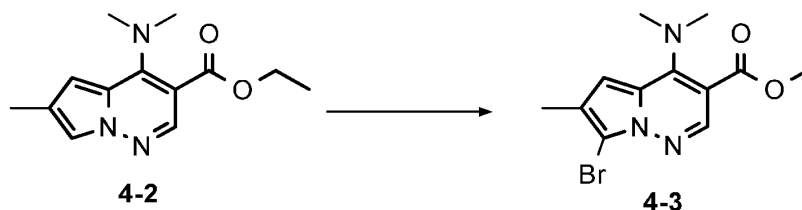
A solution of 31.0g (83.1 mmol) of ethyl 6 - chloro - 4 - (trifluoromethanesulfonyloxy)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**3-5**) in 300 mL of ethanol was added 40 mL (0.22 mol) of dimethylamine in ethanol (5.6 mol/L) and the solution heated to reflux for 15 min. After cooling to RT, the solution was diluted with ethyl acetate, washed with 1N HCl, 10% Na₂CO₃ solution and brine. After filtering through Celite, the solvent was evaporated under reduced pressure. Silica gel chromatography (CH/Ea 9:1-2:8) yielded 22.3 g (70 %) of **4-1** as yellow solid. (ESI, m/z): 268 [M+H]⁺.

3. Synthesis of ethyl 4 - (dimethylamino) - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**4-2**)



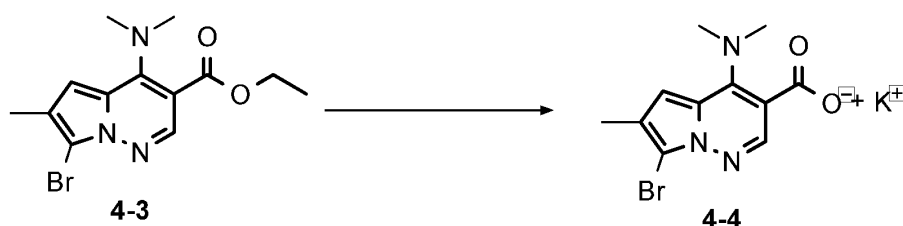
To a solution of 7.4 g (27.6 mmol) ethyl 6 - chloro - 4 - (dimethylamino)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**4-1**) in 150 mL of dioxane in a three-necked flask was added 10 mL trimethylboroxine and 80 mL of 1M Na₂CO₃ solution. The mixture was purged with Argon for 5 min then heated to 50 °C and treated with 3.0 g (3.5 mmol) XPHOS Pd G3 under Argon and stirred for 1 h at 90 °C. After cooling to RT, the solution was diluted with ethyl acetate, washed with 10% Na₂CO₃ solution and brine. After filtering through Celite, the solvent was evaporated under reduced pressure. Silica gel chromatography (CH/Ea 95:5-1:9) yielded 5.6 g (81 %) of the title compound (**4-2**) as yellow oil that solidifies upon standing. (ESI, m/z): 248 [M+H]⁺.

4. Synthesis of ethyl 7 - bromo - 4 - (dimethylamino) - 6 - methylpyrrolo[1,2 -

b]pyridazine - 3 - carboxylate (4-2)

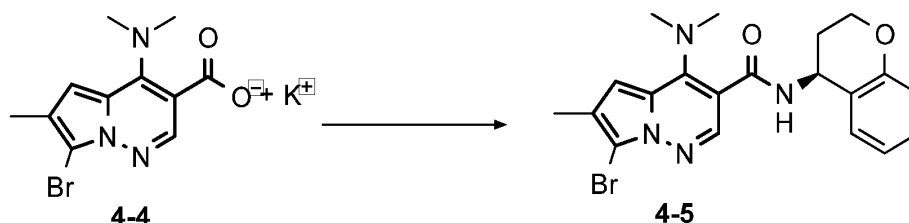
To a solution of 5.6 g (22.6 mmol) ethyl 4 - (dimethylamino) - 6 - methylpyrrolo[1,2 -
b]pyridazine - 3 - carboxylate (**4-2**) in 120 mL DMF was added 3.9 g (21.9 mmol) NBS at 0 °C
5 and the mixture stirred for 1 h at RT. The solution was diluted with ethyl acetate, washed with 10%
Na₂CO₃ solution and brine. After filtering through Celite, the solvent was evaporated under
reduced pressure. Silica gel chromatography (CH/EA 95:5-2:8) yielded 6.4 g (86 %) of the title
compound (**4-3**) as yellow solid. (ESI, m/z): 327 [M+H]⁺.

5. Synthesis of potassium 7 - bromo - 4 - (dimethylamino) - 6 - methylpyrrolo[1,2 -
10 **b]pyridazine - 3 - carboxylate (4-4)**



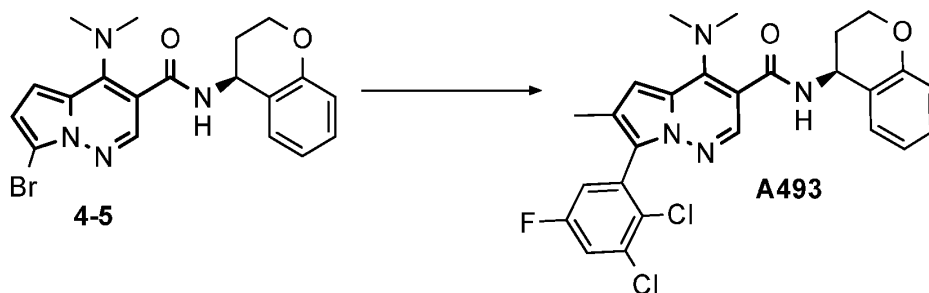
To a solution of 14.6 g (44.7 mmol) of ethyl 7 - bromo - 4 - (dimethylamino) - 6 -
methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**4-3**) in 400 mL THF was added 12.7 g (89.0
mmol) TMSOK and the mixture stirred at 70 °C for 7 h. After evaporation of volatiles 15 g of
15 crude product (**4-4**) was obtained and directly used in the next step. (ESI, m/z): 337 [M+H]⁺.

6. Synthesis of 7 - bromo - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 4 -
(dimethylamino) - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxamide (4-5)



To a solution of 15 g (35.6 mmol) potassium 7 - bromo - 4 - (dimethylamino) - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**4-4**) in 400 mL of DMF was added 28 mL (159.9 mmol) DIPEA and 24.0 g (63.1 mmol) HATU at RT. After stirring for 5 min at RT 13 g (70.0 mmol) (S)-chroman-4-amine hydrochloride were added and the mixture stirred for 30 min at 50 °C. After cooling to RT, the solution was diluted with ethyl acetate, washed with 1N HCl, 10% Na₂CO₃ solution and brine. After filtering through Celite, the solvent was evaporated under reduced pressure to about 200 mL and the product crystallized. The filtered solids were washed with little EA and dried to yield 10.6 g of product which was combined with the remaining mother liquor purified via silica gel chromatography (CH/EA 85:15-3:7) to yield a total of 11.9 g (77 %) of the title compound (**4-5**) as beige solid. (ESI, m/z): 430 [M+H]⁺.

7. Synthesis of 7 - (2,3 - dichloro-5-fluorophenyl)-N-[(4S)-3,4-dihydro-2H-1-benzopyran-4-yl]-4-(dimethylamino)-6-methylpyrrolo[1,2-b]pyridazine-3-carboxamide (A493)



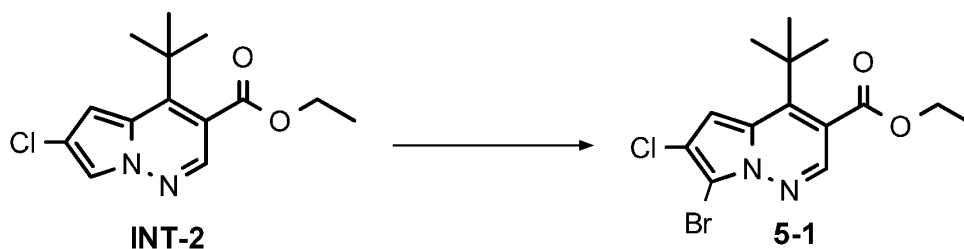
To a solution of 720 mg (1.5 mmol) of 7-bromo-N-[(4S)-3,4-dihydro-2H-1-benzopyran-4-yl]-4-(dimethylamino)-6-methylpyrrolo[1,2-b]pyridazine-3-carboxamide (**4-5**) in 25 mL of dioxane was added 430 mg (2.0 mmol) 2,3-dichloro-5-fluorophenylboronic acid under Argon followed by 200 mg (0.3 mmol) of 1,1' -Bis-(di-tert-butylphosphino)-ferrocen-palladiumdichloride and 3 mL Na₂CO₃ solution (2 mol/L). The mixture was stirred for 2 h at 80 °C in a sealed vessel. After

cooling to RT, the solution was diluted with water and extracted with EA. After combining the organic layers, the solvent was evaporated under reduced pressure. Silica gel chromatography (CH to CH/EA 8:2) yielded 680 mg (51 %) of the title compound (**A493**) as brown solid. (ESI, m/z): 514 [M+H]⁺.

5 **Preparation Example 5: Synthesis of 4 - tert - butyl - 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl) - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl]pyrrolo[1,2 - b]pyridazine - 3 - carboxamide (A502)**

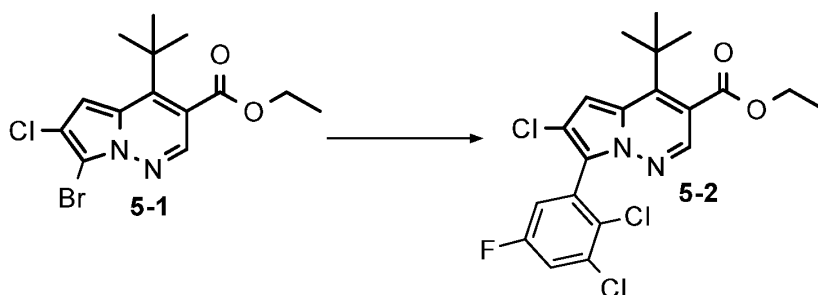
Compound A502 was prepared according to the general process described in Scheme 2. The specific synthesis details are provided below.

10 **1. Synthesis of ethyl 7 - bromo - 4 - tert - butyl - 6 - chloropyrrolo[1,2 - b]pyridazine - 3 - carboxylate (5-1)**



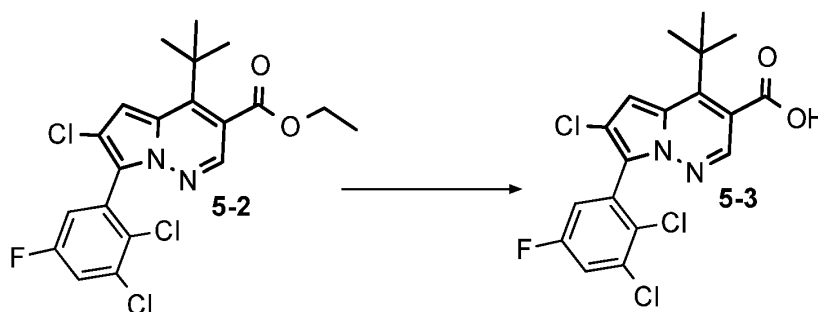
To a solution of 325 mg (1.0 mmol) ethyl 4-tert-butyl-6-chloropyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-2**) in 5 mL DMF was added 166 mg (0.9 mmol) NBS at RT and the mixture stirred for 1 h at RT. The solution was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄ and the solvent was evaporated under reduced pressure. Preparative HPLC (ACN/H₂O/TFA) yielded 323 mg (86 %) of the title compound (**5-1**) as yellow solid. (5-1, ESI, m/z): 360 [M+H]⁺.

20 **2. Synthesis of ethyl 4 - tert - butyl - 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (5-2)**



To a solution of 100 mg (0.27 mmol) of ethyl 7 - bromo - 4 - tert - butyl - 6 - chloropyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**5-1**) in 3 mL of dioxane was added 63 mg (0.3 mmol) 2,3-dichloro-5-fluorophenyl)boronic acid under Argon followed by 0.5 mL Na₂CO₃ solution (2 mol/L) and 45 mg (0.05 mmol) of 1,1' -Bis-(di-tert-butylphosphino)-ferrocene-palladiumdichloride. The mixture was stirred for 2 h at 80 ° C in a sealed vessel. After cooling to RT, the solution was diluted with water and extracted with EA. After combining the organic layers were dried over Na₂SO₄ and the solvent was evaporated under reduced pressure. Preparative HPLC (ACN/H₂O/TFA) yielded 45 mg (37 %) of the title compound (**5-2**) as brown solid. (ESI, m/z): 444 [M+H]⁺.

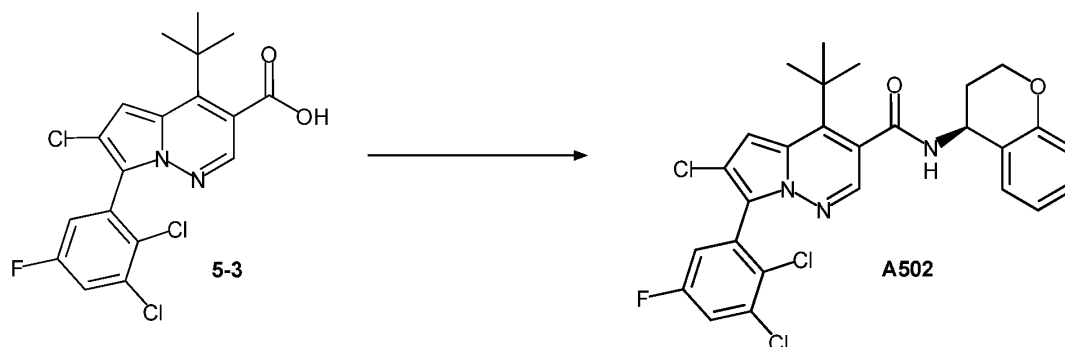
3. Synthesis of 4 - tert - butyl - 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylic acid (**5-3**)



To a solution of 45 mg (0.1 mmol) ethyl 4 - tert - butyl - 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**5-2**) in 1 mL dioxane/ethanol was added 0.5 mL NaOH-solution (4 mol/L) at RT and the mixture stirred for 12 h at 90 °C. After cooling to RT, the solution was treated with HCl (4 mol/L) until acidic pH at 0 °C and diluted with

DCM. After filtration through a phase separation cartridge, the organic phase was evaporated under reduced pressure and the crude title product (**5-3**) directly used in the subsequent step. (ESI, m/z): 416 [M+H]⁺.

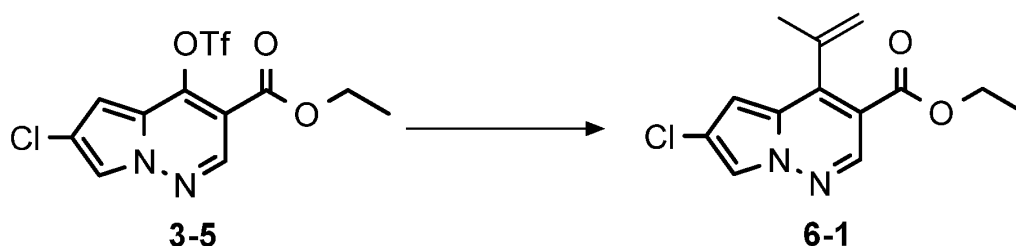
4. Synthesis of 4 - tert - butyl - 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl) - N -
 5 [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl]pyrrolo[1,2 - b]pyridazine - 3 -
 carboxamide (**A502**)



To a solution of 42 mg (0.1 mmol) 4 - tert - butyl - 6 - chloro - 7 - (2,3 - dichloro - 5 -
 fluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylic acid (**5-3**) in 1.5 mL DMF was added 51
 10 μ L (0.3 mmol) DIPEA and 38 mg (0.1 mmol) HATU at RT. After stirring for 5 min at RT 28 mg
 (0.15 mmol) (S)-chroman-4-amine hydrochloride were added and the mixture stirred for 2 h at RT.
 After acidifying with TFA, the mixture was directly purified via preparative HPLC
 (ACN/H₂O/TFA) to yield 10 mg (18 %) of the title compound (**A502**) as yellow solid. (ESI, m/z):
 547 [M+H]⁺.

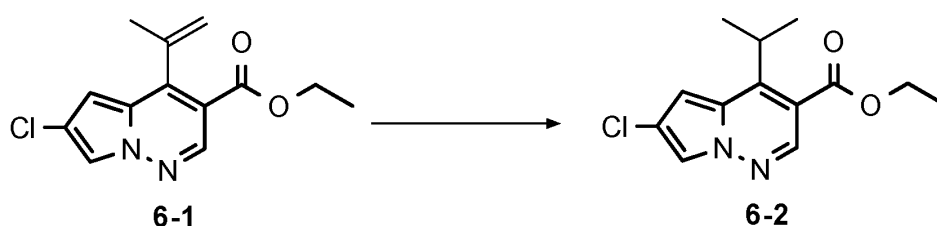
15 **Preparation Example 6: Synthesis of N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 -
 yl] - 6 - methyl - 4 - (propan - 2 - yl) - 7 - (2,3,5 - trifluorophenyl)pyrrolo[1,2 -
 b]pyridazine - 3 - carboxamide (**A513**)**

1. Synthesis of ethyl 6 - chloro - 4 - (prop - 1 - en - 2 - yl)pyrrolo[1,2 - b]pyridazine -
 3 - carboxylate (**6-1**)



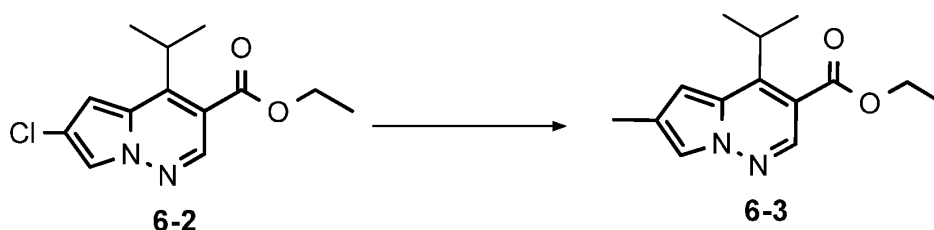
A solution of 1.55 g (8.1 mmol) of ethyl 6 - chloro - 4 - (trifluoromethanesulfonyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**3-5**) in 25 mL 1,2-Dimethoxyethane was treated with 9.24 g (28.3 mmol) Cs₂CO₃ dissolved in 5 mL of water under Argon, followed by addition of 2.59 mL (13.7 mmol) of Isopropenylboronic acid pinacol ester. After degassing for 5 min, 794 mg (1.0 mmol) of 1,1' -Bis-(di-tert-butylphosphino)-ferrocenepalladiumdichloride were added under Argon and the sealed vessel stirred for 3 h at 80 °C. After cooling to RT, the solution was diluted with ethyl acetate and washed with 10% Na₂CO₃ solution and brine. The solvent was dried over Na₂SO₄ and the evaporated under reduced pressure. Preparative HPLC (ACN/H₂O/TFA) yielded 578 mg (27 %) of the title compound (**6-1**) as solid. (ESI, m/z): 265 [M+H]⁺.

2. Synthesis of ethyl 6 - chloro - 4 - (propan - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (6-2)



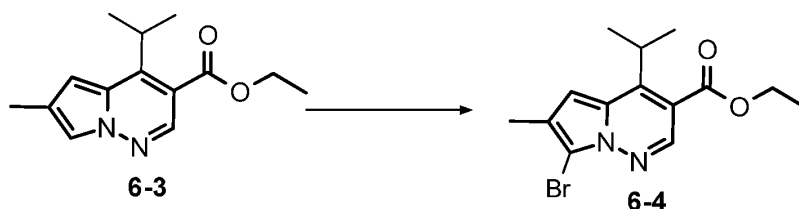
A solution of 578 mg (2.1 mmol) ethyl 6 - chloro - 4 - (prop - 1 - en - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**6-1**) in 25 mL of acetic acid was treated with 50 mg of PtO₂ and stirred for 30 min at RT under 50 psi of hydrogen. The crude mixture was filtrated, and the filtrate evaporated. Preparative HPLC (ACN/H₂O/TFA) yielded 337 mg (57 %) of the title compound (**6-2**) as solid. (ESI, m/z): 267 [M+H]⁺.

3. Synthesis of ethyl 6 - methyl - 4 - (propan - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (6-3)



To a solution of 2.0 g (7.5 mmol) ethyl 6 - chloro - 4 - (propan - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**6-2**) in 22 mL of dioxane in a vial was added 505 mg (0.75 mmol) XPHOS Pd G3 under Argon, followed by 3.5 mL (24.7 mmol) trimethylboroxine and 11.2 mL of 2M Na₂CO₃ solution. The mixture was purged with Argon for 5 min then heated for 6 h at 80 °C. After cooling to RT, the solution was diluted with water and extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄ and the solvent was evaporated under reduced pressure. Silica gel chromatography (CH/EA 9:1) yielded 1.43 g (69 %) of the title compound (**6-3**) as solid. (ESI, m/z): 247 [M+H]⁺.

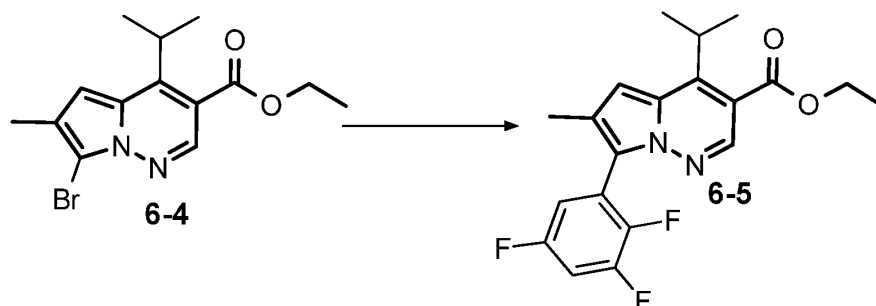
4. Synthesis of ethyl 7 - bromo - 6 - methyl - 4 - (propan - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (6-4)



To a solution of 1.43 g (5.2 mmol) of ethyl 6-methyl-4-(propan-2-yl)pyrrolo[1,2-b]pyridazine-3-carboxylate (**6-3**) in 14 mL DMF was added 837 mg (4.7 mmol) NBS at RT and the mixture stirred for 30 min at RT. After acidifying with TFA, the mixture was directly purified via preparative HPLC (ACN/H₂O/TFA) to yield a total of 1.14 g (67 %) of the title compound (**6-4**) as yellow oil. (ESI, m/z): 326 [M+H]⁺.

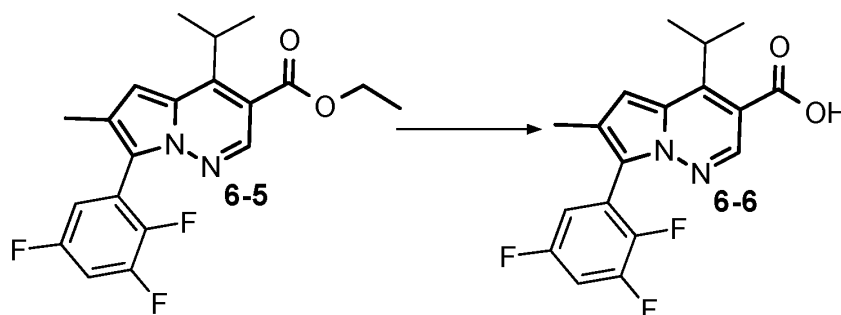
5. Synthesis of ethyl 6 - methyl - 4 - (propan - 2 - yl) - 7 - (2,3,5 -

trifluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (6-5)



To a solution of 25 mg (0.1 mmol) of ethyl 7 - bromo - 6 - methyl - 4 - (propan - 2 -
yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**6-4**) in 1 mL of dioxane was added 20 mg (0.1
5 mmol) 2,3-dichloro-5-fluorophenyl)boronic acid under Argon followed by 153 μ L Na_2CO_3
solution (2 mol/L) and 10 mg (0.015 mmol) of 1,1' -Bis-(di-tert-butylphosphino)-ferrocen-
palladiumdichloride. The mixture was stirred for 1 h at 80 ° C in a sealed vessel. After cooling to
RT, the solution was diluted with DCM and brine. After filtration through a phase separation
cartridge, the organic phase was evaporated under reduced pressure and the mixture purified via
10 preparative HPLC (ACN/ H_2O /TFA) to yield 10 mg (34 %) of the title compound (**6-5**) as brown
solid. (ESI, m/z): 377 $[\text{M}+\text{H}]^+$.

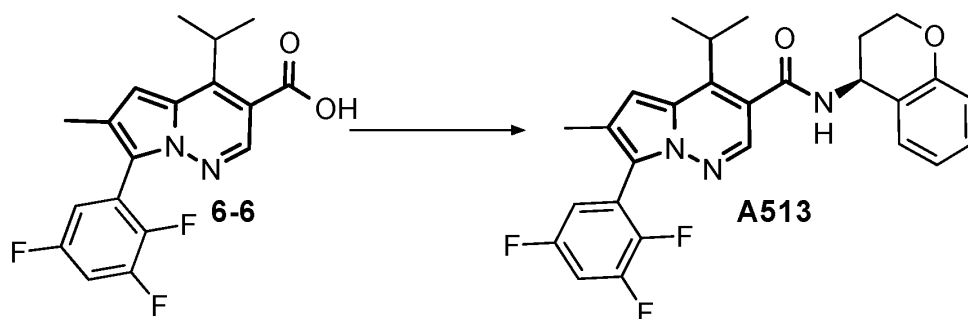
**6. Synthesis of 6 - methyl - 4 - (propan - 2 - yl) - 7 - (2,3,5 -
trifluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylic acid (6-6)**



15 To a solution of 10 mg (0.02 mmol) ethyl 6 - methyl - 4 - (propan - 2 - yl) - 7 - (2,3,5 -
trifluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**6-5**) in 2 mL ethanol was added 0.13

mL NaOH-solution (4 mol/L) at RT and the mixture stirred for 2 h at 90 °C. After cooling to RT, the solution was treated with HCl (4 mol/L) until acidic pH at 0 °C and diluted with DCM. After filtration through a phase separation cartridge, the organic phase was evaporated under reduced pressure and the crude title product (**6-6**) directly used in the subsequent step. (ESI, m/z): 349 [M+H]⁺.

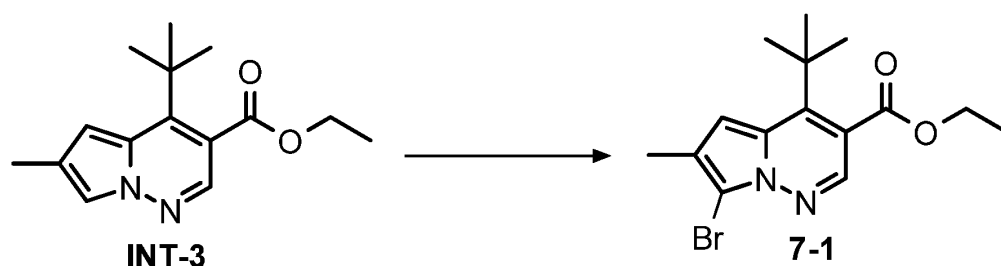
7. Synthesis of N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methyl - 4 - (propan - 2 - yl) - 7 - (2,3,5 - trifluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxamide (A513)



To a solution of 9 mg (0.02 mmol) 6 - methyl - 4 - (propan - 2 - yl) - 7 - (2,3,5 - trifluorophenyl)pyrrolo[1,2 - b]pyridazine - 3 - carboxylic acid (**6-6**) in 1 mL DMF was added 13 µL (0.078 mmol) DIPEA and 9.8 mg (0.026 mmol) HATU at RT. After stirring for 10 min at RT 5.7 mg (0.03 mmol) (S)-chroman-4-amine hydrochloride were added and the mixture stirred at RT overnight. After diluting with ACN and acidifying with TFA, the mixture was directly purified via preparative HPLC (ACN/H₂O/TFA) to yield 9 mg (72 %) of the title compound (**A513**) as solid. (ESI, m/z): 480 [M+H]⁺.

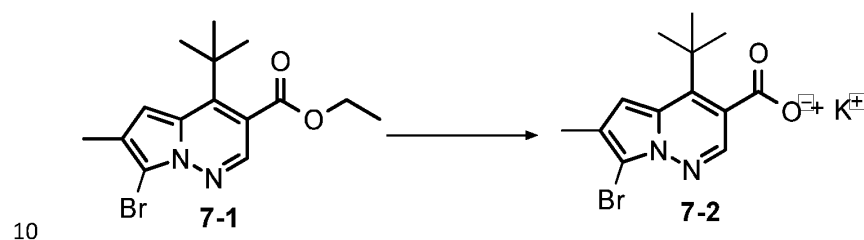
Preparation Example 7: Synthesis of 4 - tert - butyl - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methyl - 7 - (piperidin - 1 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxamide (A524)

1. Synthesis of ethyl 7 - bromo - 4 - tert - butyl - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (7-1)



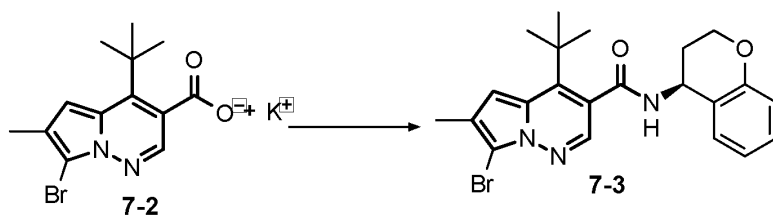
To a solution of 680 mg (2.6 mmol) of ethyl 4-tert-butyl-6-methylpyrrolo[1,2-b]pyridazine-3-carboxylate (**INT-3**) in 10 mL DMF was added 360 mg (2.0 mmol) NBS at RT and the mixture stirred for 30 min at RT. The solution was diluted with ethyl acetate and washed with 10% Na₂CO₃ solution and brine. The combined organic layers were filtered over Celite and the solvent was evaporated under reduced pressure. Silica gel chromatography (CH/EA gradient) yielded 730 mg (74 %) of the title compound (**7-1**) as yellow oil. (ESI, m/z): 340 [M+H]⁺.

2. Synthesis of potassium 7 - bromo - 4 - tert - butyl - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**7-2**)



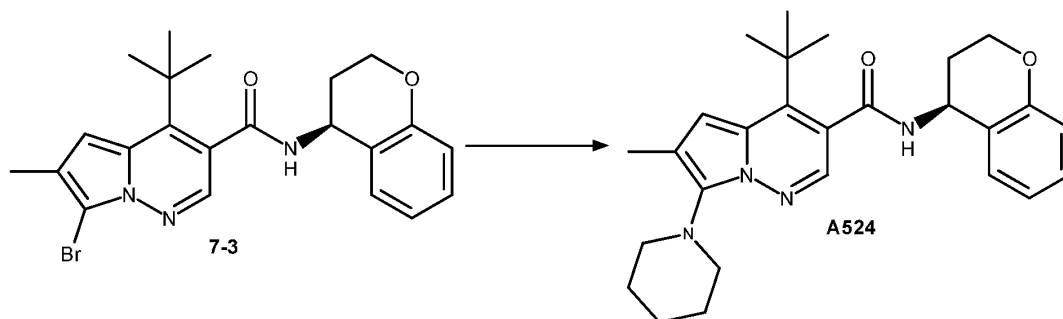
To a solution of 3 g (7.0 mmol) of ethyl 7 - bromo - 4 - tert - butyl - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**7-1**) in 100 mL THF was added 3.0 g (21.2 mmol) TMSOK and the mixture stirred at 70 °C for 7 h. After evaporation of volatiles 2.2 g of crude product (**7-2**) was obtained and directly used in the next step. (ESI, m/z): 350 [M+H]⁺.

3. Synthesis of 7 - bromo - 4 - tert - butyl - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxamide (**7-3**)



To a solution of 2.2 g (6.8 mmol) potassium 7 - bromo - 4 - tert - butyl - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxylate (**7-2**) in 85 mL DMF was added 4.2 mL (24.7 mmol) DIPEA and 3.78 g (9.9 mmol) HATU at RT. After stirring for 5 min at RT 2.0 g (11.0 mmol) (S)-chroman-4-amine hydrochloride were added and the mixture stirred for 1 h at 50 °C. The mixture was diluted with ethyl acetate, washed with 1N HCl, 10% Na₂CO₃ solution and brine. The organic layer was dried over Na₂SO₄ and the solvent was evaporated under reduced pressure. Silica gel chromatography (CH/EA gradient) yielded 2.0 g (68 %) of the title compound (**7-3**) as solid. (ESI, m/z): 443 [M+H]⁺.

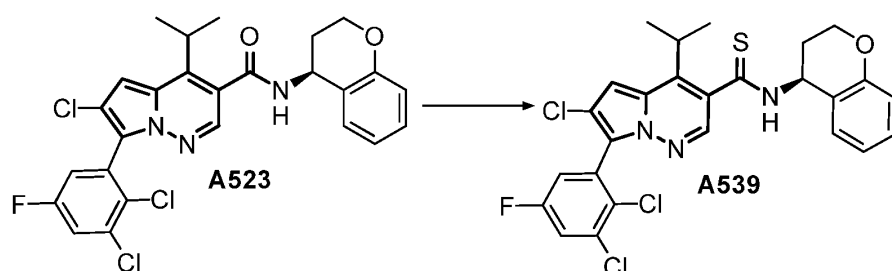
4. Synthesis of 4 - tert - butyl - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methyl - 7 - (piperidin - 1 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxamide (**A524**)



A 5 mL vial was charged with 50 mg (0.1 mmol) 7 - bromo - 4 - tert - butyl - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxamide (**7-3**), dioxane 1 mL, 11 µL (0.1 mmol) piperidine and degassed with Argon. After addition of 43 mg (0.45 mmol) of *t*-BuONa and additional degassing with Argon, 1.45 mg (0.002 mmol) of Pd-PEPPSI-IPent Cl were added and the sealed vial heated to 80 °C over night. After cooling to RT the mixture was diluted with MeOH and directly purified via preparative HPLC

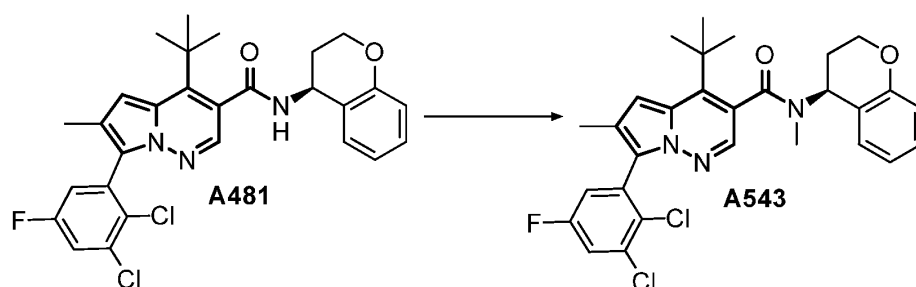
(ACN/H₂O/TFA) to yield 3 mg (6 %) of the title compound (**A524**) as solid. (ESI, m/z): 447 [M+H]⁺.

Preparation Example 8: Synthesis of 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl) - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 4 - (propan - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carbothioamide (A539**)**



To a solution of 48 mg (0.1 mmol) of 6 - chloro - 7 - (2,3 - dichloro - 5 - fluorophenyl) - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 4 - (propan - 2 - yl)pyrrolo[1,2 - b]pyridazine - 3 - carboxamide (**A523**) in 3 mL of THF was added 54 mg (0.14 mmol) Lawesson's reagent. The mixture was stirred for 3 h at RT, then heated to 50 °C overnight. After cooling to RT, the mixture was acidified with TFA and directly purified via preparative HPLC (ACN/H₂O/TFA) to yield 16.5 mg (33 %) of the title compound (**A539**) as yellow solid. (ESI, m/z): 549 [M+H]⁺.

Preparation Example 9: Synthesis of 4 - tert - butyl - 7 - (2,3 - dichloro - 5 - fluorophenyl) - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - N,6 - dimethylpyrrolo[1,2 - b]pyridazine - 3 - carboxamide (A543**)**

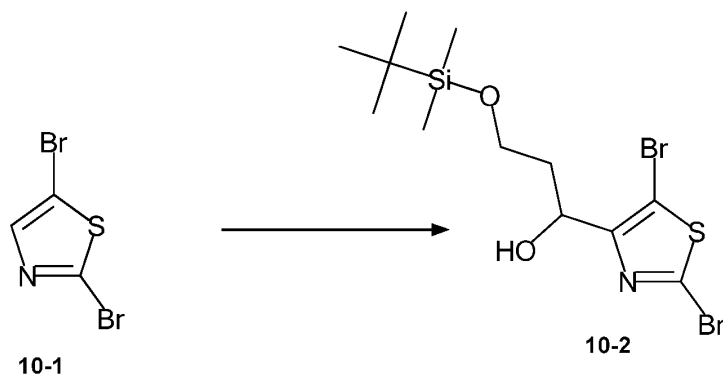


To a solution of 20 mg (0.03 mmol) 4 - tert - butyl - 7 - (2,3 - dichloro - 5 - fluorophenyl) - N - [(4S) - 3,4 - dihydro - 2H - 1 - benzopyran - 4 - yl] - 6 - methylpyrrolo[1,2 - b]pyridazine - 3 - carboxamide (**A481**) in 3 mL of DMF was added 3.3 mg (0.077 mmol) of NaH. After addition of 2.6 μ L (0.042 mmol) MeI the mixture was stirred for 1 h at RT and then directly purified via preparative HPLC (ACN/H₂O/TFA) to yield 9.5 mg (41 %) of the title compound (**A543**) as yellow solid. (ESI, m/z): 541 [M+H]⁺.

Preparation Example 10: Synthesis of 5H,6H,7H-pyrano[3,2-d][1,3]thiazol-7-amine (11-9)

The amine group (11-9) used in the preparation of Ring System U in Compound A550 is synthesized from commercially available starting materials via the following reaction process:

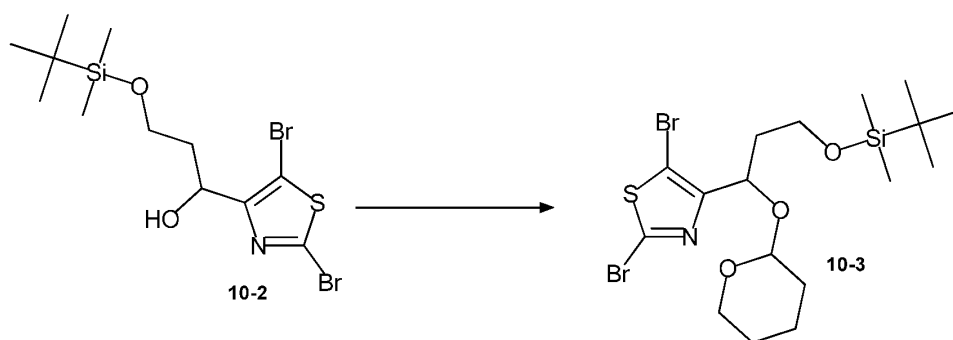
1. Synthesis of 3-[(tert-butyldimethylsilyl)oxy]-1-(2,5-dibromo-1,3-thiazol-4-yl)propan-1-ol (10-2)



Into a 250-mL 3-necked round-bottom flask, was placed LDA (2 M) (15.50 mL, 30.9 mmol) in THF (20.00 mL). The resulting solution was cooled to -78 °C. Then a solution of 2,5-dibromo-1,3-thiazole (**10-1**, 5.00 g, 20.6 mmol) in 15 mL THF was added. The resulting solution was stirred

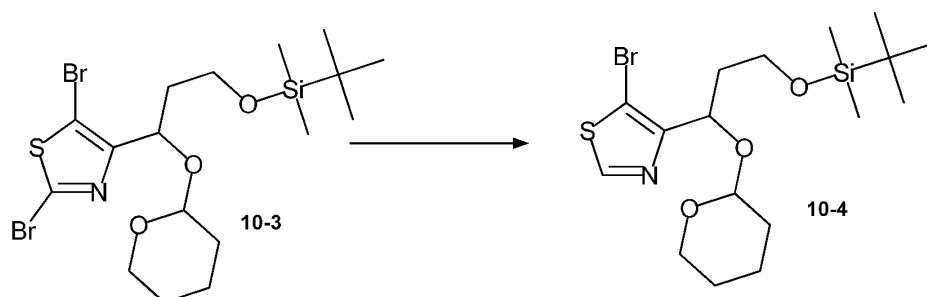
for 30 min at -78 °C. A solution of 3-[(tert-butyldimethylsilyl)oxy] propanal (3.88 g, 20.6 mmol) in 15 mL THF was added. The resulting solution was stirred for 1 h at -78 °C. The resulting solution was allowed to react, with stirring, for an additional 15 hours at room temperature. The pH value of the solution was adjusted to 6-7 with HCl (1 mol/L). The resulting solution was extracted with 2 x 100 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 100 ml of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:15). This resulted in 4.00 g (45 %) of 3-[(tert-butyldimethylsilyl)oxy]-1-(2,5-dibromo-1,3-thiazol-4-yl)propan-1-ol (**10-2**) as yellow oil.

2. Synthesis of 2,5-dibromo-4-[3-[(tert-butyl dimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (10-3)



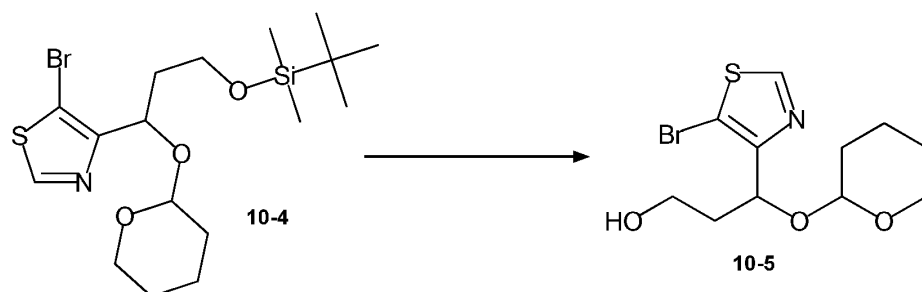
Into a 250-mL round-bottom flask, was placed 3-[(tert-butyldimethylsilyl)oxy]-1-(2,5-dibromo-1,3-thiazol-4-yl)propan-1-ol (**10-2**, 4.0 g, 9.3 mmol), DCM (40.00 mL), DHP (3.90 g, 46.4 mmol), PPTS (0.23 g, 0.9 mmol). The resulting solution was stirred for 3 h at 40 °C. The resulting mixture was washed with 30 ml of H₂O and 30 mL of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:10). This resulted in 3.62 g (75 %) of 2,5-dibromo-4-[3-[(tert-butyl dimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (**10-3**) as yellow oil.

3. Synthesis of 5-bromo-4-[3-[(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (10-4)



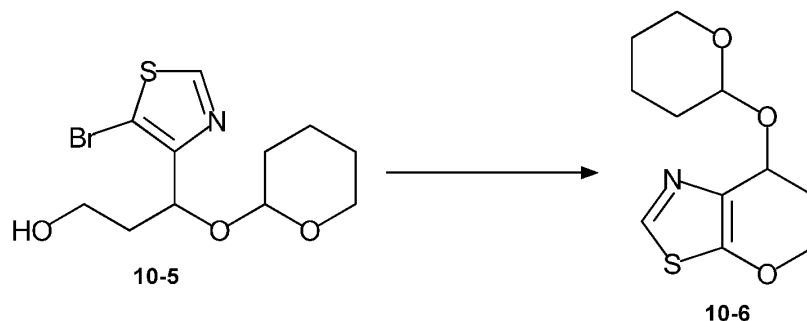
Into a 100-mL 3-necked round-bottom flask, was placed 2,5-dibromo-4-[3-[(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (**10-3**, 3.60 g, 7.0 mmol) in 40 mL THF. The resulting solution was cooled to -10 °C. And *i*-PrMgCl (2 M) (3.70 mL, 7.3 mmol) was added. The resulting solution was stirred for 1 h at -10 °C. The reaction was then quenched by the addition of 100 mL of saturated aqueous NH₄Cl. The resulting solution was extracted with 2x50 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 50 ml of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. This resulted in 2.60 g (85 %) of 5-bromo-4-[3-[(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (**10-4**) as yellow oil.

4. Synthesis of 3-(5-bromo-1,3-thiazol-4-yl)-3-(oxan-2-yloxy)propan-1-ol (**10-5**)



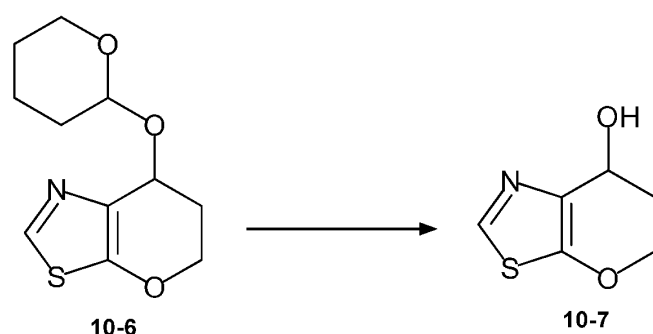
Into a 250-mL round-bottom flask, was placed 5-bromo-4-[3-[(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (**10-4**, 2.60 g, 6.0 mmol), THF (30.00 mL) and TBAF (1 M) (7.20 mL, 7.2 mmol). The resulting solution was stirred for 2 h at room temperature. The resulting mixture was washed with 30 mL of H₂O and 30 mL of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). This resulted in 1.55 g (81 %) of 3-(5-bromo-1,3-thiazol-4-yl)-3-(oxan-2-yloxy)propan-1-ol (**10-5**) as yellow oil.

5. Synthesis of 7-(oxan-2-yloxy)-5H,6H,7H-pyrano[3,2-d][1,3]thiazole (10-6)



Into a 40-mL vial, was placed 3-(5-bromo-1,3-thiazol-4-yl)-3-(oxan-2-yloxy)propan-1-ol (**10-5**, 1.55 g, 4.8 mmol), toluene (16.00 mL), Cs₂CO₃ (2.35 g, 7.2 mmol), *t*-BuBrettPhos Pd G3 (0.33 g, 0.4 mmol). The resulting solution was stirred for 15 h at 120 °C. The solids were filtered out and washed with 20 mL of EA. The filtrate was concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:4). This resulted in 0.60 g (52 %) of 7-(oxan-2-yloxy)-5H,6H,7H-pyrano[3,2-d][1,3]thiazole (**10-6**) as yellow oil.

6. Synthesis of 5H,6H,7H-pyrano[3,2-d][1,3]thiazol-7-ol (10-7)



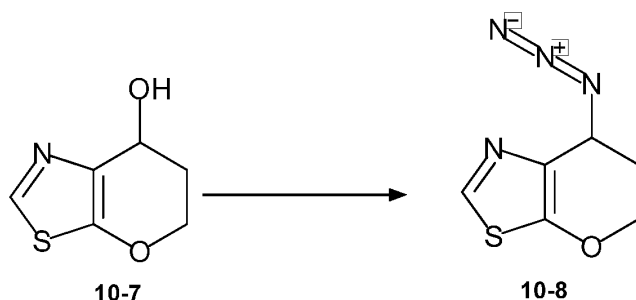
10

15

Into a 20-mL vial, was placed 7-(oxan-2-yloxy)-5H,6H,7H-pyrano[3,2-d][1,3]thiazole (**10-6**, 0.60 g, 2.5 mmol), THF (3.00 mL), H₂O (3.00 mL), PTSA (85.63 mg, 0.35 mmol). The resulting solution was stirred for 2 h at room temperature. The resulting solution was diluted with 10 mL of H₂O. The resulting solution was extracted with 3x15 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 30 mL of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with

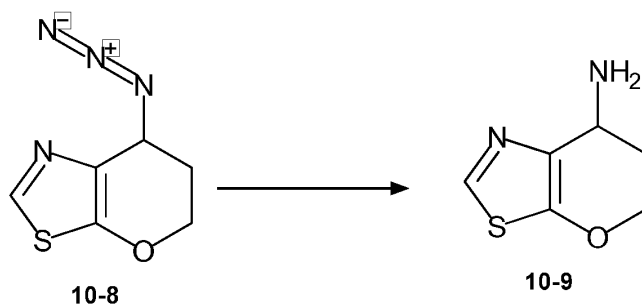
ethyl acetate/petroleum ether (1:1). This resulted in 0.20 g (51 %) of 5H,6H,7H-pyrano[3,2-d][1,3]thiazol-7-ol (**10-7**) as yellow oil.

7. Synthesis of 7-azido-5H,6H,7H-pyrano[3,2-d][1,3]thiazole (**10-8**)



- 5 Into a 20-mL vial, was placed 5H,6H,7H-pyrano[3,2-d][1,3]thiazol-7-ol (**10-7**, 200 mg, 1.3 mmol), THF (4.00 mL), DPPA (420 mg, 1.5 mmol). The resulting solution was cooled to 0 °C and DBU (232 mg, 1.5 mmol) was added. The resulting solution was stirred for 15 h at room temperature. The resulting solution was added 10 mL of 10% HCl. The resulting solution was extracted with 2x10 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 20
10 ml of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:4). This resulted in 110 mg (47 %) of 7-azido-5H,6H,7H-pyrano[3,2-d][1,3]thiazole (**10-8**) as yellow oil.

8. Synthesis of 5H,6H,7H-pyrano[3,2-d][1,3]thiazol-7-amine (**10-9**)



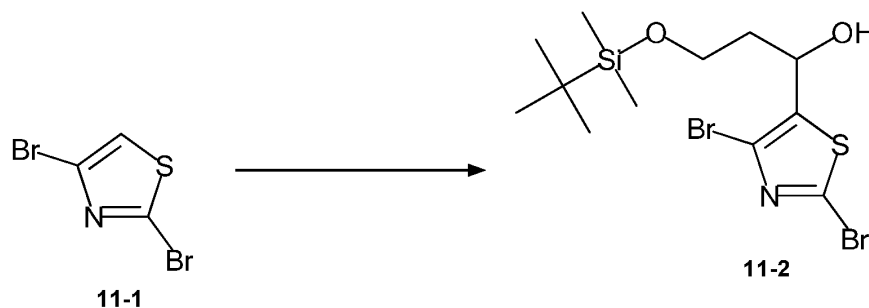
- 15 Into a 50-mL pressure tank reactor, was placed 7-azido-5H,6H,7H-pyrano[3,2-d][1,3]thiazole (**10-8**, 0.30 g, 1.65 mmol), EtOH (9.00 mL), Pd/C (30 mg, 10 w%). The resulting solution was stirred for 6 h at 40 °C under 10 atm hydrogen pressure. The solids were filtered out and washed with 10 mL of EtOH. The filtrate was concentrated. The crude product was purified by Flash-Prep-

HPLC with the following conditions (IntelFlash-1): Column, C18 silica gel; mobile phase, H₂O:ACN=100:0 increasing to H₂O:ACN=70:30 within 15 min; Detector, 254nm. This resulted in 206.2 mg (80 %) of 5H,6H,7H-pyrano[3,2-d][1,3]thiazol-7-amine (**10-9**) as yellow solid. MS (ES, m/z): 157 [M+H]⁺; ¹H NMR (300 MHz, CDCl₃, ppm) δ: 8.53 (s, 1H), 4.44-4.28 (m, 2H), 4.21 (t, *J* = 5.4 Hz, 1H), 2.23 (m, 1H), 1.86 (m, 1H).

Preparation Example 11: Synthesis of 5H,6H,7H-pyrano[2,3-d][1,3]thiazol-7-amine

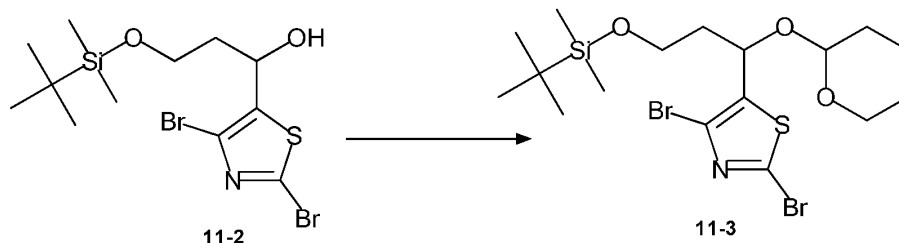
The amine group used in the preparation of Ring System V in Compound A551 is synthesized from commercially available starting materials via the following reaction process:

1. Synthesis of 3-[(tert-butyldimethylsilyl)oxy]-1-(2,4-dibromo-1,3-thiazol-5-yl)propan-1-ol (**11-2**)



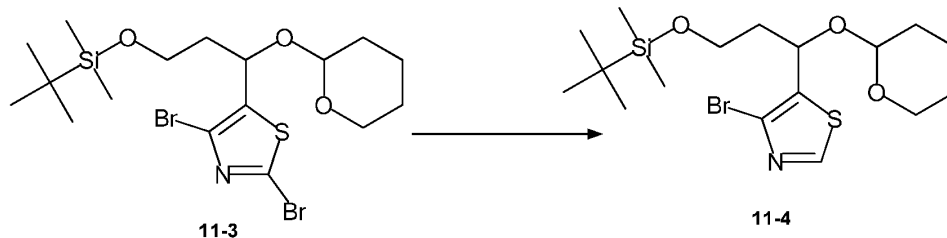
Into a 250-mL 3-necked round-bottom flask, was placed LDA (2 M, 15.50 mL, 30.9 mmol), THF (20 mL). The resulting solution was cooled to -78 °C. Then the solution of 2,4-dibromo-1,3-thiazole (**11-1**, 5.00 g, 20.6 mmol) in THF (15 mL) was added. The resulting solution was stirred for 30 min at -78 °C. To the above solution, 3-[(tert-butyl dimethylsilyl)oxy]propanal (3.88 g, 20.6 mmol) in THF (15.00 mL) was added. The resulting solution was stirred for 1 h at -78 °C. The resulting solution was allowed to react, with stirring, for an additional 15 h at room temperature. The pH value of the solution was adjusted to 6-7 with HCl (1 mol/L). The resulting solution was extracted with 2 x 100 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 100 ml of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:12). This resulted in 5.00 g (56 %) of 3-[(tert-butyldimethylsilyl)oxy]-1-(2,4-dibromo-1,3-thiazol-5-yl)propan-1-ol (**11-2**) as yellow oil

2. Synthesis of 2,4-dibromo-5-[3-[(tert-butyldimethyl silyl)oxy]-1-(oxan-2-yloxy)propyl]-

1,3-thiazole (11-3)

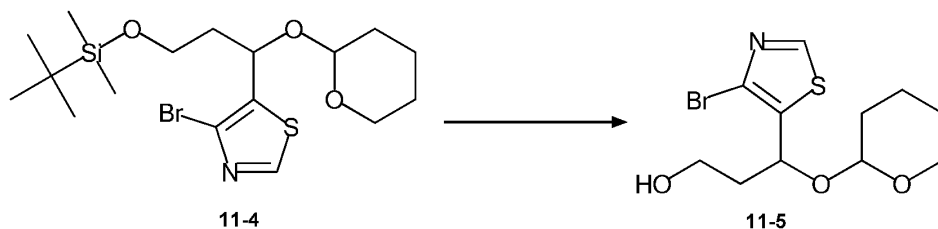
Into a 250-mL round-bottom flask, was placed 3-[(tert-butyldimethylsilyl)oxy]-1-(2,4-dibromo-1,3-thiazol-5-yl)propan-1-ol (**11-2**, 4.00 g, 9.3 mmol), DCM (60 mL), DHP (3.90 g, 46.4 mmol), PPTS (0.23 g, 0.9 mmol). The resulting solution was stirred for 2 h at 40 °C. The resulting mixture was washed with 1x50 mL of H₂O and 1x50 mL of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:15). This resulted in 4.30 g (90 %) of 2,4-dibromo-5-[3-[(tert-butyldimethyl silyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (**11-3**) as a yellow oil.

3. Synthesis of 4-bromo-5-[3- [(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl] -1,3-thiazole (11-4)



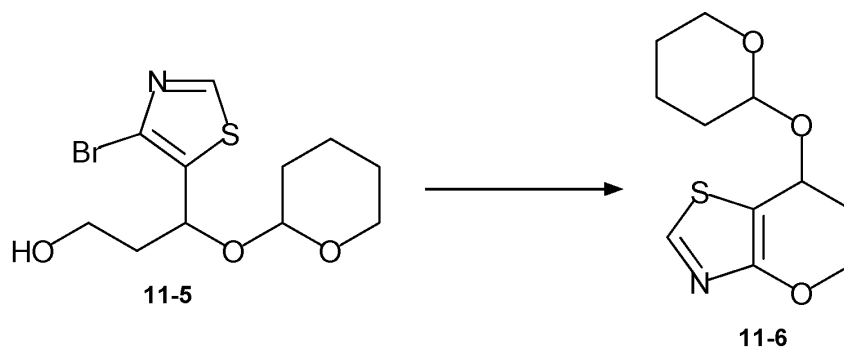
Into a 100-mL 3-necked round-bottom flask, was placed 2,4-dibromo-5-[3-[(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl]-1,3-thiazole (**11-3**, 5.46 g, 10.6 mmol), THF (50.0 mL). The resulting solution was cooled to -10 °C, and *i*-PrMgCl (2 M) (5.60 mL, 11.1 mmol) was added. The resulting solution was stirred for 1 h at -10 °C. The reaction was then quenched by the addition of 100 mL of saturated aqueous NH₄Cl. The resulting solution was extracted with 2x50 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 50 mL of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. This resulted in 4.00 g (86 %) of 4-bromo-5-[3- [(tert-butyldimethylsilyl)oxy]-1-(oxan-2-yloxy)propyl] -1,3-thiazole (**11-4**) as yellow oil.

4. Synthesis of 3-(4-bromo-1,3-thiazol-5-yl)-3-(oxan-2-yloxy)propan-1-ol (11-5)



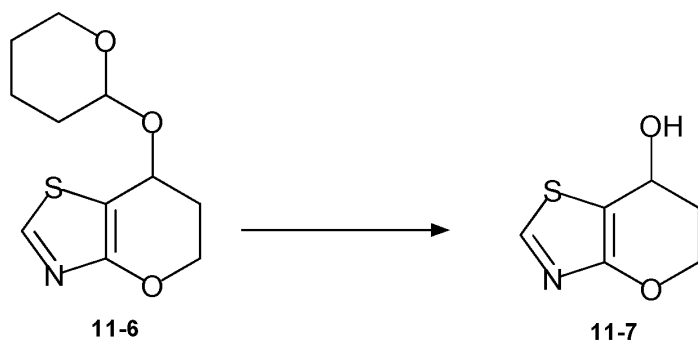
Into a 250-mL round-bottom flask, was placed 4-bromo-5-[3-[(tert-butyl)dimethylsilyl]oxy]-1,3-thiazole (**11-4**, 4.00 g, 9.2 mmol), THF (40 mL), TBAF (1 M) (11 mL, 11.1 mmol). The resulting solution was stirred for 2 hrs at room temperature. The resulting mixture was washed with 30 mL of H₂O and 30 mL of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). This resulted in 2.75 g (93 %) of 3-(4-bromo-1,3-thiazol-5-yl)-3-(oxan-2-yloxy)propan-1-ol (**11-5**) as yellow oil.

5. Synthesis of 7-(oxan-2-yloxy)-5H,6H,7H-pyrano[2,3-d][1,3]thiazole (11-6)



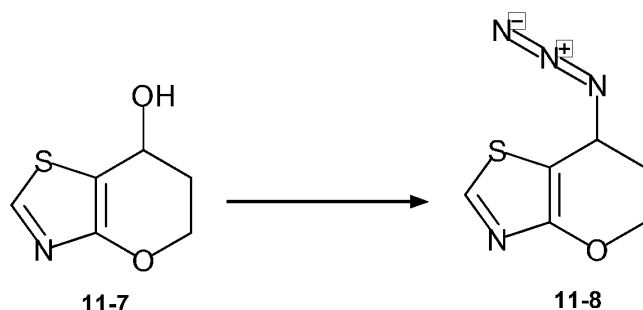
Into a 40-mL vial, was placed 3-(4-bromo-1,3-thiazol-5-yl)-3-(oxan-2-yloxy)propan-1-ol (**11-5**, 2.75 g, 8.5 mmol), toluene (25.00 mL), Cs₂CO₃ (4.17 g, 12.8 mmol), t-BuBrettPhos Pd G3 (0.58 g, 0.7 mmol). The resulting solution was stirred for 15 h at 100 °C. The solids were filtered out and washed with 20 mL of EA. The filtrate was concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:4). This resulted in 1.20 g (58 %) of 7-(oxan-2-yloxy)-5H,6H,7H-pyrano[2,3-d][1,3]thiazole (**11-6**) as yellow oil.

6. Synthesis of 5H,6H,7H-pyrano[2,3-d][1,3]thiazol-7-ol (11-7)



Into a 20-mL vial, was placed 7-(oxan-2-yloxy)-5H,6H,7H-pyrano[2,3-d][1,3]thiazole (**11-6**, 1.20 g, 5.0 mmol), THF (4 mL), H₂O (4 mL), PTSA (0.17 g, 1.0 mmol). The resulting solution was stirred for 15 h at room temperature. The resulting solution was diluted with 10 mL of H₂O. The resulting solution was extracted with 3x15 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 30 ml of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (9:1). This resulted in 0.40 g (51 %) of 5H,6H,7H-pyrano[2,3-d][1,3]thiazol-7-ol (**11-7**) as yellow oil.

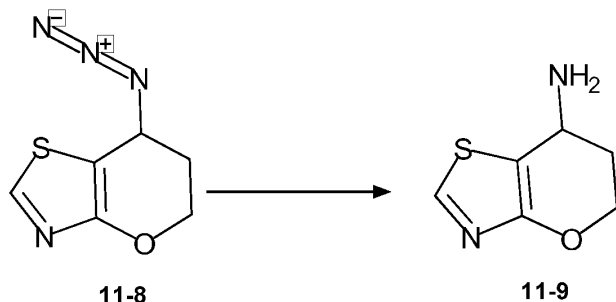
10 **7. 7-azido-5H,6H,7H-pyrano[2,3-d][1,3]thiazole (11-8)**



Into a 40-mL vial, was placed 5H,6H,7H-pyrano[2,3-d][1,3]thiazol-7-ol (**11-7**, 400 mg, 2.5 mmol), THF (8 mL), DBU (465 mg, 3.0 mmol). The resulting solution was cooled to 0 °C. Then DPPA (840 mg, 3.0 mmol) was added. The resulting solution was stirred for 2 h at room temperature. The resulting solution was added 20 mL of 10% HCl. The resulting solution was extracted with 2 x20 mL of ethyl acetate and the organic layers combined. The organic layer was washed with 20 ml of brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The

residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:3). This resulted in 0.22 g (47 %) of 7-azido-5H,6H,7H-pyrano[2,3-d][1,3]thiazole (**11-8**) as a yellow oil.

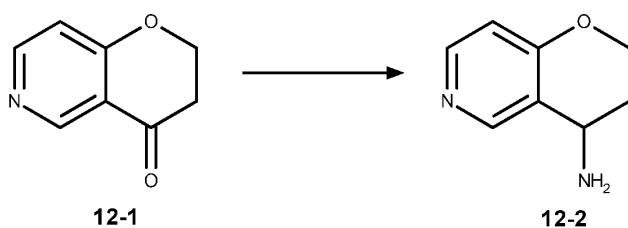
8. Synthesis of 5H,6H,7H-pyrano[2,3-d][1,3]thiazol-7-amine (**11-9**)



- 5 Into a 30-mL pressure tank reactor, was placed 7-azido-5H,6H,7H-pyrano[2,3-d][1,3]thiazole (**11-8**, 300 mg, 1.65 mmol), EtOH (6 mL), Pd/C (30 mg, 0.3 mmol). The resulting solution was stirred for 15 h at room temperature under 5 atm of hydrogen pressure. The solids were filtered out and washed with 20 mL of EtOH. The filtrate was concentrated. The crude product was purified by Flash-Prep-HPLC with the following conditions (IntelFlash-1): Column, C18 silica gel; mobile phase, H₂O:ACN=80:20 increasing to H₂O:ACN=40:60 within 15 min; Detector, 254nm.
- 10 This resulted in 210.6 mg (82 %) of 5H,6H,7H-pyrano[2,3-d][1,3]thiazol-7-amine (**11-9**) as a light-yellow solid. MS (ES, m/z): 157 [M+H]⁺; ¹H NMR (300 MHz, CDCl₃, ppm) δ: 8.47 (s, 1H), 4.41-4.29 (m, 2H), 4.21 (t, *J* = 5.4 Hz, 1H), 2.23 (m, 1H), 1.83(m, 1H).

Preparation Example 12: Synthesis of 2H,3H,4H-pyrano[3,2-c]pyridin-4-amine (**12-2**)

- 15 The bicyclic amine used in the preparation of Ring System AF present in compound A569 (see Table 3) is prepared from commercially available materials according to the process shown below.



To a solution of 400 mg (2.6 mmol) 2H-Pyrano[3,2-c]pyridin-4(3H)-one (**12-1**) and 1.35 g (21.4 mmol) ammonium formate in 13.4 mL methanol were added 887 mg (13.4 mmol) sodium

cyanoborohydride at RT and the mixture was then stirred at 60 °C over night. After addition of further same amount of ammonium formate and sodium cyanoborohydride and stirring for 3 h at 60 °C, the reaction mixture was cooled to RT, diluted with ethyl acetate and quenched with water. After phase separation the organic phase was dried over anhydrous Na₂SO₄ and the solvent was evaporated to yield 120 mg (23 %) of the title compound (**12-2**) as crude oil. The crude material was used without further purification. (ESI, m/z): 151 [M+H]⁺.

Table 4 below includes ¹H NMR data for certain compounds shown in Table 3 and prepared according to the processes outlined in schemes 1, 2 and 3 and the preparation examples shown above:

10 **Table 4:** ¹H NMR data for Compounds of the Invention

Compound	¹ H NMR Spectra
A461	(400 MHz, DMSO-d ₆ , ppm) δ 9.93 (s, 1H), 7.99 (s, 1H), 7.68 (d, J=2.03 Hz, 2H), 7.57 (t, J=1.90 Hz, 1H), 6.75 - 7.26 (m, 5H), 4.30 - 4.43 (m, 1H), 4.17 (s, 1H), 3.99 (s, 1H), 3.34 - 3.47 (m, 1H), 2.52 - 2.55 (m, 3H), 2.11 - 2.32 (m, 2H), 1.36 - 1.46 (m, 6H)
A462	(400 MHz, DMSO-d ₆ , ppm) δ 9.93 (s, 1H), 7.99 (s, 1H), 7.68 (d, J=2.03 Hz, 2H), 7.57 (t, J=1.90 Hz, 1H), 6.75 - 7.26 (m, 5H), 4.30 - 4.43 (m, 1H), 4.17 (s, 1H), 3.99 (s, 1H), 3.34 - 3.47 (m, 1H), 2.52 - 2.55 (m, 3H), 2.11 - 2.32 (m, 2H), 1.36 - 1.46 (m, 6H)
A463	(400 MHz, DMSO-d ₆) δ ppm 9.02 (d, J=8.11 Hz, 1 H) 8.27 (s, 1 H) 7.77 (d, J=1.90 Hz, 2 H) 7.68 (t, J=1.90 Hz, 1 H) 7.31 (d, J=7.37 Hz, 1 H) 7.20 (s, 1 H) 7.17 (dt, J=7.80, 1.63 Hz, 1 H) 6.91 (t, J=7.08 Hz, 1 H) 6.79 (dd, J=8.17, 1.08 Hz, 1 H) 5.15 - 5.27 (m, 1 H) 4.25 (br d, J=3.42 Hz, 2 H) 3.42 - 3.58 (m, 1 H) 2.12 - 2.24 (m, 1 H) 1.96 - 2.08 (m, 1 H) 1.44 (dd, J=10.52, 7.10 Hz, 6 H)
A464	(400 MHz, DMSO-d ₆) δ ppm 9.03 (d, J=8.11 Hz, 1 H) 7.98 (s, 1 H) 7.65 (d, J=1.90 Hz, 2 H) 7.58 - 7.62 (m, 1 H) 7.33 (d, J=7.10 Hz, 1 H) 7.16 (t, J=7.42 Hz, 1 H) 6.89 - 6.94 (m, 2 H) 6.79 (dd, J=8.17, 0.95 Hz, 1 H) 5.13 - 5.19 (m, 1 H) 4.17 - 4.29 (m, 2 H) 2.33 - 2.44 (m, 3 H) 2.09 - 2.22 (m, 1 H) 1.95 - 2.09 (m, 1 H) 1.57 (s, 9 H)

A465	(400 MHz, DMSO-d6) δ ppm 8.95 (d, J=8.24 Hz, 1 H) 8.12 (s, 1 H) 7.68 (d, J=1.90 Hz, 2 H) 7.60 (t, J=1.90 Hz, 1 H) 7.30 (d, J=7.22 Hz, 1 H) 7.16 (t, J=7.69 Hz, 1 H) 6.88 - 6.94 (m, 2 H) 6.79 (d, J=7.96 Hz, 1 H) 5.18 - 5.24 (m, 1 H) 4.20 - 4.30 (m, 2 H) 3.49 - 3.64 (m, 1 H) 2.39 (s, 3 H) 2.09 - 2.22 (m, 1 H) 1.98 - 2.09 (m, 1 H) 1.45 (dd, J=10.27, 7.10 Hz, 6 H)
A466	(400 MHz, DMSO-d6) δ ppm 9.04 (br d, J=7.86 Hz, 1 H) 8.39 (s, 1 H) 8.01 (s, 2 H) 7.58 - 7.63 (m, 1 H) 7.32 (br d, J=7.60 Hz, 1 H) 7.12 - 7.21 (m, 1 H) 7.09 (s, 1 H) 6.92 (t, J=7.41 Hz, 1 H) 6.79 (d, J=8.24 Hz, 1 H) 5.17 - 5.26 (m, 1 H) 4.17 - 4.32 (m, 2 H) 3.44 - 3.60 (m, 1 H) 2.11 - 2.22 (m, 1 H) 1.94 - 2.11 (m, 1 H) 1.44 - 1.53 (m, 6 H)
A467	(400 MHz, DMSO-d6) δ ppm 9.10 (d, J=8.11 Hz, 1 H) 8.32 (s, 1 H) 8.18 (d, J=1.90 Hz, 2 H) 7.70 (s, 1 H) 7.57 (t, J=1.90 Hz, 1 H) 7.36 (d, J=7.48 Hz, 1 H) 7.16 - 7.22 (m, 1 H) 6.86 - 6.96 (m, 1 H) 6.80 (dd, J=8.17, 0.82 Hz, 1 H) 5.15 - 5.23 (m, 1 H) 4.05 - 4.33 (m, 3 H) 2.11 - 2.24 (m, 1 H) 1.97 - 2.11 (m, 1 H) 1.42 - 1.52 (m, 6 H)
A468	(400 MHz, DMSO-d6) δ ppm 9.14 (d, J=7.98 Hz, 1 H) 8.54 (s, 1 H) 8.22 (d, J=1.77 Hz, 2 H) 8.02 (s, 1 H) 7.62 (s, 1 H) 7.38 (d, J=7.60 Hz, 1 H) 7.18 (t, J=7.73 Hz, 1 H) 6.93 (t, J=7.48 Hz, 1 H) 6.80 (d, J=8.11 Hz, 1 H) 5.18 - 5.24 (m, 1 H) 4.18 - 4.32 (m, 2 H) 3.54 (dt, J=13.97, 7.02 Hz, 1 H) 2.14 - 2.25 (m, 1 H) 2.02 - 2.14 (m, 1 H) 1.48 (t, J=7.03 Hz, 6 H)
A469	(400 MHz, DMSO-d6) δ ppm 9.02 (d, J=7.98 Hz, 1 H) 8.16 - 8.24 (m, 3 H) 7.49 (t, J=1.84 Hz, 1 H) 7.44 (s, 1 H) 7.36 (d, J=7.48 Hz, 1 H) 7.15 - 7.27 (m, 1 H) 6.93 (t, J=7.41 Hz, 1 H) 6.80 (d, J=7.98 Hz, 1 H) 5.15 - 5.23 (m, 1 H) 4.18 - 4.33 (m, 2 H) 3.79 (dt, J=14.04, 6.99 Hz, 1 H) 2.58 (s, 3 H) 2.11 - 2.25 (m, 1 H) 1.99 - 2.11 (m, 1 H) 1.23 - 1.52 (m, 6 H)
A470	(400 MHz, DMSO-d6) δ ppm 9.00 (d, J=8.11 Hz, 1 H) 8.34 (s, 1 H) 8.25 (d, J=1.77 Hz, 2 H) 7.60 (d, J=4.82 Hz, 1 H) 7.51 (t, J=1.84 Hz, 1 H) 7.33 (d, J=7.48 Hz, 1 H) 7.12 - 7.19 (m, 1 H) 7.07 (d, J=4.82 Hz, 1 H) 6.90 - 7.00 (m, 1 H) 6.79 (d, J=7.99 Hz, 1 H) 5.20 - 5.26 (m, 1 H) 4.21 - 4.31 (m, 2 H) 3.59 (spt, J=7.03 Hz, 1 H) 2.12 - 2.24 (m, 1 H) 1.99 - 2.12 (m, 1 H) 1.41 - 1.52 (m, 6 H)

A472	(400 MHz, DMSO-d ₆ , ppm) δ 9.03-9.08 (m, 1H), 7.96 (d, 1H), 7.89-7.90 (d, 1H), 7.56-7.61 (dd, 1H), 7.29-7.33 (t, 1H), 7.13-7.17 (t, 1H), 6.89-6.92 (m, 2H), 6.77-6.79 (d, 1H), 5.13-5.17 (m, 1H), 4.17-4.27 (m, 2H), 2.21 (s, 3H), 1.99-2.14 (m, 2H), 1.58 (s, 9H)
A471	(400 MHz, DMSO-d ₆) δ ppm 9.05 (d, J=7.98 Hz, 1 H) 7.94 (s, 1 H) 7.56 - 7.69 (m, 1 H) 7.25 - 7.37 (m, 2 H) 7.16 (t, J=7.67 Hz, 1 H) 6.86 - 6.96 (m, 2 H) 6.78 (d, J=8.11 Hz, 1 H) 5.12 - 5.19 (m, 1 H) 4.15 - 4.30 (m, 2 H) 2.29 (s, 3 H) 2.09 - 2.25 (m, 1 H) 1.94 - 2.09 (m, 1 H) 1.58 (s, 9 H)
A475	(400 MHz, DMSO-d ₆ , ppm) δ 8.80-8.82 (d, 1H), 8.00 (s, 1H), 7.74-7.75 (d, 2H), 7.65-7.66 (t, 1H), 7.29-7.30 (d, 1H), 7.16-7.18 (t, 1H), 7.11 (s, 1H), 6.88-6.92 (t, 1H), 6.78-6.80 (d, 1H), 5.15-5.19 (m, 1H), 4.18-4.28 (m, 2H), 3.18 (s, 6H), 1.99-2.16 (m, 2H)
A473	(400 MHz, DMSO-d ₆ , ppm) δ 8.79-8.81 (dd, 1H), 8.01-8.02 (d, 1H), 7.90 (s, 1H), 7.60-7.62 (dd, 1H), 7.26-7.28 (m, 1H), 7.13-7.17 (t, 1H), 7.11 (s, 1H), 8.86-8.90 (t, 1H), 6.77-6.79 (d, 1H), 5.15-5.17 (m, 1H), 4.19-4.27 (m, 2H), 3.19 (d, 6H), 1.91-2.17 (m, 2H)
A474	(400 MHz, DMSO-d ₆ , ppm) δ 8.80-8.82 (d, 1H), 7.94 (s, 1H), 7.66-7.73 (m, 1H), 7.27-7.32 (m, 2H), 7.14-7.18 (m, 2H), 6.87-6.91 (t, 1H), 6.77-6.79 (d, 1H), 5.14-5.19 (m, 1H), 4.20-4.24 (m, 2H), 3.19 (s, 6H), 1.98-2.16 (m, 2H)
A522	(400 MHz, DMSO-d ₆) δ ppm 9.12 (t, J=9.08 Hz, 1 H) 8.07 (d, J=7.10 Hz, 1 H) 8.04 (d, J=2.53 Hz, 1 H) 7.69 (dd, J=12.04, 2.41 Hz, 1 H) 7.32 (t, J=8.17 Hz, 1 H) 7.20 (s, 1 H) 7.16 (t, J=7.60 Hz, 1 H) 6.87 - 6.92 (m, 1 H) 6.78 (d, J=7.35 Hz, 1 H) 5.11 - 5.18 (m, 1 H) 4.15 - 4.28 (m, 2 H) 2.52 - 2.65 (m, 3 H) 2.14 (br d, J=3.42 Hz, 1 H) 1.98 - 2.07 (m, 1 H) 1.57 (s, 9 H)
A525	(400 MHz, DMSO-d ₆) δ ppm 8.83 (dd, J=8.11, 3.17 Hz, 1 H) 7.95 (d, J=2.41 Hz, 1 H) 7.83 (d, J=1.14 Hz, 1 H) 7.54 (dd, J=8.17, 2.47 Hz, 1 H) 7.29 (d, J=7.73 Hz, 1 H) 7.15 (t, J=7.30 Hz, 1 H) 6.89 (td, J=7.45, 1.08 Hz, 1 H) 6.78 (dd, J=8.17, 0.82 Hz, 1 H) 6.75 (s, 1 H) 5.13 (br d, J=5.70 Hz, 1 H) 4.75 - 4.93 (m, 4 H) 4.23 (br t, J=4.50 Hz, 2 H) 2.05 - 2.23 (m, 4 H) 1.94 - 2.04 (m, 1 H) 1.40 (s, 1 H)

A526	(400 MHz, DMSO-d6) δ ppm 8.84 (dd, J=8.05, 4.12 Hz, 1 H) 7.79 - 7.85 (m, 2 H) 7.40 (td, J=8.46, 2.98 Hz, 1 H) 7.29 (d, J=7.73 Hz, 1 H) 7.15 (t, J=7.73 Hz, 1 H) 6.89 (t, J=7.45 Hz, 1 H) 6.78 (d, J=7.98 Hz, 1 H) 6.75 (s, 1 H) 5.13 (br d, J=5.45 Hz, 1 H) 4.72 - 4.94 (m, 4 H) 4.23 (br t, J=4.44 Hz, 2 H) 2.07 - 2.23 (m, 4 H) 1.92 - 2.05 (m, 1 H)
A527	(400 MHz, DMSO-d6) δ ppm 8.93 (d, J=8.11 Hz, 1 H) 7.86 (s, 1 H) 7.32 (d, J=7.48 Hz, 1 H) 7.16 (t, J=7.74 Hz, 1 H) 6.91 (t, J=7.18 Hz, 1 H) 6.78 (d, J=7.98 Hz, 1 H) 6.62 (s, 1 H) 5.11 - 5.18 (m, 1 H) 4.16 - 4.28 (m, 2 H) 3.27 - 3.34 (m, 5 H) 2.25 (s, 3 H) 1.95 - 2.20 (m, 6 H) 1.53 (s, 9 H) 0.97 - 1.12 (m, 1 H) 0.66 - 0.76 (m, 1 H)
A528	(400 MHz, DMSO-d6) δ ppm 8.89 (br s, 1 H) 7.81 (br s, 1 H) 7.32 (br d, J=7.35 Hz, 1 H) 7.16 (t, J=7.37 Hz, 1 H) 6.92 (t, J=7.04 Hz, 1 H) 6.78 (d, J=8.11 Hz, 1 H) 6.59 (br s, 1 H) 5.15 (br d, J=6.59 Hz, 1 H) 4.11 - 4.34 (m, 2 H) 2.72 - 3.06 (m, 4 H) 2.12 - 2.27 (m, 3 H) 1.66 - 1.83 (m, 3 H) 1.41 - 1.63 (m, 9 H) 0.84 (br s, 5 H)
A524	(400 MHz, DMSO-d6) δ ppm 8.91 (d, J=8.11 Hz, 1 H) 7.81 (s, 1 H) 7.32 (d, J=7.48 Hz, 1 H) 7.16 (t, J=7.36 Hz, 1 H) 6.81 - 6.95 (m, 1 H) 6.78 (d, J=8.11 Hz, 1 H) 6.59 (s, 1 H) 5.11 - 5.18 (m, 1 H) 4.11 - 4.35 (m, 2 H) 3.15 (br d, J=5.20 Hz, 5 H) 2.20 - 2.35 (m, 4 H) 2.11 - 2.18 (m, 1 H) 1.95 - 2.03 (m, 1 H) 1.62 (br d, J=4.56 Hz, 4 H) 1.45 - 1.58 (m, 11 H) 0.68 - 0.82 (m, 1 H)
A529	(400 MHz, DMSO-d6) δ ppm 8.93 (d, J=8.11 Hz, 1 H) 7.84 (s, 1 H) 7.32 (d, J=7.35 Hz, 1 H) 7.16 (t, J=7.72 Hz, 1 H) 6.91 (t, J=7.17 Hz, 1 H) 6.78 (d, J=7.48 Hz, 1 H) 6.61 (s, 1 H) 5.12 - 5.18 (m, 1 H) 4.12 - 4.28 (m, 2 H) 3.64 - 3.77 (m, 4 H) 3.10 - 3.29 (m, 5 H) 2.27 (s, 3 H) 2.09 - 2.19 (m, 1 H) 1.94 - 2.03 (m, 1 H) 1.53 (s, 9 H)
A530	¹ H NMR (400 MHz, DMSO-d6) δ ppm 9.05 (dd, J=10.46, 8.17 Hz, 1 H) 7.96 (d, J=2.53 Hz, 1 H) 7.89 (d, J=5.20 Hz, 1 H) 7.60 (d, J=2.53 Hz, 1 H) 7.31 (t, J=6.65 Hz, 1 H) 7.15 (t, J=7.73 Hz, 1 H) 6.87 - 6.93 (m, 2 H) 6.78 (d, J=7.95 Hz, 1 H) 5.12 - 5.18 (m, 1 H) 4.17 - 4.28 (m, 2 H) 2.67 (dt, J=3.61, 1.74 Hz, 1 H) 2.31 - 2.34 (m, 1 H) 2.21 (s, 3 H) 1.58 (s, 9 H)

A531	(400 MHz, DMSO-d6) δ ppm 9.01 (d, J=8.11 Hz, 1 H) 8.50 (s, 1 H) 8.16 (s, 1 H) 7.98 (s, 1 H) 7.34 (d, J=7.48 Hz, 1 H) 7.17 (t, J=7.69 Hz, 1 H) 6.93 (t, J=7.23 Hz, 1 H) 6.88 (s, 1 H) 6.79 (d, J=8.29 Hz, 1 H) 5.15 - 5.29 (m, 3 H) 4.18 - 4.30 (m, 2 H) 2.47 (s, 3 H) 2.10 - 2.22 (m, 1 H) 1.96 - 2.08 (m, 1 H) 1.58 (s, 9 H)
A532	(400 MHz, DMSO-d6) δ ppm 9.03 (d, J=8.11 Hz, 1 H) 8.79 (d, J=1.65 Hz, 1 H) 8.55 (dd, J=4.82, 1.65 Hz, 1 H) 8.02 (dt, J=7.98, 1.96 Hz, 1 H) 7.90 (s, 1 H) 7.52 (dd, J=7.98, 4.82 Hz, 1 H) 7.32 (d, J=7.48 Hz, 1 H) 7.16 (t, J=7.75 Hz, 1 H) 6.88 - 6.94 (m, 2 H) 6.78 (d, J=8.30 Hz, 1 H) 5.12 - 5.19 (m, 1 H) 4.16 - 4.31 (m, 2 H) 2.38 (s, 3 H) 2.29 (s, 1 H) 1.52 - 1.62 (m, 10 H)
A533	(400 MHz, DMSO-d6) δ ppm 9.10 (t, J=7.10 Hz, 1 H) 8.95 (d, J=2.15 Hz, 1 H) 7.82 (dd, J=8.30, 2.98 Hz, 1 H) 7.73 (d, J=6.21 Hz, 1 H) 7.44 (ddd, J=8.74, 5.96, 3.04 Hz, 1 H) 6.91 (s, 1 H) 5.24 (br d, J=4.56 Hz, 1 H) 2.69 - 2.81 (m, 2 H) 2.21 (s, 3 H) 1.77 - 1.90 (m, 2 H) 1.57 (s, 9 H)
A534	(400 MHz, DMSO-d6) δ ppm 9.12 (dd, J=9.70, 8.30 Hz, 1 H) 8.06 (d, J=6.59 Hz, 1 H) 7.90 (dd, J=8.30, 2.98 Hz, 1 H) 7.55 (ddd, J=11.94, 8.71, 3.04 Hz, 1 H) 7.32 (t, J=7.86 Hz, 1 H) 7.20 (s, 1 H) 7.16 (t, J=7.73 Hz, 1 H) 6.90 (tdd, 1 H) 6.78 (dd, J=8.24, 0.89 Hz, 1 H) 5.11 - 5.18 (m, 1 H) 4.15 - 4.28 (m, 2 H) 2.52 - 2.55 (m, 1 H) 2.15 (ddd, J=11.03, 5.45, 2.53 Hz, 1 H) 1.95 - 2.04 (m, 1 H) 1.57 (s, 9 H)
A535	(400 MHz, DMSO-d6) δ ppm 8.90 (s, 1 H) 7.80 (dd, J=8.30, 2.98 Hz, 1 H) 7.71 (d, J=0.76 Hz, 1 H) 7.50 (d, J=2.28 Hz, 1 H) 7.41 (ddd, J=8.68, 2.98, 1.65 Hz, 1 H) 6.90 (dd, J=8.49, 3.42 Hz, 1 H) 6.80 (s, 1 H) 4.97 (q, J=6.93 Hz, 1 H) 3.99 - 4.06 (m, 1 H) 2.68 - 2.79 (m, 2 H) 2.52 - 2.65 (m, 1 H) 2.18 (s, 3 H) 1.87 - 2.08 (m, 3 H) 1.69 - 1.87 (m, 2 H) 1.56 (s, 9 H) 1.51 - 1.61 (m, 1 H)
A536a	(400 MHz, DMSO-d6) δ ppm 8.95 (d, J=7.98 Hz, 1 H) 7.81 (dd, J=8.30, 2.98 Hz, 1 H) 7.73 (d, J=2.66 Hz, 1 H) 7.44 (dt, J=8.62, 3.30 Hz, 1 H) 6.90 (s, 1 H) 5.27 - 5.35 (m, 1 H) 2.92 - 3.01 (m, 1 H) 2.79 - 2.90 (m, 2 H) 2.23 - 2.31 (m, 1 H) 2.21 (s, 3 H) 1.57 (s, 9 H)

A537	(400 MHz, DMSO-d ₆) δ ppm 8.86 (dd, J=11.85, 8.43 Hz, 1 H) 7.79 - 7.85 (m, 2 H) 7.44 (ddd, J=16.51, 8.71, 3.04 Hz, 1 H) 7.27 (dd, J=5.13, 2.72 Hz, 1 H) 6.98 (dd, J=7.29, 5.26 Hz, 1 H) 6.88 (s, 1 H) 5.05 (br s, 1 H) 2.66 - 2.79 (m, 2 H) 2.65 - 2.79 (m, 1 H) 2.21 (s, 3 H) 1.89 - 2.04 (m, 2 H) 1.71 - 1.84 (m, 2 H) 1.56 - 1.63 (m, 9 H) 1.52 (br s, 1 H)
A536b	(400 MHz, DMSO-d ₆) δ ppm 8.95 (d, J=7.98 Hz, 1 H) 7.81 (dd, J=8.30, 2.98 Hz, 1 H) 7.73 (d, J=2.66 Hz, 1 H) 7.44 (dt, J=8.62, 3.30 Hz, 1 H) 6.90 (s, 1 H) 5.27 - 5.35 (m, 1 H) 2.92 - 3.01 (m, 1 H) 2.79 - 2.90 (m, 2 H) 2.23 - 2.31 (m, 1 H) 2.21 (s, 3 H) 1.57 (s, 9 H)
A538	(400 MHz, DMSO-d ₆) δ ppm 8.92 (dd, J=18.31, 8.43 Hz, 1 H) 7.87 (d, J=4.31 Hz, 1 H) 7.81 (dd, J=8.36, 2.91 Hz, 1 H) 7.44 - 7.51 (m, 1 H) 7.35 - 7.43 (m, 1 H) 6.90 - 7.07 (m, 2 H) 6.89 (s, 1 H) 5.06 - 5.13 (m, 1 H) 2.64 - 2.83 (m, 2 H) 2.21 (s, 3 H) 1.58 (s, 9 H)
A539	(400 MHz, DMSO-d ₆) δ ppm 11.06 (br s, 2 H) 8.11 (s, 1 H) 8.07 (s, 1 H) 7.88 - 7.92 (m, 2 H) 7.51 - 7.59 (m, 2 H) 7.30 (t, J=7.73 Hz, 2 H) 7.20 (t, J=7.71 Hz, 2 H) 7.12 (d, J=1.01 Hz, 2 H) 6.93 (t, J=7.44 Hz, 2 H) 6.83 (d, J=8.11 Hz, 2 H) 5.83 (br d, J=4.44 Hz, 2 H) 4.26 - 4.33 (m, 2 H) 4.16 - 4.24 (m, 2 H) 3.33 - 3.48 (m, 2 H) 2.24 - 2.30 (m, 2 H) 2.05 - 2.19 (m, 2 H) 1.45 (dd, J=6.97, 5.58 Hz, 6 H) 1.41 (dd, J=7.03, 4.88 Hz, 6 H)
A540	(400 MHz, DMSO-d ₆) δ ppm 8.97 (d, J=3.04 Hz, 1 H) 8.92 (dd, J=8.24, 2.28 Hz, 1 H) 7.81 (dd, J=8.30, 2.98 Hz, 1 H) 7.73 (d, J=3.42 Hz, 1 H) 7.44 (d, J=8.80 Hz, 1 H) 6.89 (s, 1 H) 5.31 - 5.39 (m, 1 H) 2.77 - 3.08 (m, 3 H) 2.30 - 2.38 (m, 1 H) 2.20 (s, 3 H) 1.58 (s, 9 H)
A541	(400 MHz, DMSO-d ₆) δ ppm 9.08 (dd, J=13.69, 8.24 Hz, 1 H) 7.86 (d, J=2.15 Hz, 1 H) 7.82 (dd, J=8.30, 2.98 Hz, 1 H) 7.44 (ddd, J=13.94, 8.68, 2.98 Hz, 1 H) 7.34 (t, J=6.72 Hz, 1 H) 7.04 - 7.17 (m, 3 H) 6.90 (s, 1 H) 5.19 (dq, J=8.36, 4.35 Hz, 1 H) 3.08 - 3.20 (m, 1 H) 2.98 - 3.07 (m, 1 H) 2.18 - 2.29 (m, 4 H) 1.57 (s, 9 H)
A542	(400 MHz, DMSO-d ₆) δ ppm 9.02 (dd, J=11.60, 8.05 Hz, 1 H) 7.93 (d, J=7.73 Hz, 1 H) 7.82 (dd, J=8.36, 2.91 Hz, 1 H) 7.73 (s, 1 H) 7.66 (d, J=7.86 Hz, 1 H)

	7.56 (t, J=7.35 Hz, 1 H) 7.44 (ddd, J=16.51, 8.65, 2.98 Hz, 1 H) 6.91 (s, 1 H) 5.48 (quin, J=7.45 Hz, 1 H) 2.96 - 3.05 (m, 1 H) 2.84 - 2.95 (m, 1 H) 2.52 - 2.53 (m, 1 H) 2.22 (s, 3 H) 1.88 - 1.99 (m, 1 H) 1.57 (s, 9 H)
A543	(400 MHz, DMSO-d ₆) δ ppm 8.03 (s, 1 H) 7.77 - 7.85 (m, 1 H) 7.47 - 7.54 (m, 1 H) 7.22 - 7.27 (m, 1 H) 7.12 - 7.21 (m, 1 H) 6.89 - 6.97 (m, 2 H) 6.78 - 6.86 (m, 1 H) 5.95 - 6.01 (m, 1 H) 4.15 - 4.36 (m, 2 H) 2.68 - 2.71 (m, 1 H) 2.62 - 2.66 (m, 1 H) 2.52 - 2.56 (m, 2 H) 2.20 - 2.28 (m, 4 H) 1.50 - 1.61 (m, 8 H)
A544	(400 MHz, DMSO-d ₆) δ ppm 8.89 (dd, J=8.24, 5.83 Hz, 1 H) 8.38 - 8.42 (m, 1 H) 7.79 - 7.83 (m, 2 H) 7.66 (d, J=7.60 Hz, 1 H) 7.44 (ddd, J=11.60, 8.68, 3.04 Hz, 1 H) 7.21 (ddd, J=7.38, 5.04, 2.03 Hz, 1 H) 6.90 (s, 1 H) 5.36 (quin, J=8.02 Hz, 1 H) 2.93 - 3.01 (m, 1 H) 2.81 - 2.90 (m, 1 H) 2.52 - 2.56 (m, 1 H) 2.19 - 2.23 (m, 3 H) 1.88 - 2.05 (m, 1 H) 1.60 (s, 9 H)
A545	(400 MHz, DMSO-d ₆) δ ppm 9.19 (d, J=6.94 Hz, 1 H) 7.85 (s, 1 H) 7.81 (dd, J=8.05, 2.85 Hz, 1 H) 7.44 (d, J=8.75 Hz, 1 H) 7.39 (t, J=7.03 Hz, 1 H) 7.22 (t, J=7.73 Hz, 1 H) 6.88 - 6.94 (m, 2 H) 6.85 (d, J=8.11 Hz, 1 H) 5.62 - 5.70 (m, 1 H) 4.73 (dd, J=9.57, 8.81 Hz, 1 H) 4.36 (ddd, J=9.73, 8.02, 4.82 Hz, 1 H) 2.21 (s, 3 H) 1.56 (s, 9 H)
A546	(400 MHz, DMSO-d ₆) δ ppm 9.06 (dd, J=10.46, 8.30 Hz, 1 H) 7.81 (dt, J=8.30, 2.69 Hz, 1 H) 7.70 (d, J=2.28 Hz, 1 H) 7.45 (ddd, J=18.53, 8.65, 2.98 Hz, 1 H) 7.23 (s, 1 H) 6.90 (s, 1 H) 5.20 (br t, J=8.74 Hz, 1 H) 4.40 (dt, J=12.90, 6.54 Hz, 1 H) 2.52 - 2.68 (m, 1 H) 2.19 - 2.38 (m, 4 H) 2.01 (br s, 1 H) 1.58 (s, 9 H) 1.31 - 1.43 (m, 6 H)
A547	(400 MHz, DMSO-d ₆) δ ppm 8.95 (dd, J=21.42, 8.36 Hz, 1 H) 7.96 (d, J=6.97 Hz, 1 H) 7.83 (dd, J=8.30, 2.98 Hz, 1 H) 7.46 (ddd, J=20.56, 8.65, 2.98 Hz, 1 H) 7.35 (t, J=6.17 Hz, 1 H) 7.14 (t, J=7.67 Hz, 1 H) 6.92 (s, 1 H) 6.86 - 6.91 (m, 1 H) 6.73 (dd, J=8.11, 0.89 Hz, 1 H) 5.18 - 5.28 (m, 1 H) 3.57 (s, 2 H) 2.11 - 2.18 (m, 1 H) 1.75 - 1.83 (m, 1 H) 1.60 (s, 9 H) 1.40 (s, 3 H) 1.29 (s, 3 H)

A548	(400 MHz, DMSO-d ₆) δ ppm 8.96 (dd, J=17.55, 8.30 Hz, 1 H) 7.95 (d, J=7.22 Hz, 1 H) 7.82 (dd, J=8.30, 2.98 Hz, 1 H) 7.46 (ddd, J=18.69, 8.68, 2.91 Hz, 1 H) 7.34 (t, J=6.18 Hz, 1 H) 7.13 (t, J=7.67 Hz, 1 H) 6.86 - 6.93 (m, 1 H) 6.72 (d, J=7.92 Hz, 1 H) 5.17 - 5.27 (m, 1 H) 3.57 (s, 1 H) 2.22 (s, 1 H) 2.10 - 2.18 (m, 1 H) 1.53 - 1.96 (m, 9 H)
A549	(400 MHz, DMSO-d ₆) δ ppm 8.94 (dd, J=18.76, 8.36 Hz, 1 H) 7.87 (d, J=4.31 Hz, 1 H) 7.82 (dd, J=8.36, 3.04 Hz, 1 H) 7.47 (dd, J=8.62, 2.92 Hz, 1 H) 7.34 - 7.43 (m, 2 H) 7.17 - 7.23 (m, 2 H) 6.90 (s, 1 H) 5.06 - 5.12 (m, 1 H) 2.68 - 2.79 (m, 2 H) 2.52 - 2.52 (m, 1 H) 2.21 (s, 3 H) 1.58 (s, 9 H)
A550	(400 MHz, DMSO-d ₆) δ ppm 9.13 (d, J=7.22 Hz, 1 H) 8.81 (d, J=2.79 Hz, 1 H) 7.82 (dd, J=8.36, 2.91 Hz, 1 H) 7.78 (d, J=8.24 Hz, 1 H) 7.44 (ddd, J=8.71, 5.80, 2.98 Hz, 1 H) 7.07 (br s, 1 H) 6.92 (d, J=1.14 Hz, 1 H) 5.11 - 5.18 (m, 1 H) 4.35 - 4.41 (m, 1 H) 4.23 - 4.32 (m, 1 H) 2.16 - 2.26 (m, 4 H) 1.98 - 2.08 (m, 1 H) 1.55 (s, 9 H)
A551	(400 MHz, DMSO-d ₆) δ ppm 9.13 (d, J=7.22 Hz, 1 H) 8.81 (d, J=2.92 Hz, 1 H) 7.82 (dd, J=8.36, 2.91 Hz, 1 H) 7.78 (d, J=8.36 Hz, 1 H) 7.44 (ddd, J=8.68, 5.83, 2.98 Hz, 1 H) 6.92 (s, 1 H) 5.11 - 5.19 (m, 1 H) 4.35 - 4.43 (m, 1 H) 4.22 - 4.32 (m, 1 H) 2.21 (s, 3 H) 1.96 - 2.07 (m, 1 H) 1.55 (s, 9 H)
A552	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm 9.14 (br d, J=7.10 Hz, 1 H) 8.21 (br s, 1 H) 7.80 - 7.85 (m, 2 H) 7.45 (ddd, J=8.65, 2.88, 1.27 Hz, 1 H) 7.10 (br s, 1 H) 6.92 (s, 1 H) 5.30 - 5.40 (m, 1 H) 4.20 - 4.28 (m, 1 H) 4.09 - 4.17 (m, 1 H) 2.87 - 3.06 (m, 1 H) 2.52 - 2.52 (m, 1 H) 2.21 (s, 3 H) 2.11 - 2.13 (m, 1 H) 1.54 (s, 9 H)
A553	(400 MHz, DMSO-d ₆) δ ppm 8.87 (dd, J=7.79, 1.84 Hz, 1 H) 7.77 - 7.84 (m, 2 H) 7.41 - 7.47 (m, 1 H) 7.38 (dd, J=4.88, 3.11 Hz, 1 H) 6.92 (dd, J=8.87, 4.94 Hz, 1 H) 6.89 (s, 1 H) 5.25 - 5.33 (m, 1 H) 2.93 - 3.01 (m, 1 H) 2.75 - 2.89 (m, 2 H) 2.21 (s, 3 H) 1.56 (s, 9 H)
A554	(400 MHz, DMSO-d ₆) δ ppm 9.09 (br d, J=7.98 Hz, 1 H) 7.76 - 7.84 (m, 2 H) 7.39 - 7.51 (m, 1 H) 7.17 (s, 1 H) 7.03 (br s, 1 H) 6.91 (s, 1 H) 5.23 - 5.35 (m,

	1 H) 4.04 - 4.14 (m, 1 H) 3.97 (ddd, J=10.39, 8.24, 5.70 Hz, 1 H) 2.91 - 3.03 (m, 1 H) 2.21 (s, 3 H) 1.57 (s, 9 H)
A555	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm 8.84 (dd, J=11.09, 8.30 Hz, 1 H) 7.81 (dd, J=8.36, 2.91 Hz, 1 H) 7.71 (d, J=2.28 Hz, 1 H) 7.44 (ddd, J=14.13, 8.68, 2.91 Hz, 1 H) 6.88 (s, 1 H) 5.07 (br dd, J=7.86, 4.18 Hz, 1 H) 3.57 (s, 2 H) 2.57 (d, J=3.68 Hz, 3 H) 2.20 (s, 3 H) 1.58 (s, 9 H)
A556	(400 MHz, DMSO-d ₆) δ ppm 9.11 (dd, J=11.85, 7.92 Hz, 1 H) 8.64 (br s, 1 H) 8.55 (br s, 1 H) 7.97 (d, J=9.00 Hz, 1 H) 7.83 (dd, J=8.36, 3.04 Hz, 1 H) 7.66 (dd, J=12.67, 5.20 Hz, 1 H) 7.45 (ddd, J=17.87, 8.62, 3.04 Hz, 1 H) 6.93 (s, 1 H) 5.52 (quin, J=8.52 Hz, 1 H) 3.03 - 3.15 (m, 1 H) 2.91 - 3.01 (m, 1 H) 2.52 - 2.57 (m, 1 H) 2.22 (s, 3 H) 1.58 (s, 9 H)
A557	(400 MHz, DMSO-d ₆) δ ppm 8.93 (dd, J=16.98, 8.49 Hz, 1 H) 7.86 (d, J=3.68 Hz, 1 H) 7.81 (dd, J=8.30, 2.98 Hz, 1 H) 7.44 (ddd, J=22.21, 8.65, 2.98 Hz, 1 H) 7.31 - 7.37 (m, 1 H) 7.12 - 7.20 (m, 2 H) 7.07 - 7.12 (m, 1 H) 6.89 (s, 1 H) 5.12 (br d, J=5.83 Hz, 1 H) 2.65 - 2.82 (m, 2 H) 2.21 (s, 3 H) 1.87 - 2.03 (m, 2 H) 1.70 - 1.85 (m, 2 H) 1.59 (s, 9 H)
A558	(400 MHz, DMSO-d ₆) δ ppm 8.91 (t, J=8.43 Hz, 1 H) 7.88 (d, J=4.82 Hz, 1 H) 7.82 (dd, J=8.36, 2.91 Hz, 1 H) 7.44 (ddd, J=13.56, 8.68, 2.98 Hz, 1 H) 7.36 (t, J=5.87 Hz, 1 H) 7.17 - 7.27 (m, 3 H) 6.90 (s, 1 H) 5.40 - 5.48 (m, 1 H) 2.91 - 3.07 (m, 1 H) 2.78 - 2.87 (m, 1 H) 2.37 - 2.48 (m, 1 H) 2.21 (s, 3 H) 1.84 - 1.95 (m, 1 H) 1.58 (s, 9 H)
A559	(400 MHz, DMSO-d ₆) δ ppm 9.10 (dd, J=10.84, 7.79 Hz, 1 H) 8.56 (br s, 1 H) 8.09 (dd, J=10.90, 7.86 Hz, 1 H) 7.94 (d, J=7.10 Hz, 1 H) 7.82 (dd, J=8.30, 2.98 Hz, 1 H) 7.35 - 7.58 (m, 2 H) 6.92 (s, 1 H) 5.50 (quin, J=7.76 Hz, 1 H) 3.01 - 3.19 (m, 2 H) 2.52 - 2.62 (m, 1 H) 2.22 (s, 3 H) 1.99 - 2.10 (m, 1 H) 1.57 (s, 9 H)
A560	(400 MHz, DMSO-d ₆) δ ppm 8.92 (d, J=7.60 Hz, 1 H) 7.81 (dd, J=8.36, 2.91 Hz, 1 H) 7.75 (d, J=3.42 Hz, 1 H) 7.44 (ddd, J=8.59, 4.59, 3.04 Hz, 1 H) 6.89 (s, 1 H) 5.19 - 5.28 (m, 1 H) 2.68 - 2.81 (m, 1 H) 2.52 - 2.65 (m, 1 H) 2.43 - 2.48 (m, 1 H) 2.21 - 2.31 (m, 1 H) 1.56 (s, 9 H)

A561	(400 MHz, DMSO-d6) δ ppm 8.73 (dd, J=8.11, 3.80 Hz, 1 H) 7.94 (d, J=2.41 Hz, 1 H) 7.77 (d, J=1.14 Hz, 1 H) 7.52 (dd, J=8.17, 2.47 Hz, 1 H) 7.27 (d, J=7.22 Hz, 1 H) 7.15 (t, J=7.32 Hz, 1 H) 6.71 - 6.91 (m, 3 H) 5.13 (br d, J=5.70 Hz, 1 H) 4.37 - 4.62 (m, 4 H) 4.20 - 4.26 (m, 2 H) 2.09 - 2.16 (m, 4 H) 1.95 - 2.03 (m, 1 H) 1.60 - 1.65 (m, 3 H)
A562	(400 MHz, DMSO-d6) δ ppm 8.74 (dd, J=8.17, 4.88 Hz, 1 H) 7.80 (dd, J=8.36, 2.92 Hz, 1 H) 7.77 (d, J=0.63 Hz, 1 H) 7.38 (td, J=8.52, 2.98 Hz, 1 H) 7.27 (d, J=7.48 Hz, 1 H) 7.15 (t, J=7.74 Hz, 1 H) 6.89 (td, J=7.48, 1.14 Hz, 1 H) 6.78 (d, J=7.82 Hz, 1 H) 6.71 (s, 1 H) 5.10 - 5.17 (m, 1 H) 4.37 - 4.61 (m, 4 H) 4.17 - 4.28 (m, 2 H) 2.52 - 2.52 (m, 1 H) 2.07 - 2.19 (m, 4 H) 1.94 - 2.04 (m, 1 H) 1.60 - 1.65 (m, 3 H)
A563	(400 MHz, DMSO-d6) δ ppm 8.66 (br d, J=7.10 Hz, 1 H) 7.93 (d, J=2.41 Hz, 1 H) 7.70 (s, 1 H) 7.50 (dd, J=6.97, 2.53 Hz, 1 H) 7.25 (d, J=7.35 Hz, 1 H) 7.14 (t, J=7.37 Hz, 1 H) 6.88 (t, J=7.13 Hz, 1 H) 6.77 (d, J=8.11 Hz, 1 H) 6.67 (s, 1 H) 5.09 - 5.16 (m, 1 H) 4.19 - 4.30 (m, 2 H) 4.08 - 4.17 (m, 4 H) 2.52 - 2.58 (m, 1 H) 2.08 - 2.15 (m, 4 H) 1.89 - 2.03 (m, 1 H) 1.30 (s, 6 H)
A564	(400 MHz, DMSO-d6) δ ppm 8.66 (dd, J=8.24, 2.15 Hz, 1 H) 7.78 (dd, J=8.36, 2.91 Hz, 1 H) 7.70 (s, 1 H) 7.30 - 7.44 (m, 1 H) 7.25 (d, J=7.60 Hz, 1 H) 7.14 (t, J=7.76 Hz, 1 H) 6.88 (t, J=7.09 Hz, 1 H) 6.77 (d, J=8.24 Hz, 1 H) 6.67 (s, 1 H) 5.09 - 5.16 (m, 1 H) 4.23 (br t, J=5.01 Hz, 2 H) 4.05 - 4.18 (m, 4 H) 2.52 - 2.58 (m, 1 H) 2.12 (s, 3 H) 1.93 - 2.02 (m, 1 H) 1.30 (s, 6 H)
A565	(400 MHz, DMSO-d6) δ ppm 10.55 (s, 1 H) 8.25 (s, 1 H) 7.79 (d, J=1.90 Hz, 2 H) 7.71 (t, J=1.90 Hz, 1 H) 7.29 (s, 1 H) 7.00 (dd, J=8.05, 1.20 Hz, 1 H) 6.85 (t, J=7.16 Hz, 1 H) 6.69 - 6.79 (m, 2 H) 4.30 - 4.40 (m, 2 H) 3.61 (br s, 2 H) 1.60 (s, 9 H)
A566	(400 MHz, DMSO-d6) δ ppm 9.05 (d, J=7.98 Hz, 1 H) 7.94 (s, 1 H) 7.53 - 7.71 (m, 1 H) 7.24 - 7.39 (m, 2 H) 7.16 (t, J=7.67 Hz, 1 H) 6.87 - 6.96 (m, 2 H) 6.78 (d, J=8.11 Hz, 1 H) 5.12 - 5.19 (m, 1 H) 4.15 - 4.30 (m, 2 H) 2.29 (s, 3 H) 2.09 - 2.20 (m, 1 H) 1.94 - 2.05 (m, 1 H) 1.58 (s, 9 H)

A567	(400 MHz, DMSO-d ₆) δ ppm 8.74 (dd, J=8.17, 2.60 Hz, 1 H) 7.87 (dd, J=8.30, 2.98 Hz, 1 H) 7.81 (s, 1 H) 7.45 (ddd, J=8.68, 5.96, 2.98 Hz, 1 H) 7.25 (d, J=7.48 Hz, 1 H) 7.15 (t, J=7.66 Hz, 1 H) 6.92 (s, 1 H) 6.86 - 6.90 (m, 1 H) 6.78 (dd, J=8.24, 1.01 Hz, 1 H) 5.09 - 5.16 (m, 1 H) 4.09 - 4.28 (m, 6 H) 2.89 (s, 1 H) 2.68 - 2.78 (m, 1 H) 2.05 - 2.16 (m, 1 H) 1.92 - 2.02 (m, 1 H) 1.31 (s, 6 H)
A568	¹ H NMR (400 MHz, DMSO-d ₆) δ ppm 8.73 (dd, J=8.24, 3.04 Hz, 1 H) 7.94 (d, J=2.41 Hz, 1 H) 7.80 (s, 1 H) 7.52 (dd, J=8.36, 2.41 Hz, 1 H) 7.27 (dd, J=6.97, 4.69 Hz, 1 H) 7.14 (t, J=7.72 Hz, 1 H) 6.88 (t, J=7.48 Hz, 1 H) 6.84 (s, 1 H) 6.78 (d, J=7.98 Hz, 1 H) 5.13 - 5.20 (m, 1 H) 4.43 (q, J=7.10 Hz, 1 H) 3.18 (d, J=2.15 Hz, 6 H) 2.06 - 2.21 (m, 4 H) 1.93 - 2.04 (m, 1 H)
A569	(400 MHz, DMSO-d ₆) δ ppm 9.20 (dd, J=17.81, 7.41 Hz, 1 H) 8.80 (s, 1 H) 8.56 (d, J=6.72 Hz, 1 H) 8.05 (d, J=9.13 Hz, 1 H) 7.83 (dd, J=8.36, 3.04 Hz, 1 H) 7.36 - 7.49 (m, 2 H) 6.95 (s, 1 H) 5.29 (quin, J=6.18 Hz, 1 H) 4.61 - 4.73 (m, 1 H) 4.50 - 4.60 (m, 1 H) 2.21 - 2.31 (m, 4 H) 2.07 - 2.18 (m, 1 H) 1.57 (s, 9 H)

Biological Examples

The disclosure is further illustrated by the following biological examples, which are not to be construed as limiting this disclosure in scope or spirit to the specific procedures herein described. It is to be understood that the examples are provided to illustrate certain embodiments and that no limitation to the scope of the disclosure is intended thereby. It is to be further understood that resort may be had to various other embodiments, modifications, and equivalents thereof which may suggest themselves to those skilled in the art without departing from the spirit of the present disclosure and/or scope of the appended claims.

10 Biological Example 1: Screening method to test activity of compounds against microfilaria of *Dirofilaria immitis*.

Four hundred to six hundred microfilariae of *Dirofilaria immitis* were added to wells of a microtiter plate containing RPMI media and the test compound formulated in 100% DMSO. Plates were held for three days at 37°C and 5% CO₂. The efficacy of a compound was determined based

on the motility of the microfilaria as compared to average motility of control wells containing DMSO only. A dose response assay was conducted to determine an EC₅₀ value. Compounds A468, A470, A480, A482, A508, A510, A514, A529, A536b, A538, A543, A547, A548, A552, A556, A561, A562, A563, A564 and A567 exhibited EC₅₀ values between 1000 nM and 10000 nM. 5 Compounds A465, A467, A475, A509, A527, A524, A549, A554 and A560 exhibited EC₅₀ values of between 100 and 1000 nM. Compounds A518, A497, A494, A481, A479, A478, A473, A487, A476, A483, A469, A466, A462, A492, A528, A532, A533, A539, A544, A550, A551, A555, A559 exhibited EC₅₀ values between 10 nM and 100 nM. Compounds A463, A464, A484, A485, A486, A499, A471, A472, A474, A477, A488, A489, A490, A491, A492, A493, A495, A496, 10 A498, A501, A502, A503, A504, A505, A506, A507, A513, A516, A517, A519, A522, A523, A525, A526, A530, A534, A536a, A537, A540, A541, A553, A557, A558, A565, A566, A568 and A569 exhibited EC₅₀ values of less than 10 nM.

Biological Example 2: Screening method to test activity of compounds against *Haemonchus contortus*.

15 Twenty L1 *Haemonchus contortus* larvae were added to wells of a microtiter plate containing a nutrient medium and the test compound in DMSO. An analysis was conducted at 4 days to determine the extent of development of the larvae from L1 to L3. Larvae exposed to DMSO alone served as controls. A dose response assay was conducted to determine an EC₅₀ value. Compounds A512, A515, A535, A549, A554, A563, A564 and A567 exhibited EC₅₀ values of between 1000 20 nM and 10000 nM. Compounds A462, A466, A479, A492, A482, A527, A528, A524, A532, A533, A544, A560, were found to be active with EC₅₀ values of between 100 nM and 1000 nM. Compounds A463, A465, A483, A476, A487, A475, A474, A477, A478, A488, A481, A494, A496, A497, A498, A499, A501, A503, A504, A505, A506, A513, A516, A517, A518, A525, A526, A536a, A540, A541, A550, A551, A555, A559 and A565 exhibited EC₅₀ values of between 25 10 nM and 100 nM. Compounds A484, A485, A486, A472, A471, A473, A493, A495, A502, A507, A523, A522, A530, A534, A553, A557, A558, A566 and A568 exhibited EC₅₀ values of less than 10 nM.

Biological Example 3: Screening method to test activity of compounds against L4 stage larvae of *Dirofilaria immitis*.

Four to six L4 stage *Dirofilaria immitis* worms are added to wells of a microtiter plate containing maintenance nutrient media and the test compound formulated in 100% DMSO. Plates are held at 37°C and 5% CO₂ for three days and then assessed to determine the motility of the larvae. Efficacy of a compound is determined by comparison of the treated L4 motility of the larvae relative to the average motility of worms in control wells containing DMSO only. A dose response assay is conducted to determine an EC₅₀ value. Compounds 536b, 538, A543, A545, A546, A547, A548, A552, A556, A561, A562, A563 and A564 exhibited EC₅₀ values of between 1000 nM and 10000 nM. Compounds A467, A478, A479, A480, A521, A524, A529, A532, A533, A539, A544, A549, A554 and A567 exhibited EC₅₀ values of between 100 nM and 1000 nM; compounds A462, A463, A465, A466, A469, A482, A488, A496, A527, A528, A536a, A537, A540, A550, A551, A555 and A559 were found to have EC₅₀ values of between 10 nM and 100 nM. Compounds A464, A483, A484, A485, A486, A471, A473, A474, A476, A477, A487, A489, A492, A499, A491, A481, A490, A493, A494, A495, A498, A501, A502, A503, A504, A505, A506, A507, A513, A516, and A519, A522, A523, A525, A526, A530, A534, A541, A553, A557, A558, A565 and A566 exhibited EC₅₀ values of less than 10 nM.

Biological Example 4: *In vivo* efficacy against the resistant JYD-34 isolate of *Dirofilaria immitis* in immune-deficient (NOD-scid-gama, NSG) mice.

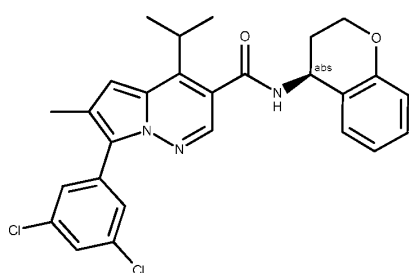
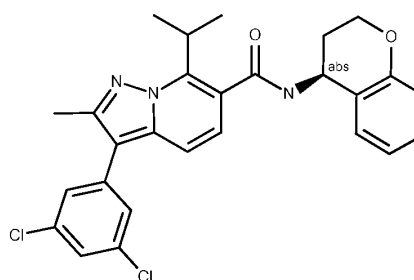
The efficacy of the compounds of the invention against a resistant isolate of *Dirofilaria immitis* (JYD-34 isolate) was evaluated in immune-deficient mice (NOD-scid-gama, NSG) as an intermediate host of the parasite (see WO 2018/148392 A1). Mice were infected with approximately 50 third stage *Dirofilaria immitis* (JYD-34 isolate) by subcutaneous injection on Day 0. Mice were treated orally with the placebo and test articles at a dosage of 25 mg/kg body weight on Day 1, Day 15, and Day 30. The dose of 25 mg/kg in the rodent model is believed to be equivalent to a dose of 5 mg/kg in dogs. Fifteen days after the last dose, at Day 45 after treatment, mice were euthanized, and live *Dirofilaria immitis* larvae were recovered from tissues and counted.

In this model, compound **A491** exhibited efficacy of < 50%; compounds **A465**, **A484** and **A495** exhibited efficacy between 50% and 70%; compounds **A464**, **A486**, **A471**, **A481**, **A489**, **A501**, **A502** and **A566** exhibited an efficacy of between 70% and 90%; and compounds **A472**, **A473**, **A493**, **A504**, **A507**, **A522** and **A530** exhibited efficacy of >90%. Mice treated with the macrocyclic lactone ivermectin dosed orally at a dosage of 0.2 mg/kg exhibited efficacy of < 50%. For comparison, the recommended minimum dose level of ivermectin for dogs in the commercial product HEARTGARD® Plus (ivermectin/pyrantel) is 6 µg/kg.

Biological Example 5: Comparison of *In vivo* efficacy against the resistant JYD-34 isolate of *Dirofilaria immitis* in immune-deficient (NOD-scid-gama, NSG) mice with closest prior art compound.

It has been found that the compounds of the invention having the bicyclic pyrrolopyridazine core structure are highly efficacious against immature stages of *Dirofilaria immitis* such as microfilaria and the L4 stage worm, including *Dirofilaria immitis* isolates that have been shown to be resistant to macrocyclic lactone treatment. Such resistant isolates of *Dirofilaria immitis* include the JYD34 isolate and others. Importantly, the compounds of the invention having the 5-6 fused bicyclic pyrrolopyridazine core structure demonstrate surprising and unexpected superior efficacy against immature stages of *Dirofilaria immitis* compared with compounds having a different 5-6 fused nitrogen-containing bicyclic core but having the same substituents around the bicyclic core.

Using the *in vivo* protocol described in Biological Example 4 above, the efficacies of Compound **A465** of the present invention and prior art compound **156** described in WO 2020/014068 (see page 124) were evaluated. The compounds described in WO 2020/014068 include a different 5-6 fused bicyclic ring core (pyrazolo[1,5-a]pyridine) compared with the pyrrolopyridazine core ring system of the compounds of the invention. With the exception of the different core ring systems, compound **A465** and prior art compound **156** contain the same substituents around the bicyclic ring. The structures of compound **A465** of the invention and prior art compound **156** are shown below for illustration:

**A465****156**

In this *in vivo* model system, compound **A465** exhibited an efficacy of 68% while compound **156** exhibited an efficacy of 29% at a dosage of 25 mg/kg. The difference in efficacy is significant in this model. This example clearly shows the importance of the pyrrolopyridazine bicyclic ring on the *in vivo* efficacy of the compounds against a resistant isolate of *Dirofilaria immitis*. As illustrated by the two structures above, with the exception of the bicyclic ring systems, the substitution pattern of the compounds is exactly the same.

Biological Example 6: *In vivo* efficacy against the resistant JYD-34 isolate of *Dirofilaria immitis* in dogs.

Beagle dogs were tested for microfilaria and heartworm antigen and received a full physical examination prior to inclusion in the study. Each dog was inoculated with 50 infective third-stage *D. immitis* larvae on Day -30 using the JYD-34 isolate which has been demonstrated to be resistant to macrocyclic lactones. Antigen testing performed on blood collected on Day 90 confirmed that animals had not been exposed to *D. immitis* prior to the induced infection.

Dogs were ranked by decreasing body weight within sex to form blocks of eight dogs each with approximately equal numbers of each sex and randomly assigned to each treatment group. Each study group contained five dogs. Dogs in the negative control group (Group 1) were untreated. Dogs in Group 2 were treated orally four times at monthly intervals with the commercial product Interceptor™ (milbemycin oxime) according to the product label. Dogs in Groups 3 and 4 were treated orally four times at monthly intervals (Days 0, 27, 55 and 84) with capsules containing an oral solution of Compound **A471** and **A464**, respectively, at a dosage of 5 mg/kg body weight. On study day 120 dogs were euthanized and necropsied for evaluation of the presence adult heartworms. The results of the study are shown in Table 5 below.

Table 5. Efficacy against *D. immitis* in beagles.

Trt. Group	Investigational Material	Dose	Geometric Mean Live Heartworm Count	% Efficacy
1	(-) control	n/a	27.1	n/a
2	Interceptor™ (milbemycin oxime)	0.5 mg/kg	21.2	21.8
3	A471	5 mg/kg	16.5	39.0
4	A464	5 mg/kg	16.7	38.2

As shown in Table 5, compounds **A471** and **A464** of the invention were found to be more effective than the commercial product Interceptor™ administered according to the label dose against the resistant JYD-34 isolate of *Dirofilaria immitis*.

- 5 **Biological Example 7:** *In vivo* efficacy at two dosages against the resistant JYD-34 isolate of *Dirofilaria immitis* in dogs.

In a further *in vivo* study conducted according to the procedure described in Biological Example 6 above, the efficacy of compounds **A481** and **A493** was tested against a resistant heartworm isolate (JYD-34) in beagles at two different dosage rates compared with a negative control group (Group 1) and a positive control group (Group 2) treated with Interceptor™ (milbemycin oxime). The objective of dosing the test compounds, in the higher dosage rate, on consecutive days was to evaluate the impact of increased exposure to the compounds on the efficacy against heartworm. Given the length of the heartworm lifecycle for the target L4 stage worm (see, for example, page 1, line 25 to page 2, line 10) and the study duration, it is considered that splitting the total dose into two administrations on consecutive days would not adversely impact the study outcome. In the study, Group 3 was treated with Compound **A481** at a dosage of 5 mg/kg body weight on days 0, 27, 55 and 84. Dogs in Group 4 were treated with Compound **A481** at a dosage

of 5 mg/kg body weight on days -1, 0, 26, 27, 54, 55, 83 and 84. Similarly, dogs in Group 5 were treated with Compound **A493** at a dosage of 5 mg/kg body weight on days 0, 27, 55 and 84, and dogs in Group 6 were treated with Compound **A493** at a dosage of 5 mg/kg body weight on days -1, 0, 26, 27, 54, 55, 83 and 84. The results of the study are shown in Table 6 below.

5 **Table 6.** Efficacy against *D. immitis* in beagles at two dosages.

Trt. Group	Investigational Material	Dose	Geometric Mean Live Heartworm Count	% Efficacy
1	(-) control	n/a	31.5	n/a
2	Interceptor™ (milbemycin oxime)	0.5 mg/kg	5.6	82.1
3	A481	5 mg/kg	11.3	64.2
4	A481	10 mg/kg (over 2 consecutive days)	0.6	98.0
5	A493	5 mg/kg	0.3	99.0
6	A493	10 mg/kg (over 2 consecutive days)	0	100.0

As shown in Table 6, compounds **A481** and **A493** are highly efficacious against the resistant JD-34 isolate of *Dirofilaria immitis* compared with the positive control. It is important to note that the Interceptor™ group (Group 2) was dosed monthly according to the product label while the optimum dosage of the test compounds has not yet been determined. It is also noted that the efficacy of the Interceptor™ group (Group 2) in the present study was significantly higher than the efficacy observed in the studies described in Biological Example 6 and Biological Example 9 (below). Compounds **A481** and **A493** exhibited efficacy of about 98% and 100% against the

resistant JYD-34 isolate of *Dirofilaria immitis* at a dosage of 5 mg/kg administered monthly for four months on two consecutive days, while Compound **A493** exhibited efficacy of 99% when one single dosage at 5 mg/kg was administered monthly for four months. These results against a resistant isolate of *Dirofilaria immitis* are significant and surprising.

5 Biological Example 8: In vivo efficacy against resistant JYD-34 isolate of *Dirofilaria immitis* in dogs.

In a further in vivo study using the procedure described in Biological Example 6, the efficacy of compound **A472** was tested for efficacy against a resistant heartworm isolate (JYD-34) in beagles compared with a negative control group (Group 1) and a positive control group (Group 2) treated with Interceptor™ (milbemycin oxime). In this study, Compound **A472** was found to be 100% efficacious at preventing infections with adult heartworm when administered in a dosage of 5 mg/kg body weight monthly for four months. In comparison, the milbemycin oxime control group was only found to be 16.6% efficacious. Table 7 below summarizes the results of the study.

Table 7. Efficacy against *D. immitis* (JYD-34 isolate) in beagles.

Trt. Group	Investigational Material	Dose	Live Heartworm Count (geo. mean)	% Efficacy
1	(-) control	n/a	33.9	n/a
2	Interceptor™ (milbemycin oxime)	0.5 mg/kg	28.3	16.6
3	A472	5 mg/kg	0	100.0

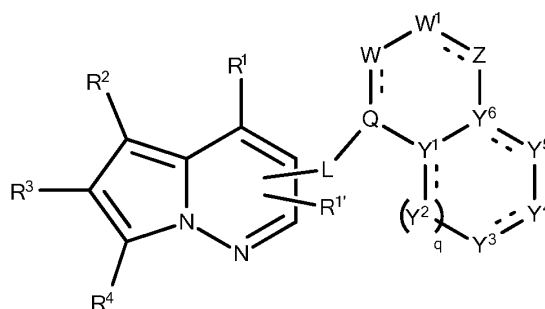
As shown above in comparison with the commercial product Interceptor™ (milbemycin oxime), the excellent *in vivo* efficacy of the compounds of the invention against a resistant isolate of *Dirofilaria immitis* is noteworthy and demonstrates the inventiveness of the compounds described herein.

* * *

Having thus described in detail preferred embodiments of the present invention, it is to be understood that the invention defined by the above paragraphs is not to be limited to particular details set forth in the above description as many apparent variations thereof are possible without
5 departing from the spirit or scope of the present invention.

WHAT IS CLAIMED IS:

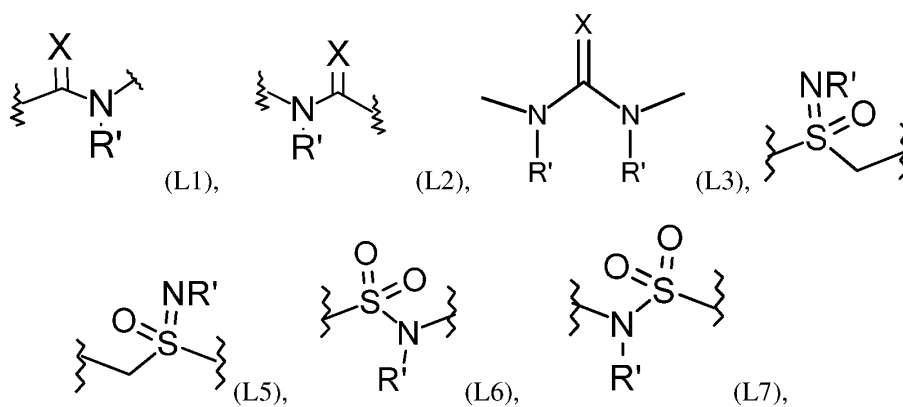
1. A compound of Formula I:

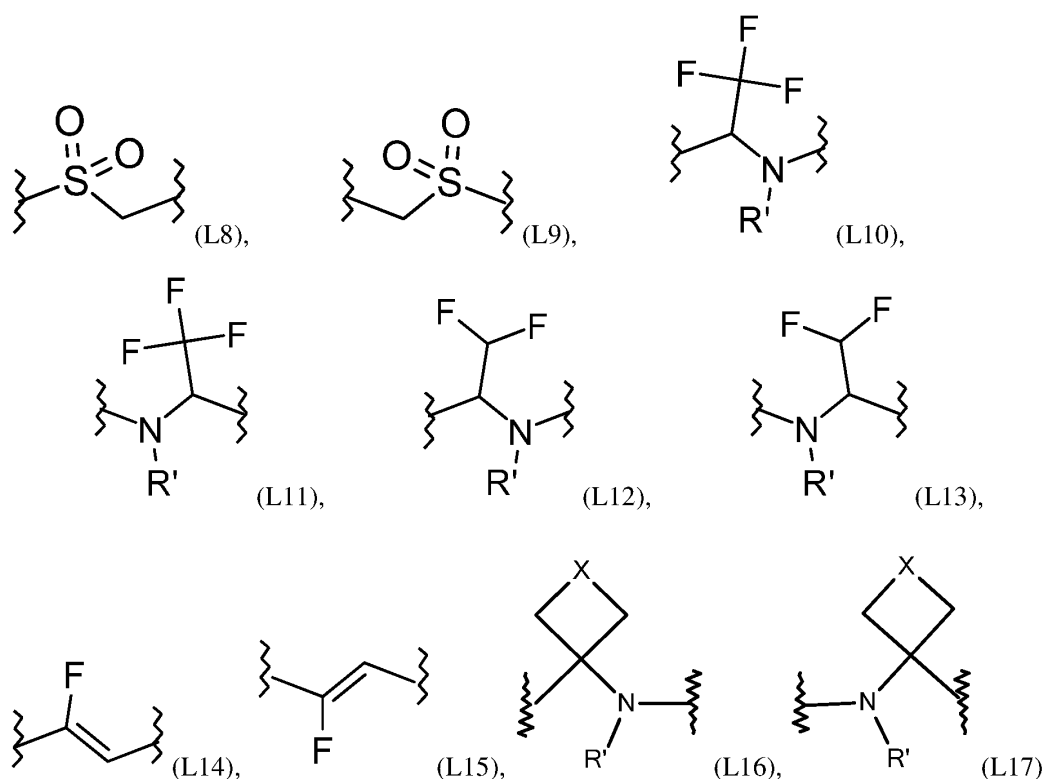


(I)

wherein:

L is L1, L2, L3, L4, L5, L6, L7, L8, L9, L10, L11, L12, L13, L14, L15, L16 or L17:





R' is hydrogen, optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, optionally substituted aralkyl, optionally substituted aryl, or two R' on the same L group together may form a 2- to 4-membered carbon chain to make a heterocycle;

R¹ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted

dialkylaminocarbonyl, optionally substituted trialkylsilyl, optionally substituted trialkylsilyloxy, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl), $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

- $\text{R}^{1'}$ is hydrogen, halogen, alkyl or haloalkyl;
- R^2 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl; optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, optionally substituted aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl), $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;
- R^3 is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl; optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted cycloalkoxy, optionally substituted heterocyclyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, optionally substituted aminocarbonyl, optionally substituted

alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl), $-\text{SF}_5$, or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^4 is hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted dialkylaminocarbonyl, $-\text{S}(\text{O})_p$ (optionally substituted alkyl), $-\text{SF}_5$, optionally substituted heterocyclyl, optionally substituted aryl, optionally substituted 5- to 10-membered heteroaryl, a spirocyclic heterocyclyl-carbocyclyl group, a spirocyclic heterocyclyl-heterocyclyl group, a spirocyclic carbocyclyl-carbocyclyl group, a spirocyclic carbocyclyl-heterocyclyl group or $-\text{NR}^a\text{R}^b$, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^5 and $\text{R}^{5'}$ are independently in each occurrence, hydrogen, halogen, cyano, nitro, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkoxy, optionally substituted alkylcarbonyl, optionally substituted alkoxy carbonyl, optionally substituted aminocarbonyl, optionally substituted alkylaminocarbonyl, optionally substituted di(alkyl)aminocarbonyl, optionally substituted alkylcarbonyloxy, optionally substituted alkylcarbonylamino, optionally substituted aryl, optionally substituted heteroaryl, $-\text{SF}_5$, $-\text{SO}_p$ (optionally substituted alkyl or haloalkyl); or R^5 together with $\text{R}^{5'}$ together form a 2-6-membered chain optionally containing one or two heteroatoms selected

from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached; or $-NR^cR^d$, wherein R^c and R^d are independently H or optionally substituted alkyl; or R^c and R^d may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^9 is hydrogen, halogen, alkyl, haloalkyl, cycloalkyl, alkenyl or alkynyl;

R^6 and R^7 are independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkoxy, or optionally substituted cycloalkoxy, or R^6 together with R^7 form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;

Q is $C-R^9$ or N;

X is O, S or $N-R'$;

Y^1 and Y^6 are each independently N, C, or $-CR^5$;

Y^2 , Y^3 , Y^4 and Y^5 are each independently N, NR' , S, O, $-CR^5$ - or $CR^5R^{5'}$;

W is CR^6 , CR^6R^7 , O, SO_p , N or $N-R^8$, or W is absent;

W^1 is CR^6 , CR^6R^7 , O, SO_p , N or $N-R^8$;

Z is CR^7 , CR^6R^7 , O, SO_p , N or $N-R^8$,

R^8 is hydrogen or C_1 - C_4 -alkyl; and

wherein at most three of Y^1 , Y^2 , Y^3 , Y^4 , Y^5 and Y^6 are heteroatoms;

q is 0 or 1;

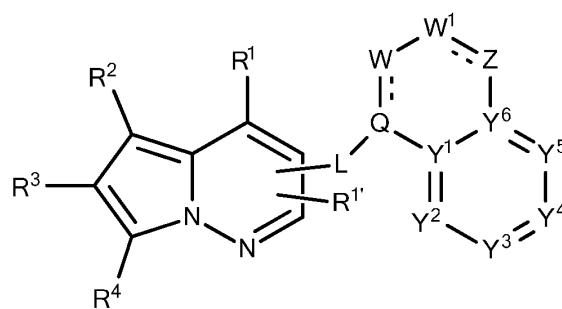
p is independently in each occurrence is 0, 1, or 2; and

the dashed bonds (---) signifies a single or double bond;

or a salt thereof;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with halogen, hydroxyl, oxo, alkyl, haloalkyl, cycloalkyl, cycloalkenyl, carboxyl, acyl, acyloxy, acetyl, alkylcarbonyl, haloalkylcarbonyl, alkoxy, alkoxy, haloalkoxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, haloalkylaminocarbonyl, dihaloalkylaminocarbonyl, amino, alkyl- or dialkylamino, amido, arylamino, alkoxy, haloalkoxy, alkylthio, haloalkylthio, aryloxy, nitro, cyano, azido, thiol, thioamido, imino, amidino, guanidino, carbonate, silyl, silyl ether, SF₅, R₃Si- or R₃SiO- where R is alkyl, haloalkyl or aryl, SF₅, sulfate, alkylsulfonyl, haloalkylsulfonyl, sulfate, alkylsulfonyl, haloalkylsulfonyl, alkoxy, alkoxy, alkylsulfinyl, haloalkylsulfinyl, sulfamoyl, sulfoximine, sulfinimine, sulfonimidamide, sulfonediimine, phosphonyl, phosphinyl, phosphoryl, phosphine, phosphonamidate, phosphinamidate, phosphinate, phosphine oxide, thioester, anhydride, oxime, hydrazine, carbamate, phosphate, phosphonate, aryl, heteroaryl or heterocyclyl.

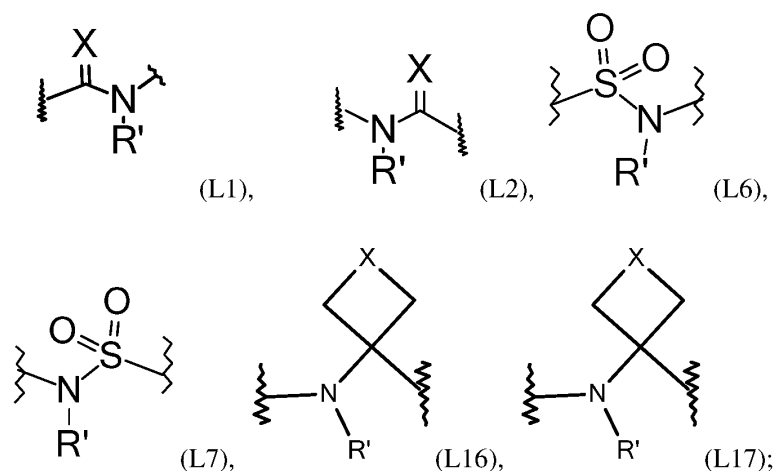
2. The compound of Formula (I) according to claim 1, wherein the compound has the structure of Formula (IA):



(IA)

wherein:

L is L1, L2, L6, L7, L16 or L17:



R' is hydrogen, optionally substituted alkyl, optionally substituted haloalkyl or optionally substituted aralkyl;

R¹ is hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted alkenyloxy, optionally substituted alkynyloxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl or -NR^aR^b, wherein R^a and R^b are independently H or optionally substituted alkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted;

R^{1'} is hydrogen, halogen, alkyl or haloalkyl;

R² is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R³ is hydrogen, cyano, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted alkoxyalkyl, optionally substituted aminoalkyl, optionally substituted alkylaminoalkyl, optionally substituted dialkylaminoalkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R⁴ is optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted heterocyclyl, optionally substituted phenyl or optionally substituted 5- or 6-membered heteroaryl;

R⁵ and R^{5'} are independently in each occurrence, hydrogen, halogen, cyano, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl or optionally substituted alkoxy;

R⁹ is hydrogen, halogen, alkyl or haloalkyl;

R⁶ and R⁷ are independently hydrogen, halogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, or R⁶ together with R⁷ form a 2-6-membered chain optionally containing one or two heteroatoms selected from the group consisting of N, O, Si and S to form carbocyclic or heterocyclic ring together with the carbon atom to which they are attached, wherein the carbon or nitrogen atoms in the chain may be optionally substituted;

Q is C-R⁹ or N;

X is O, S or N-R⁹;

Y¹ and Y⁶ are independently N or C;

Y², Y³, Y⁴ and Y⁵ are each independently N or -CR⁵;

W is CR⁶ or CR⁶R⁷ or W is absent;

W¹ is CR⁶ or CR⁶R⁷;

Z is CR⁶, CR⁶R⁷ or O;

wherein at most three of Y¹, Y², Y³, Y⁴, Y⁵ and Y⁶ are N; and

the dashed bonds (---) signifies a single or double bond;

or a salt thereof;

wherein “optionally substituted” indicates that the group recited may be optionally substituted with one or more halogen, hydroxyl, alkyl, haloalkyl, cycloalkyl, carboxyl, acyl, acyloxy, acetyl, $\text{R}_3\text{Si-}$ or $\text{R}_3\text{SiO-}$ where R is alkyl, haloalkyl or aryl, SF_5 , sulfate, alkylsulfonyl, haloalkylsulfonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, haloalkylaminocarbonyl, dihaloalkylaminocarbonyl, amino, alkyl- or dialkylamino, amido, alkoxy, haloalkoxy, alkylthio, haloalkylthio, cyano, thiol, thioamido, SF_5 , alkylsulfonyl, alkoxysulfonyl, or alkylsulfinyl.

3. The compound of Formula (I) or Formula (IA) according to claim 1 or 2, wherein Q is N.

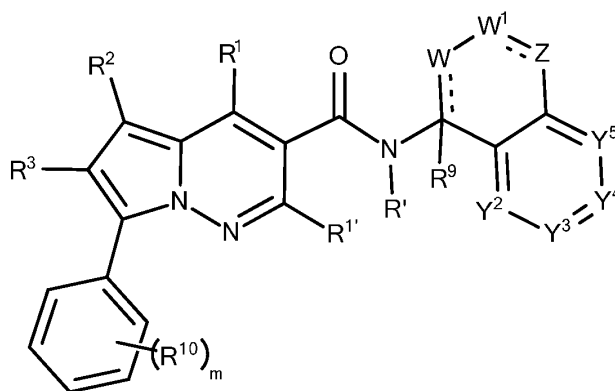
4. The compound of Formula (I) or Formula (IA) according to claim 1 or 2, wherein Q is C-R^9 .

5. The compound of Formula (I) or Formula (IA) according to any one of claims 1 to 4, wherein X is O or S.

6. The compound of Formula (I) or Formula (IA) according to any one of claims 1 to 5, wherein L is L1 or L2.

7. The compound of Formula (I) or Formula (IA) according to any one of claims 1 to 6, wherein W and W^1 are independently CR^6R^7 and Z is O.

8. The compound of Formula (I) or Formula (IA) according to claim 1 or 2, which is represented by the compound of formula (Ie):



(Ie)

wherein:

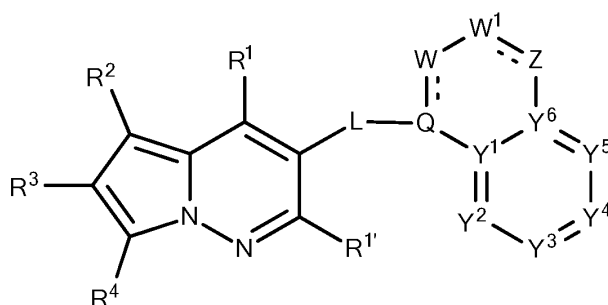
each R^{10} is independently halogen, cyano, hydroxyl, optionally substituted C₃-C₈-cycloalkyl, optionally substituted C₃-C₈-cycloalkyloxy, C₁-C₄-alkyl, C₁-C₄-haloalkyl, C₃-C₈-halocycloalkyl, C₁-C₄-alkoxy, C₁-C₄-haloalkoxy, C₂-C₆-alkenyl, C₂-C₆-haloalkenyl, C₂-C₆-alkynyl, C₂-C₆-haloalkynyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-haloalkoxy-C₁-C₆-alkyl, optionally substituted phenyl, optionally substituted phenyloxy, optionally substituted 5- or 6-membered heteroaryl, optionally substituted 3- to 7-membered heterocyclyl containing from one to three heteroatoms selected from the group consisting of N, O, Si and S, C₁-C₆-alkylcarbonyl, C₁-C₆-haloalkylcarbonyl, C₁-C₆-alkoxycarbonyl, C₁-C₆-haloalkoxycarbonyl, aminocarbonyl, C₁-C₆-alkylaminocarbonyl, C₁-C₆-haloalkylaminocarbonyl, di-C₁-C₆-alkylaminocarbonyl, di-C₁-C₆-haloalkylaminocarbonyl, -SO_p(optionally substituted C₁-C₆-alkyl or C₁-C₆-haloalkyl) where p is 0, 1 or 2, SF₅, or -NR^aR^b, wherein R^a and R^b are independently H, C₁-C₆-alkyl or C₁-C₆-haloalkyl; or R^a and R^b may form, with the nitrogen to which they are attached, a 3-, 4-, 5-, 6-, 7-, or 8-membered-heterocyclyl group, which may include one to three additional heteroatoms selected from the group consisting of N, O, Si and S and may be optionally substituted; and

m is 0, 1, 2, 3, 4 or 5.

9. The compound according to claim 8, wherein each R^{10} is independently halogen and m is 2 or 3.
10. The compound according to claim 8, wherein:
each R^{10} is independently chloro or fluoro;
m is 2 or 3;
 R^1 is C_1 - C_4 -alkyl or $-NR^aR^b$;
 $R^{1'}$ is hydrogen;
 R^2 is hydrogen, halogen, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl;
 R^3 is hydrogen, halogen, C_1 - C_3 -alkyl or C_1 - C_3 -haloalkyl;
W is CH_2 ;
 W^1 is CH_2 ; and
Z is O.
11. The compound according to claim 10, wherein:
 R^{10} is chloro or fluoro, wherein the chloro or fluoro substituents are located on the 2, 3 and 5 positions of the phenyl ring;
 R^2 is hydrogen;
 R^3 is C_1 - C_3 -alkyl or halogen.
12. The compound according to claim 11, wherein:
 R^1 is *iso*-propyl, *tert*-butyl, $-N(CH_3)_2$ or azetidiny, which may be substituted by one or more methyl or fluoro.
13. The compound of any of claims 1 to 12, wherein each of Y^2 , Y^3 , Y^4 and Y^5 are independently $-C-R^5$.
14. The compound of any of claims 1 to 12, wherein Y^2 is N and Y^3 , Y^4 and Y^5 are independently $-C-R^5$; or wherein Y^3 is N and Y^2 , Y^4 and Y^5 are independently $-CR^5$; or wherein Y^4 is N and Y^2 , Y^3 and Y^5 are independently $-CR^5$; or wherein Y^5 is N and Y^2 , Y^3 and Y^4 are independently $-CR^5$; or wherein Y^2 and Y^3 are N; and Y^4 and

Y^5 are independently $-CR^5$; or wherein Y^3 and Y^4 are N; and Y^2 and Y^5 are independently $-CR^5$; or wherein Y^4 and Y^5 are N; and Y^2 and Y^3 are independently $-CR^5$; or wherein Y^2 and Y^4 are N; and Y^3 and Y^5 are independently $-CR^5$; or wherein Y^3 and Y^5 are N; and Y^2 and Y^4 are independently $-CR^5$; or wherein Y^3 and Y^4 are N; and Y^2 and Y^5 are independently $-CR^5$.

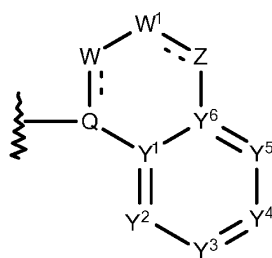
15. The compound of claim 1 which has the Formula (IA-1):



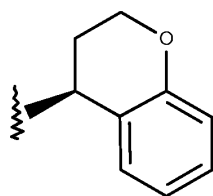
Formula (IA-1)

wherein L, R^1 , $R^{1'}$, R^2 , R^3 and R^4 are as defined in the table below; X is oxygen unless otherwise noted in the table, R' is hydrogen unless otherwise noted in the table; and

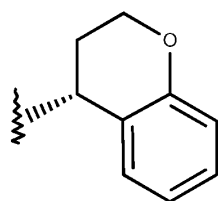
the group



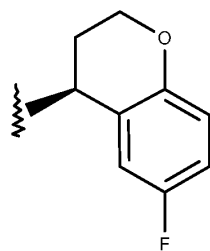
represents the following Ring Systems:



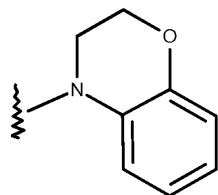
Ring System A;



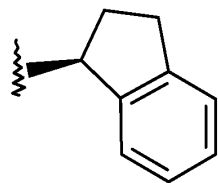
Ring System B;



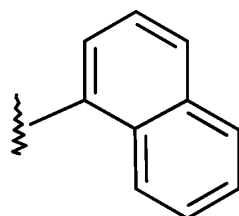
Ring System C;



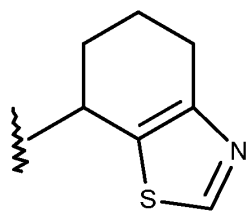
Ring System D;



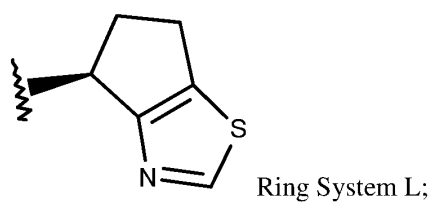
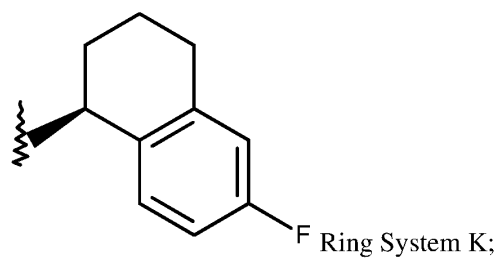
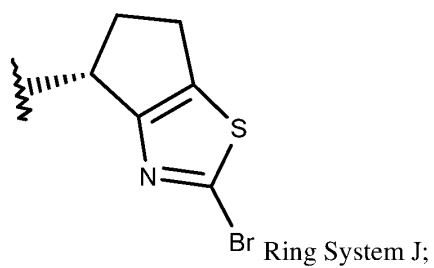
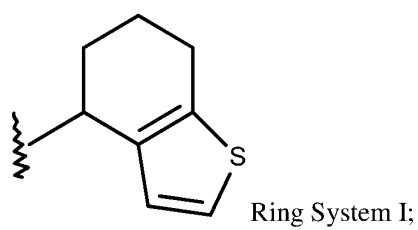
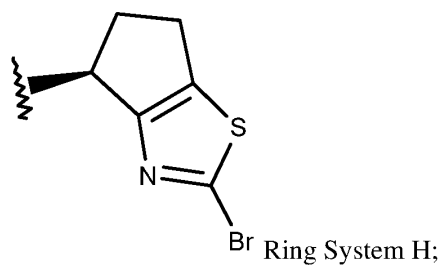
Ring System E;

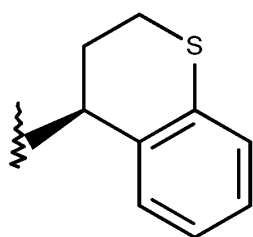


Ring System F;

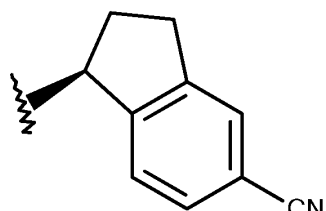


Ring System G;

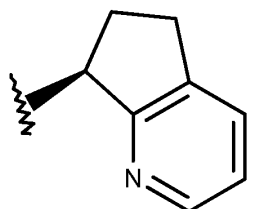




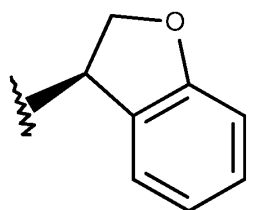
Ring System M;



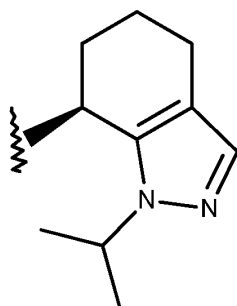
CN Ring System N;



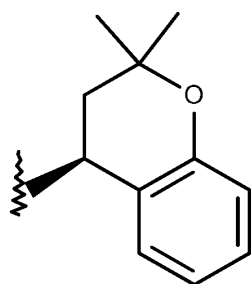
Ring System O;



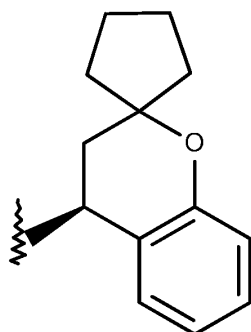
Ring System P;



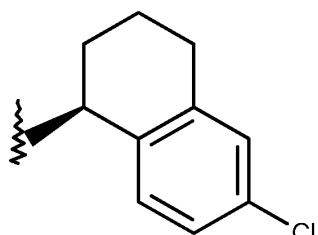
Ring System Q;



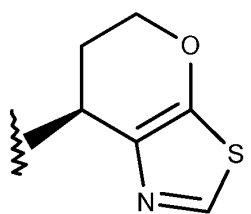
Ring System R;



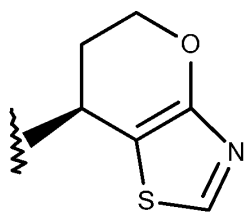
Ring System S;



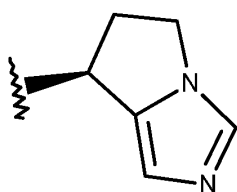
Ring System T;



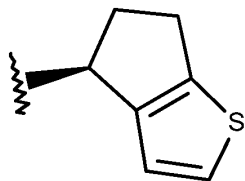
Ring System U;



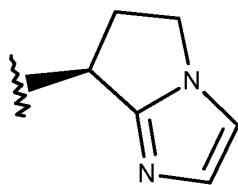
Ring System V;



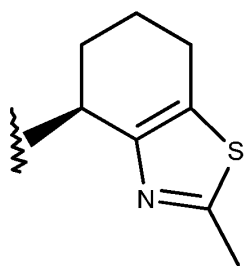
Ring System W;



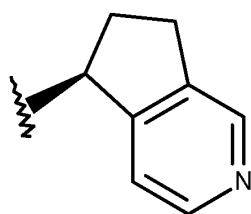
Ring System X;



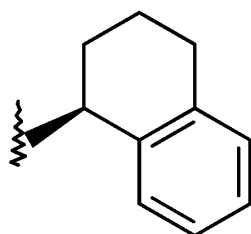
Ring System Y;



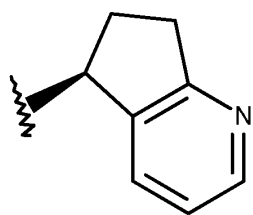
Ring System Z;



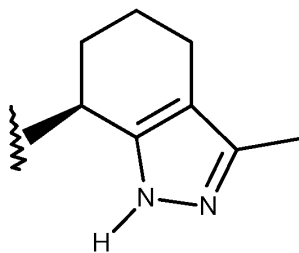
Ring System AA;



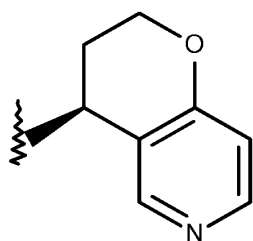
Ring System AB;



Ring System AC;



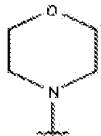
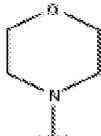
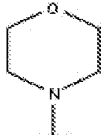
Ring System AD;



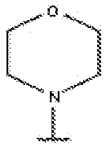
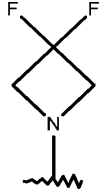
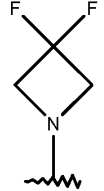
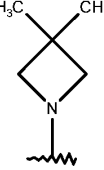
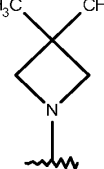
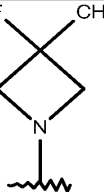
Ring System AE;

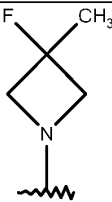
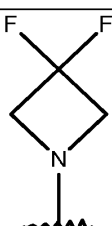
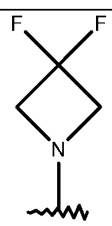
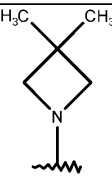
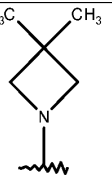
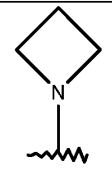
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A461	L2	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	B
A462	L2	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	A
A463	L1	<i>i</i> -Pr	H	H	Cl	3,5-di-Cl- Ph	A
A464	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	A
A465	L1	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	A
A466	L1	<i>i</i> -Pr	H	H	F	3,5-di-Cl-	A

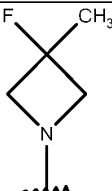
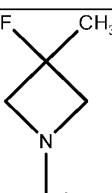
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
						Ph	
A467	L1	<i>i</i> -Pr	H	Cl	H	3,5-di-Cl- Ph	A
A468	L1	<i>i</i> -Pr	H	CF ₃	H	3,5-di-Cl- Ph	A
A469	L1	<i>i</i> -Pr	H	Me	H	3,5-di-Cl- Ph	A
A470	L1	<i>i</i> -Pr	H	H	H	3,5-di-Cl- Ph	A
A483	L1	<i>t</i> -Bu	H	H	CF ₃	3,5-di-Cl- Ph	A
A482	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	D
A484	L1	<i>t</i> -Bu	H	H	Cl	2,4,6-tri-F- Ph	A
A485	L1	<i>t</i> -Bu	H	H	Cl	2,6-di-Cl-4- F-Ph	A
A486	L1	<i>t</i> -Bu	H	H	Cl	2,3,5-tri-F- Ph	A
A472	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-Cl- Ph	A
A471	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-F- Ph	A
A476	L1	<i>t</i> -Bu	H	H	Me	2,4,6-tri-F- Ph	A
A487	L1	<i>t</i> -Bu	H	H	Me	2,6-di-Cl-4- F-Ph	A

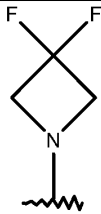
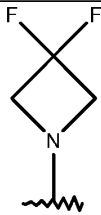
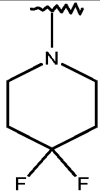
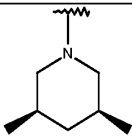
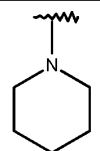
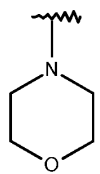
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A499	L1		H	H	Me	3,5-di-Cl- Ph	A
A475	L1	-N(CH ₃) ₂	H	H	Cl	3,5-di-Cl- Ph	A
A473	L1	-N(CH ₃) ₂	H	H	Cl	2,3,5-tri-Cl- Ph	A
A474	L1	-N(CH ₃) ₂	H	H	Cl	2,3,5-tri-F- Ph	A
A477	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	A
A478	L1	-N(CH ₃) ₂	H	H	Cl	2,3-di-Cl-5- F-Ph	A
A490	L1		H	H	Me	2,3-di-Cl-5- F-Ph	A
A491	L1		H	H	Me	2,3,5-tri-F- Ph	A
A488	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5- F-Ph	C
A479	L1	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl-5- F-Ph	D
A489	L1	<i>i</i> -Pr	H	H	Me	2,3-di-Cl-5- F-Ph	A

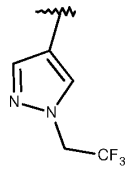
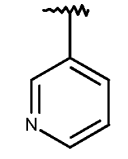
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A480	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	E
A481	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5- F-Ph	A
A502	L1	<i>t</i> -Bu	H	H	Cl	2,3-di-Cl-5- F-Ph	A
A492	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	E
A493	L1	-N(CH ₃) ₂	H	H	Me	2,3-di-Cl-5- F-Ph	A
A516	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	D
A494	L1	<i>t</i> -Bu	H	H	Cl	2,3-di-Cl-5- F-Ph	D
A482	L1	<i>t</i> -Bu	H	H	Me	3,5-di-Cl- Ph	D
A495	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5- F-Ph	D
A496	L1	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl-5- F-Ph	D
A497	L1	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	D
A498	L1	<i>i</i> -Pr	H	H	Me	2,3-di-Cl-5- F-Ph	D

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A501	L1		H	H	Me	2,3,5-tri-Cl- Ph	A
A505	L1		H	H	Me	2,3,5-tri-Cl- Ph	A
A504	L1		H	H	Me	2,3-di-Cl-5- F-Ph	A
A511	L1		H	H	Me	2,3,5-tri-Cl- Ph	A
A512	L1		H	H	Me	2,3-di-Cl-5- F-Ph	A
A508	L1		H	H	Me	2,3,5-tri-Cl- Ph	A

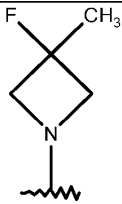
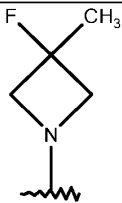
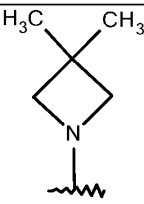
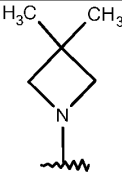
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A510	L1		H	H	Me	2,3-di-Cl-5-F-Ph	A
A506	L1		H	H	Cl	2,3,5-tri-Cl-Ph	A
A507	L1		H	H	Cl	2,3-di-Cl-5-F-Ph	A
A515	L1		H	H	Cl	2,3,5-tri-Cl-Ph	A
A520	L1		H	H	Cl	2,3-di-Cl-5-F-Ph	A
A503	L1		H	H	Cl	2,3-di-Cl-5-F-Ph	A

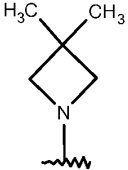
Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A509	L1		H	H	Cl	2,3,5-tri-Cl- Ph	A
A514	L1		H	H	Cl	2,3-di-Cl-5- F-Ph	A
A521	L1	<i>i</i> -Pr	H	H	Me	3,5-di-Cl- Ph	F
A513	L1	<i>i</i> -Pr	H	H	Me	2,3,5-tri-F- Ph	A
A517	L1	<i>i</i> -Pr	H	H	Me	2,3,5-tri-Cl- Ph	A
A518	L1	<i>t</i> -Bu	H	Br	Me	2,3-di-Cl- Ph	A
A519	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl- Ph	A
A522	L1	<i>t</i> -Bu	H	H	Cl	2,3,5-tri-Cl- Ph	A
A523	L1	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl-5- F-Ph	A
A500	L1	H	<i>i</i> -Pr	H	H	3,5-di-Cl- Ph	A

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A525	L1		H	H	Me	2,3,5-tri-Cl- Ph	A
A526	L1		H	H	Me	2,3-di-Cl-5- F-Ph	A
A527	L1	<i>t</i> -Bu	H	H	Me		A
A528	L1	<i>t</i> -Bu	H	H	Me		A
A524	L1	<i>t</i> -Bu	H	H	Me		A
A529	L1	<i>t</i> -Bu	H	H	Me		A
A530	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-Cl- Ph	A

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A531	L1	<i>t</i> -Bu	H	H	Me		A
A532	L1	<i>t</i> -Bu	H	H	Me		A
A533	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	G
A534	L1	<i>t</i> -Bu	H	H	Cl	2,3-di-Cl-5-F-Ph	A
A535	L3	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	G
A536a	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	H
A537	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	I
A536b	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	J
A538	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	K
A539	L1; X=S	<i>i</i> -Pr	H	H	Cl	2,3-di-Cl-5-F-Ph	A
A540	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	L
A541	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-Cl-Ph	M

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A542	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	N
A543	L1; R'=Me	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	A
A544	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	O
A545	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	P
A546	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	Q
A547	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	R
A548	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	S
A549	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	T
A550	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	U
A551	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	V
A552	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	W
A553	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	X
A554	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	Y
A555	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-	Z

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
						F-Ph	
A556	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	AA
A557	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	AB
A558	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	E
A559	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	AC
A560	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5-F-Ph	AD
A561	L1		H	H	Me	2,3,5-tri-Cl-Ph	A
A562	L1		H	H	Me	2,3-di-Cl-5-F-Ph	A
A563	L1		H	H	Me	2,3,5-tri-Cl-Ph	A
A564	L1		H	H	Me	2,3-di-Cl-5-F-Ph	A

Cmpd. #	L	R ¹	R ^{1'}	R ²	R ³	R ⁴	Ring Sys.
A565	L1	<i>t</i> -Bu	H	H	Cl	3,5-di-Cl- Ph	D
A566	L1	<i>t</i> -Bu	H	H	Me	2,3,5-tri-F- Ph	A
A567	L1		H	H	Cl	2,3-di-Cl-5- F-Ph	A
A568	L1	-N(CH ₃) ₂	H	H	Me	2,3,5-tri-Cl- Ph	A
A569	L1	<i>t</i> -Bu	H	H	Me	2,3-di-Cl-5- F-Ph	AE

16. A veterinary composition comprising the compound of any one of claims 1 to 15, or a salt thereof, and a pharmaceutically acceptable carrier.

17. A veterinary composition comprising the compound of any one of claims 1 to 15, or a salt thereof, one or more additional active agent(s), and a pharmaceutically acceptable carrier.

18. A method for the treatment, control and/or prevention of a parasitic infection and/or infestation in an animal in need thereof, which comprises administering to said animal an effective amount of the compound of any one of claims 1 to 15, or a salt thereof.

19. Use of a compound of any one of claims 1 to 15 in the preparation of a medicament for the treatment, control and/or prevention of a parasitic infection and/or infestation in an animal.

20. A compound of Formula (I) of any of claims 1 to 15, for use in a method for the treatment, control and/or prevention of a parasitic infection and/or infestation in an animal.