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(54) **Titre : PRODUIT DE COMBINAISON DESTINE A LA LUTTE CONTRE LES PARASITES CHEZ L'ANIMAL**
(54) **Title: COMBINATION PRODUCT FOR CONTROLLING PARASITES ON ANIMALS**

(57) **Abrégé/Abstract:**

The invention relates to novel compositions for controlling parasites on animals, comprising an N-arylpyrazole and also a pyrethroid in a formulation comprising aliphatic cyclic carbonates and aliphatic cyclic or acyclic polyethers.



Combination product for controlling parasites on animals

Abstract

The invention relates to novel compositions for controlling parasites on animals, comprising an N-arylpyrazole and also a pyrethroid in a formulation comprising aliphatic cyclic carbonates and aliphatic cyclic or acyclic polyethers.

Combination product for controlling parasites on animals

The invention relates to novel compositions for controlling parasites on animals, comprising an N-arylpyrazole and also a pyrethroid in a formulation comprising
5 aliphatic cyclic carbonates and aliphatic cyclic or acyclic polyethers.

N-Arylpyrazoles and their good insecticidal and acaricidal activity are known from US 2006014802 A1, WO2005090313 A1, FR2834288 A1, WO09828277, US06069157, WO200031043, DE19824487, WO09804530, WO09962903,
10 EP00933363, EP00911329, WO09856767, US05814652, WO09845274, WO9840359, WO09828279, WO09828278, DE19650197, WO09824767, EP00846686, EP00839809, WO09728126, EP00780378, GB02308365, US05629335, WO09639389, US05556873, EP00659745, US05321040, EP00511845, EP-A-234119, EP-A-295117 and WO 98/24769. In spite of this
15 abundance of applications with numerous N-arylpyrazole structures, there is a superior structure type which, for most indications, shows, by comparison, the best activity. 1-[2,6-Dichloro-4-(trifluoromethyl)phenyl]-3-cyano-4-[(trifluoromethyl)-sulphiny]-5-aminopyrazole (INN: fipronil) is generally acknowledged to be the most effective compound of this class for controlling most parasites.

20

N-Arylpyrazoles have been marketed as ectoparasiticides for more than 10 years (Hunter, J.S., III, D.M. Keister and P. Jeannin. 1994. Fipronil: A new compound for animal health. Proc. Amer. Assoc. Vet. Parasitol. 39th Ann. Mtg. San Francisco, CA. Pg. 48.). They are distinguished by good and broad activity and acceptable
25 compatibility. It is known that the existing formulations having a high content of DEE (Transcutol) contain a strong transdermal (FR 1996-11446 A; Sicherheitsdatenblatt [Safety data sheet]: ISO/DIS 11014/29 CFR 1910.1200/ANSI Z400.1 Printing date 10/23/2001: FRONTLINE® TOP SPOT™: fipronil 9.7% w/w) component. This facilitates, via the formulation, penetration into the sebaceous
30 glands and the epithelium (Skin distribution of fipronil by microautoradiography following topical administration to the beagle dog. Cochet, Pascal; Birckel, P.; Bromet-Petit, M.; Bromet, N.; Weil, A.; European Journal of Drug Metabolism and Pharmacokinetics (1997), 22(3), 211-216.). Via sebum excretion from the sebaceous

glands, a high concentration in the sebaceous glands may contribute to a long-lasting availability of the active compound if the active compound is carried along. However, in the case of the customary formulations, penetration of N-arylpyrazoles into the circulation is also likely, since each hair follicle is supplied by a blood vessel and the follicles are thus separated from the circulation only by a very thin barrier (Transfollicular drug delivery - Is it a reality? Meidan, Victor M.; Bonner, Michael C.; Michniak, Bozena B.; International Journal of Pharmaceutics (2005), 306(1-2), 1-14). Thus, the availability of the active compound on the animal is limited, too, both with respect to duration and concentration, since the active compound passes into the circulation and its available concentration in the sebum is lowered accordingly.

It is further known that the efficacy of the N-arylpyrazoles against representatives of the genus *Ixodes* is less than that against other genera of ticks (Endris RG, Matthewson, Cooke D & Amodie D (2000). Relency and efficacy of 65% permethrin and 9.7% fipronil against *Ixodes ricinus*. Vet. Therapeutics, Vol. 1 (No, 3): 159-168); Endris RG, Cooke D, Amodie D, Sweenwy DL & Katz TL (2002). Repellency and efficacy of 65% permethrin and selamectin spot-on formulations against *Ixodes ricinus* on dogs. Vet. Therapeutics. Vol. 3 (No. 1): 64-71).

Pyrethroids do likewise have a relatively broad insecticidal action, and some representatives also show good acaricidal effects; however, with these compounds there are frequently incompatibilities, and only particularly non-toxic representatives with limited efficacy can be used for cats. Recently, WO 04/098290 described a solution of this problem where a dosage tolerated by cats could be achieved with the aid of a synergist, an acaricidal pyrethroid and a neonicotinoid. The different physicochemical properties of the materials used require special formulations.

Furthermore, it is generally known that, compared to N-arylpyrazoles, pyrethroids are less active against ticks of the genus *Dermacentor*. Recently, it has furthermore been found that there is no cross-resistance between pyrethroids and N-arylpyrazoles in pyrethroid-resistant insects. On the other hand, selection of such mosquito strains with N-arylpyrazoles even leads to partial reversion of the pyrethroid resistance.

[Laboratory evaluation of fipronil, a phenylpyrazole insecticide, against adult Anopheles (Diptera: Culicidae) and investigation of its possible cross-resistance with dieldrin in Anopheles stephensi. Kolaczinski, Jan; Curtis, Chris. London School of Hygiene and Tropical Medicine, London, UK. Pest Management Science (2001),
5 57(1), 41-45].

WO 2001/065941 A1 and EP 1013170 A1 propose the combination of an N-arylpyrazole and a pyrethroid in applications against plant pests. JP 11049618 A2 uses similar mixtures to prevent feeding damage on timber constructions.
10 WO 95/22902 A1 uses such mixtures for the direct control of termites. FR 2713891 A1 and WO 95/22902 A1 even claim a synergistic effect of such mixtures, but without demonstrating it clearly.

However, [Antagonism of fipronil toxicity by piperonyl butoxide and S,S,S-tributyl
15 phosphorotrithioate in the German cockroach (Dictyoptera: Blattellidae). Valles, Steven M.; Koehler, Philip G.; Brenner, Richard J. Center for Medical, Agricultural and Veterinary Entomology, USDA-ARS, Gainesville, FL, USA. Journal of Economic Entomology (1997), 90(5), 1254-1258] indicates that inhibitors of the oxidative metabolism (P450 oxidase inhibitors) have an antagonistic effect in
20 cockroaches on the action of N-arylpyrazoles. Since most pyrethroids are detoxified via the p450 oxidase path, they, like MGK264 or piperonyl butoxide, have to be considered to be antagonists rather than synergists of the N-arylpyrazoles.

GB2396557 A1 teaches that the treatment of ectoparasites with mixtures of
25 N-arylpyrazoles and pyrethroids (if appropriate also with addition of synergists, such as MGK264 or piperonyl butoxide) is possible when concentrated powder formulations are used. WO 95/22902 A1 describes a soil treatment with improved activity by combined application of phenylpyrazoles and pyrethroids for control of termites. Here, too, the mixture used is unsuitable for application on homeotherms.

30

Since such formulations are difficult to apply in practice and, owing to the particles (GB 2396557), involve additional toxicological risks, it has to be the object to prepare a self-spreading liquid formulation having a good user safety profile which

combines the positive activity properties of the pyrethroids with those of the N-arylpyrazoles and does not result in a reduction of the efficacy of the N-arylpyrazoles even in the presence of further synergists from the class of the p450 oxidase inhibitors.

5

To this end, by intensive analyses and test series, we have now identified, from a large number of additives, solvents and spreading agents, formulations which, in general, can improve the good arthropodicidal efficacy properties of the N-arylpyrazoles in combination with pyrethroids. Surprisingly, the expected
10 antagonistic effects were not observed here.

The invention relates to novel compositions for controlling parasites on animals, comprising an N-arylpyrazole and a pyrethroid in a formulation comprising:

- an aliphatic cyclic carbonate
- 15 - an aliphatic cyclic or acyclic polyether.

The arthropodicidal compositions according to the invention are novel and, compared to the formulations hitherto described, have considerably better and longer-lasting efficacy, with simultaneously improved user and target animal safety
20 profile.

For the compositions, the combination partners of the N-arylpyrazoles are preferably arthropodicidal pyrethroids, in particular of the cyanopyrethroid (for example flumethrin), type-I pyrethroid (for example permethrin) or non-ester pyrethroid
25 (etofenprox) type.

Here, α -cyanopyrethroids (for example alpha-cypermethrin, cyfluthrin, beta-cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, fenvalerate, flucythrinate, flumethrin, tau-fluvalinate) are preferably employed in a concentration range of from
30 0.01 to 5% by weight, and a synergist is added, if appropriate (as described, for example, in WO 04/098290). Particular preference is given to using cypermethrin, cyfluthrin, deltamethrin and flumethrin in a concentration range of from 0.025 to

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- 5 -

0.25% by weight. Very particular preference is given to using flumethrin in a concentration range of from 0.05 to 1.25% by weight.

5 Type-1 pyrethroids (for example allethrin, bioallethrin, permethrin, phenothrin, resmethrin, tetramethrin, transfluthrin) are preferably employed in a concentration range of from 20 to 70% by weight. Particular preference is given here to permethrin, cyphenothrin in a concentration range of from 30 to 60% by weight. Very particular preference is given to using permethrin in concentrations of from 40 to 50% by weight.

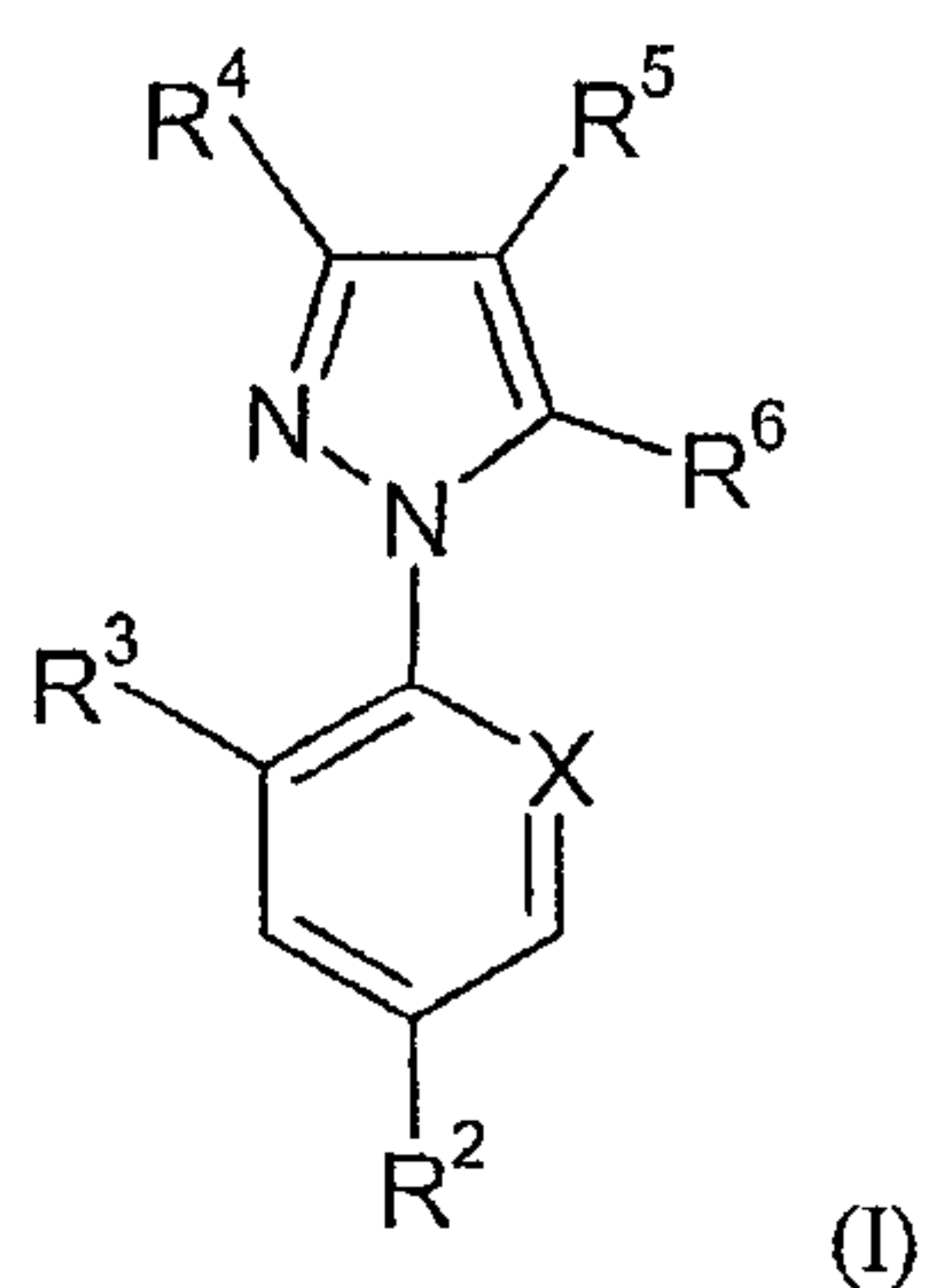
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Non-ester pyrethroids (for example etofenprox, halfenprox, silafluofen) are usually employed in a concentration range of from 10 to 60% by weight. Preference is given to etofenprox or halfenprox; particular preference is given to etofenprox in a concentration range of 25-55%.

15

To the person skilled in the art, N-arylpyrazoles are known per se as arthropodically active compounds, for example from the documents mentioned above.

20 Preferred phenylpyrazoles are those of the formula (I):



in which

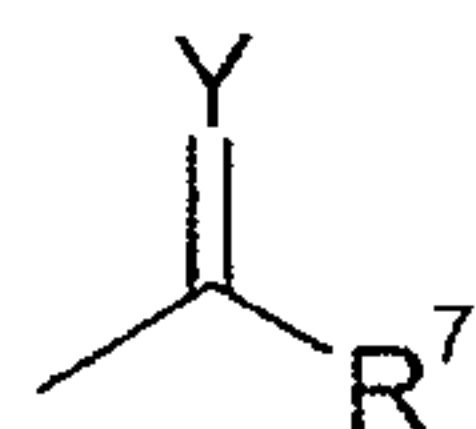
X represents =N- or C-R¹,

R¹ and R³ independently of one another represent halogen,

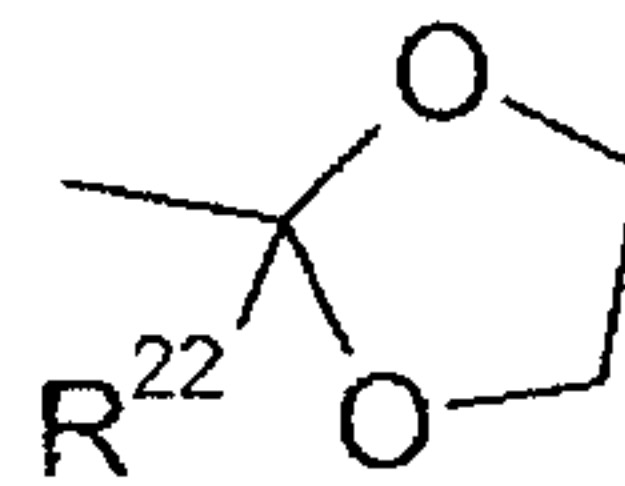
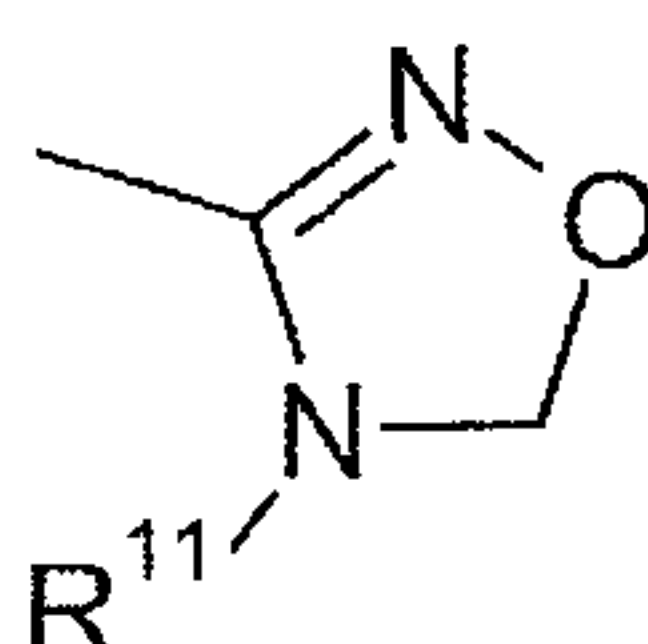
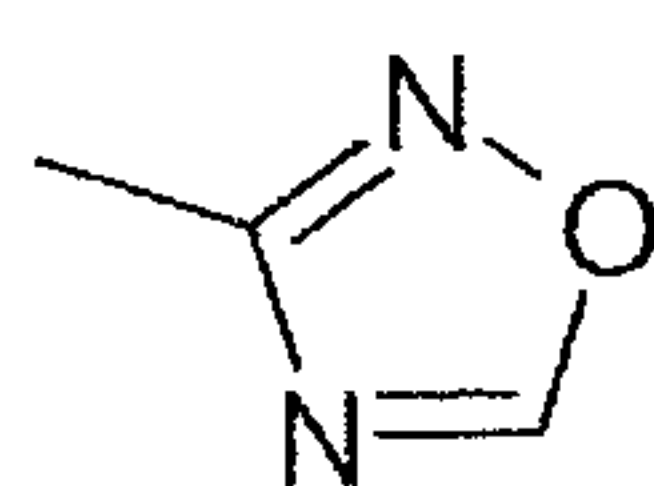
25 R² represents halogen, C₁₋₃-haloalkyl, S(O)_nCF₃ or SF₅,

n represents 0, 1 or 2,

R⁴ represents hydrogen, cyano or a radical of the formula

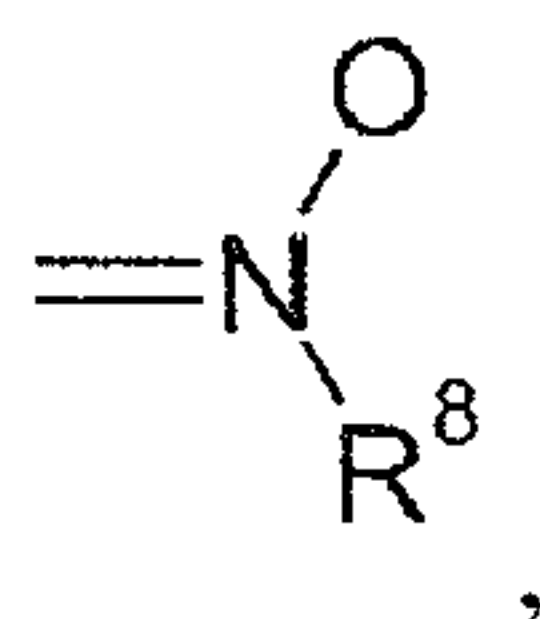


or one of the cyclic substituents below:



5

- R⁵ represents hydrogen, C₂₋₄-alkynyl, C₂₋₄-alkenyl which may optionally be mono- or polysubstituted by halogen or C₁₋₃-alkyl, or R⁵ represents C₁₋₄-alkyl-(C=O)-, C₁₋₄-alkyl-S-, C₁₋₄-haloalkyl-S-, -S(=O)-C₁₋₄-alkyl or -S(=NH)-C₁₋₄-alkyl, optionally halogen-substituted phenyl, optionally halogen-substituted furyl, the radical -NR¹⁴R¹⁵, an oxiranyl radical which is optionally mono- or polysubstituted by C₁₋₄-alkyl or C₁₋₄-haloalkyl, or a cyclopropyl radical which is optionally mono- or polysubstituted by halogen, C₁₋₄-alkyl or C₁₋₄-haloalkyl,
- 10 R⁶ represents hydrogen, C₁₋₄-alkylcarbonyl or a radical -NR¹⁶R¹⁷,
- 15 R⁷ represents hydrogen, C₁₋₄-alkyl, C₁₋₄-alkyl-S- or -NR⁹R¹⁰,
- Y represents =S, =O, =NH, =N-C₁₋₄-alkyl, =N-OH or



- R⁸ represents C₁₋₄-alkyl,
- R⁹ and R¹⁰ independently of one another represent hydrogen, hydroxyl or C₁₋₄-alkyl,
- 20 R¹¹ represents hydrogen, C₁₋₄-alkyl, -COO-C₁₋₄-alkyl or -CONR¹²R¹³,
- R¹² and R¹³ independently of one another represent hydrogen or C₁₋₄-alkyl,
- R¹⁴ and R¹⁵ independently of one another represent hydrogen, C₁₋₄-alkyl, C₁₋₄-haloalkyl or C₁₋₄-alkyl-SO₂-,
- R¹⁶ and R¹⁷ independently of one another represent hydrogen, C₁₋₄-alkoxy or C₁₋₄-alkyl, where the C₁₋₄-alkyl may optionally be substituted by phenyl,
- 25

- pyranzinyll or pyridyl, where phenyl, pyranzinyll or pyridyl may be mono- or polysubstituted by hydroxyl, C₁₋₄-alkyl, C₁₋₄-haloalkyl and/or C₁₋₄-alkoxy, or R¹⁶ and R¹⁷ represent C₁₋₄-alkylcarbonyl, C₁₋₄-alkoxycarbonyl, C₁₋₄-alkoxy-C₁₋₄-alkylcarbonyl or the radical -(C=O)NR²⁰R²¹ or
- 5 R¹⁶ and R¹⁷ together represent the group =CR¹⁸R¹⁹ which is attached by a double bond to the nitrogen,
- R¹⁸ and R¹⁹ independently of one another represent phenyl which is optionally mono- or polysubstituted by hydroxyl, C₁₋₄-alkyl, C₁₋₄-haloalkyl and/or C₁₋₄-alkoxy, and/or R¹⁸ and R¹⁹ represent hydrogen, C₁₋₄-alkyl, C₁₋₄-alkenyl or C₁₋₄-alkoxy, where C₁₋₄-alkyl, C₁₋₄-alkenyl or C₁₋₄-alkoxy may optionally be substituted by phenyl which is optionally mono- or polysubstituted by hydroxyl, C₁₋₄-alkyl, C₁₋₄-haloalkyl and/or C₁₋₄-alkoxy,
- 10 R²⁰ and R²¹ independently of one another represent hydrogen, C₁₋₄-alkyl or phenyl which is optionally mono- or polysubstituted by hydroxyl, C₁₋₄-alkyl, C₁₋₄-haloalkyl and/or C₁₋₄-alkoxy,
- 15 R²² represents C₁₋₄-alkyl.

Halogen preferably represents fluorine, chlorine, bromine or iodine, in particular fluorine, chlorine or bromine.

20

C₁₋₄-Alkyl represents straight-chain or branched alkyl having 1 to 4 carbon atoms, such as, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl.

C₁₋₄-Haloalkyl represents straight-chain or branched alkyl having 1 to 4 carbon atoms which is substituted by one or more identical or different halogen atoms; this also includes perhaloalkyl compounds. Preference is given to fluoroalkyls. Examples are -CF₂H, -CF₃, -CH₂CF₃, -CF₂CF₃.

25

Preferably, the substituents have the following meanings:

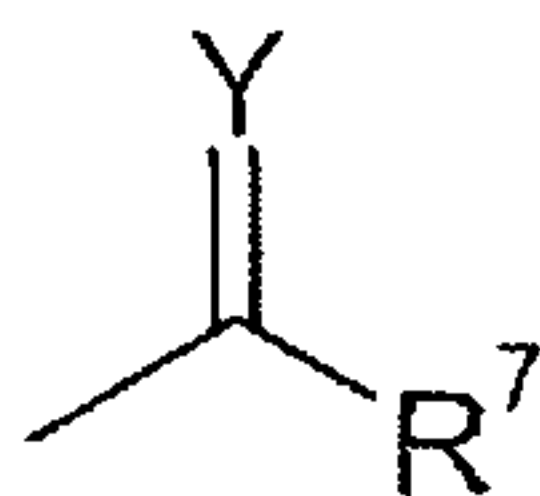
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X preferably represents C-R¹.

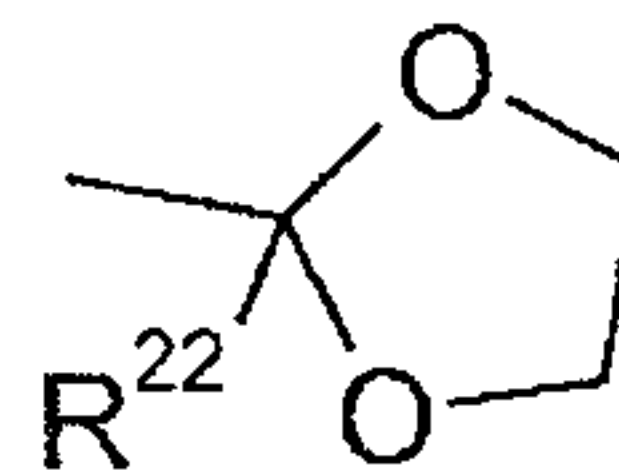
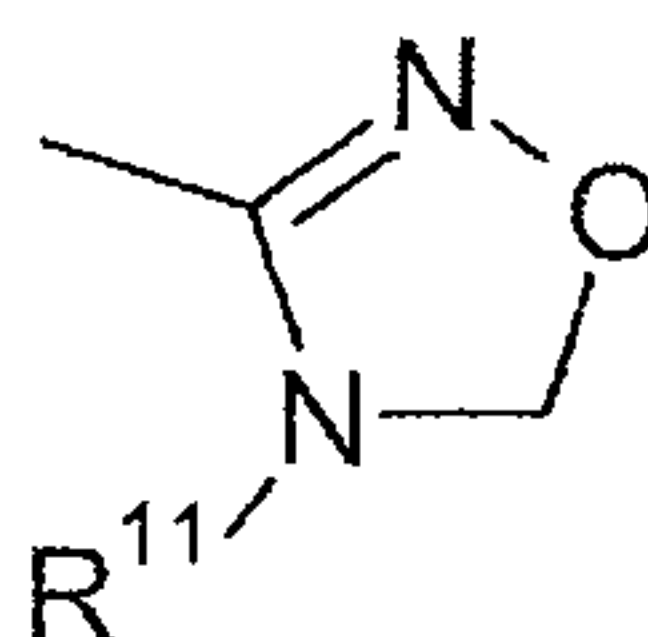
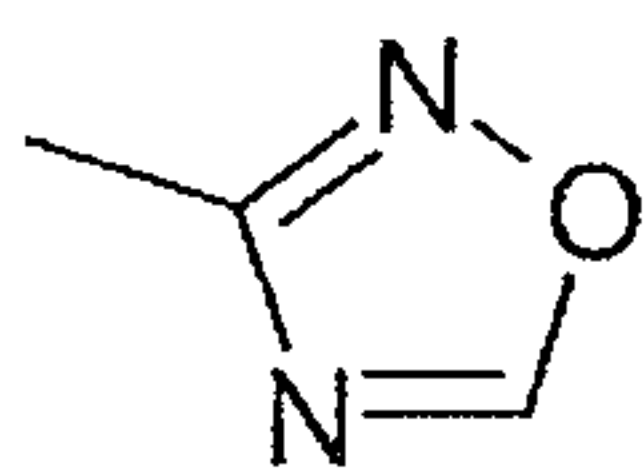
R¹ and R³ independently of one another preferably represent chlorine or bromine.

R² preferably represents C₁₋₃-haloalkyl or SF₅.

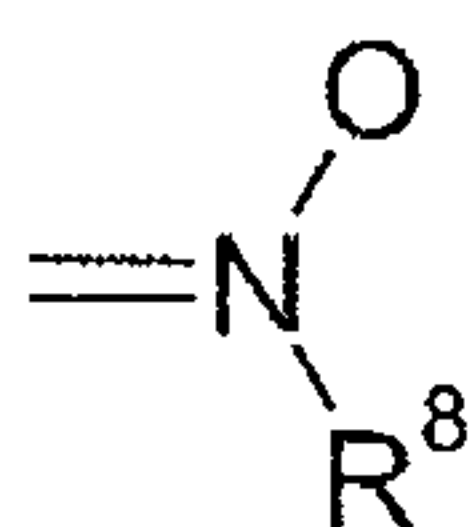
R⁴ preferably represents hydrogen, cyano or a radical of the formula



or one of the cyclic substituents below:



- 5 R⁵ preferably represents hydrogen, C₂₋₃-alkynyl, C₂₋₃-alkenyl which may optionally be monosubstituted by halogen or C₁₋₃-alkyl, or R⁵ preferably represents C₁₋₃-alkyl-(C=O)-, C₁₋₃-alkyl-S-, C₁₋₃-haloalkyl-S-, -S(=O)-C₁₋₃-alkyl or -S(=NH)-C₁₋₃-alkyl, optionally halogen-substituted phenyl, optionally halogen-substituted furyl, the radical -NR¹⁴R¹⁵, an optionally C₁₋₃-haloalkyl-substituted oxiranyl radical or a cyclopropyl radical which is optionally mono- or polysubstituted by halogen, C₁₋₄-alkyl or C₁₋₄-haloalkyl.
- 10 R⁶ preferably represents hydrogen, C₁₋₃-alkylcarbonyl or a radical -NR¹⁶R¹⁷.
- R⁷ preferably represents hydrogen, C₁₋₄-alkyl, C₁₋₄-alkyl-S- or -NR⁹R¹⁰.
- Y preferably represents =S, =O, =NH, =N-OH or



- 15 R⁸ preferably represents C₁₋₃-alkyl.
- R⁹ and R¹⁰ independently of one another preferably represent hydrogen, hydroxyl or C₁₋₃-alkyl.
- R¹¹ preferably represents hydrogen, C₁₋₄-alkyl or -CONR¹²R¹³.
- 20 R¹² and R¹³ independently of one another preferably represent hydrogen or C₁₋₃-alkyl.
- R¹⁴ and R¹⁵ independently of one another preferably represent hydrogen, C₁₋₃-alkyl, C₁₋₃-haloalkyl or C₁₋₃-alkyl-SO₂-.
- R¹⁶ and R¹⁷ independently of one another preferably represent hydrogen, C₁₋₃-alkoxy or C₁₋₃-alkyl, where the C₁₋₃-alkyl may optionally be substituted by phenyl,
- 25

pyrazinyl or pyridyl, where phenyl, pyrazinyl or pyridyl may be mono- or disubstituted by hydroxyl, C₁₋₃-alkyl, C₁₋₃-haloalkyl and/or C₁₋₃-alkoxy,

or

R¹⁶ and R¹⁷ represent C₁₋₄-alkylcarbonyl, C₁₋₄-alkoxycarbonyl, C₁₋₄-alkoxy-C₁₋₄-alkylcarbonyl or the radical -(C=O)NR²⁰R²¹ or

R¹⁶ and R¹⁷ together represent the group =CR¹⁸R¹⁹ which is attached by a double bond to the nitrogen.

R¹⁸ and R¹⁹ independently of one another preferably represent phenyl which is optionally mono- or disubstituted by hydroxyl, C₁₋₃-alkyl, C₁₋₃-haloalkyl and/or C₁₋₃-alkoxy, and/or R¹⁸ and R¹⁹ represent hydrogen, C₁₋₃-alkyl, C₁₋₃-alkenyl or C₁₋₃-alkoxy, where C₁₋₃-alkyl, C₁₋₃-alkenyl or C₁₋₃-alkoxy may optionally be substituted by phenyl which is optionally mono- or disubstituted by hydroxyl, C₁₋₄-alkyl, C₁₋₄-haloalkyl and/or C₁₋₄-alkoxy.

R²⁰ and R²¹ independently of one another preferably represent C₁₋₃-alkyl or phenyl which is optionally mono- or disubstituted by hydroxyl, C₁₋₃-alkyl, C₁₋₃-haloalkyl and/or C₁₋₃-alkoxy.

R²² preferably represents C₁₋₃-alkyl.

Particularly preferably, the substituents in formula (I) have the meaning below:

20

X represents C-R¹.

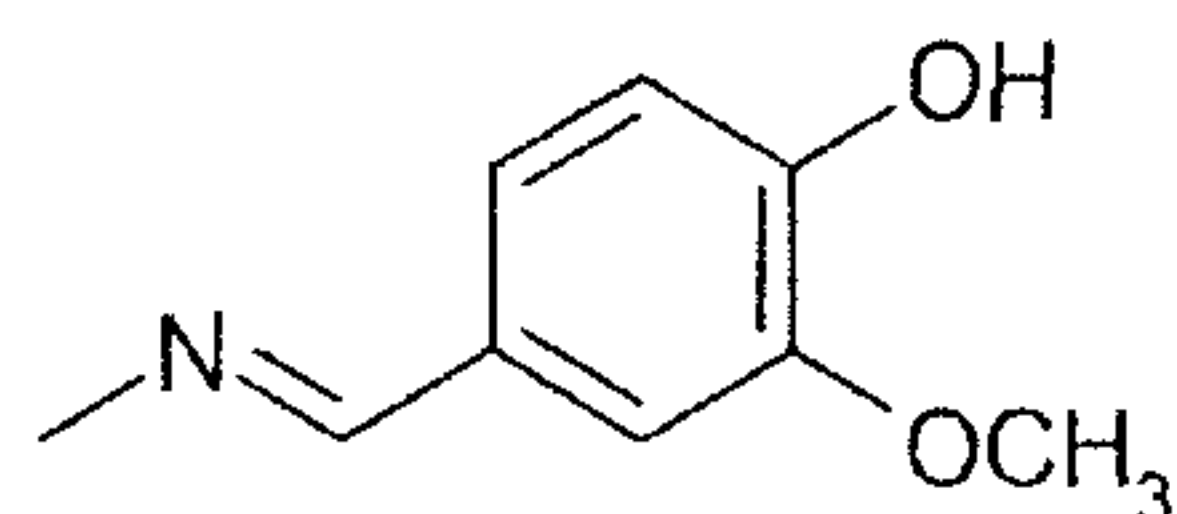
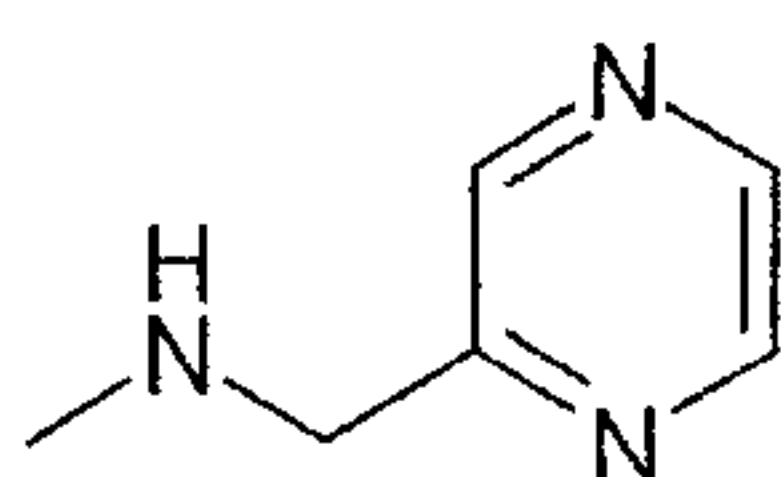
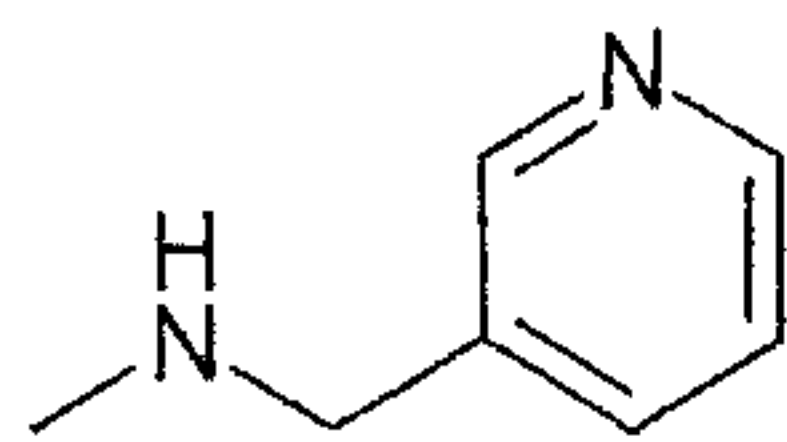
R¹ and R³ each represent Cl.

R² represents CF₃.

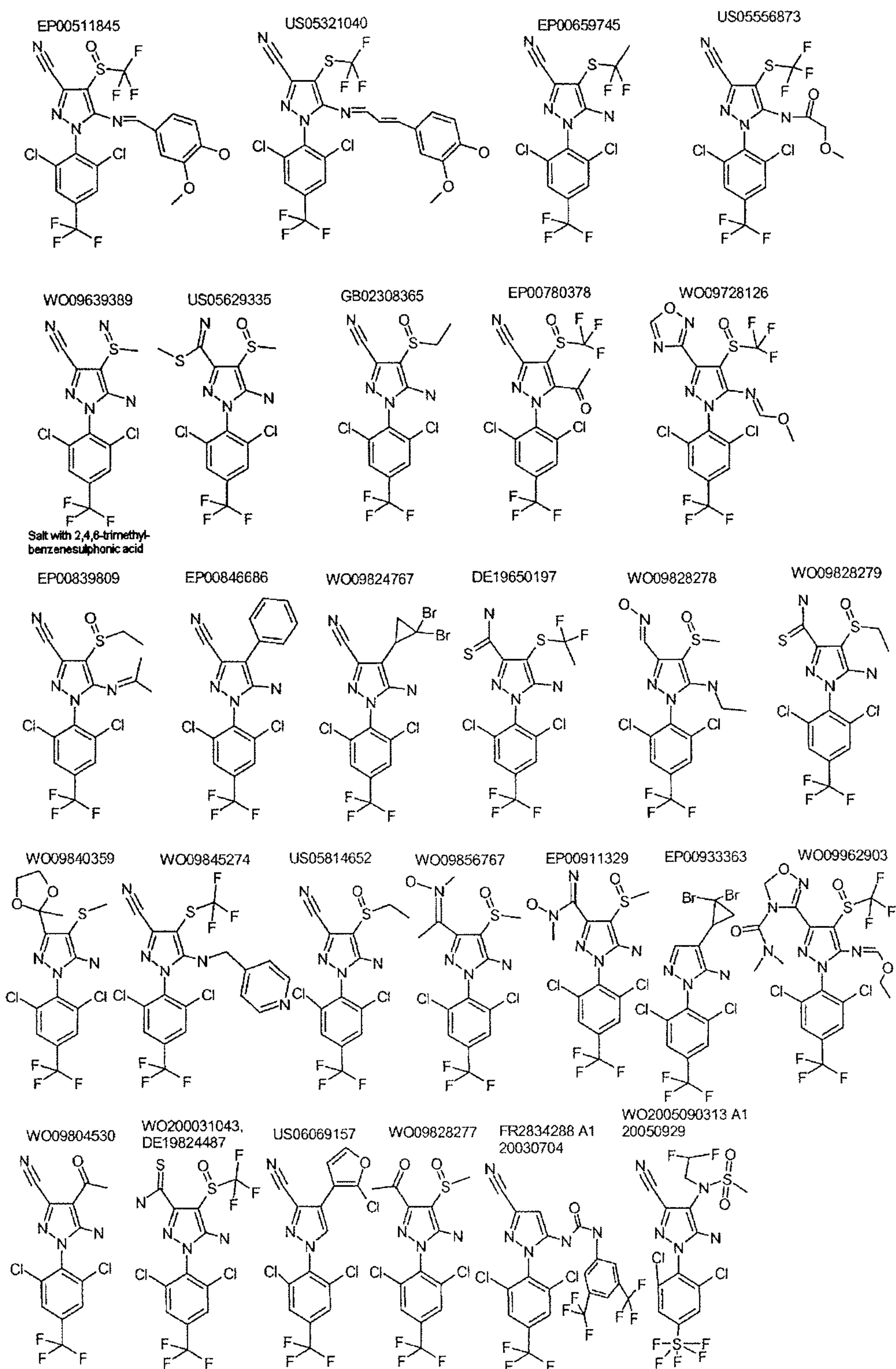
R⁴ represents CN, -C(=S)NH₂ or -C(=O)CH₃.

25 R⁵ represents -SCHF₂, -S(=O)CF₃, -S(=O)CH₃, -S(=O)CH₂CH₃ or represents the 1-trifluoromethyloxiranyl radical.

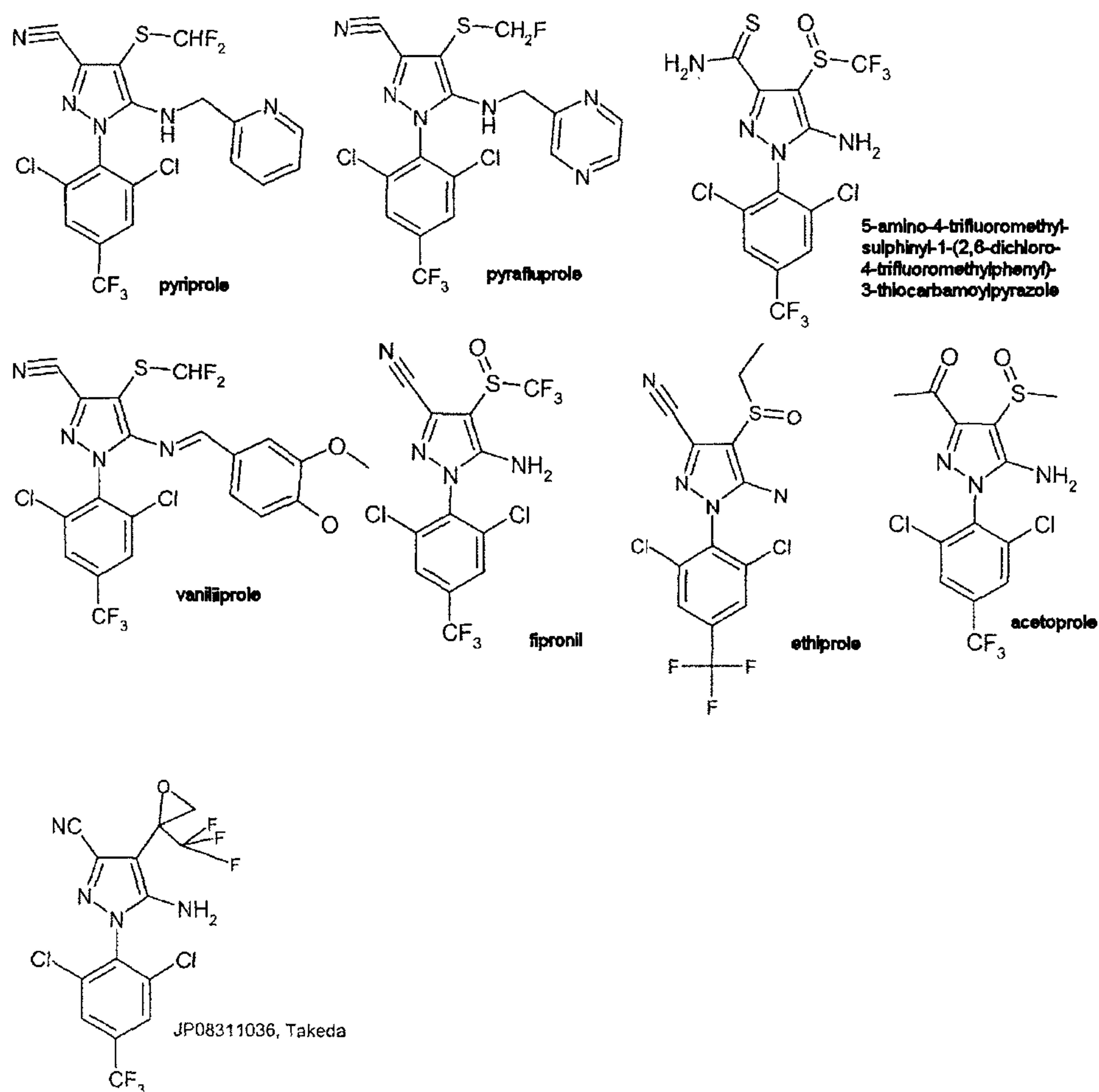
R⁶ represents an amino group or one of the radicals below



Preferred examples of compounds which can be used according to the invention are listed below:



Particularly preferred examples of compounds which can be used according to the invention are:



- 5 An example of a very particularly preferred N-arylpyrazole is fipronil.

A further example of a very particularly preferred N-arylpyrazole is 5-amino-4-trifluoromethylsulphonyl-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-thiocarbamoylpyrazole.

10

Depending on the nature and arrangement of the substituents, the active compounds may, if appropriate, be present in various stereoisomeric forms, in particular as enantiomers and racemates. According to the invention, it is possible to use both the pure stereoisomers and mixtures thereof.

15

If appropriate, the active compounds can also be employed in the form of their salts, pharmaceutically acceptable acid addition salts and basic salts being suitable.

5 Suitable pharmaceutically acceptable salts are salts of mineral acids or organic acids (for example carboxylic acids or sulphonic acids). Examples which may be mentioned are salts of hydrochloric acid, sulphuric acid, acetic acid, glycolic acid, lactic acid, succinic acid, citric acid, tartaric acid, methanesulphonic acid, 4-toluenesulphonic acid, galacturonic acid, gluconic acid, embonic acid, glutamic acid or aspartic acid. Suitable pharmaceutically acceptable basic salts are, for 10 example, the alkali metal salts, for example the sodium or potassium salts, and the alkaline earth metal salts, for example the magnesium or calcium salts.

It is furthermore also possible to use the active compounds in the form of their solvates, in particular hydrates. Solvates are to be understood as meaning both the 15 solvates, in particular hydrates, of the active compounds themselves and the solvates, in particular hydrates, of their salts.

As solids, the active compounds may, in certain cases, form various crystal modifications. Advantageous for the use in medicaments are stable modifications 20 having suitable solubility properties.

Unless indicated otherwise, percentages are to be understood as per cent by weight based on the weight of the finished preparation.

25 Usually, the compositions comprise the arylpyrazole in amounts of from 1 to 27.5% by weight, preferably from 5 to 20% by weight, particularly preferably from 7.5 to 15% by weight.

The aliphatic cyclic carbonate is preferably ethylene carbonate or propylene 30 carbonate, it also being possible to use mixtures.

The amount of aliphatic cyclic carbonate in the formulation can be varied widely in the range of from 10% by weight to 70% by weight, preferably from 12.5 to 50% by weight, particularly preferably from 15 to 40% by weight.

- 5 Aliphatic cyclic and/or acyclic ethers are compounds known per se. Preferably, they are ethers derived from diols having up to 8 carbon atoms, such as, for example, ethylene glycol, diethylene glycol, propylene glycol, dipropylene glycol. In the acyclic ethers, one or both OH groups carry a C₁₋₄-alkyl group, preferably, only one OH group is etherified; particularly preferred examples are: diethylene glycol
10 monoethyl ether, diethylene glycol monopropyl ether, dipropylene glycol monopropyl ether. Preferred 5- or 6-membered cyclic ethers have a ring oxygen and 4 or 5 ring carbon atoms and optionally carry a C₁₋₄-alkyl substituent; preferably, they carry a free OH group either directly on the ring or on the C₁₋₄-alkyl substituent. A particularly preferred example is tetrahydrofurfuryl alcohol. The amount of
15 aliphatic, cyclic and/or acyclic ether in the compositions according to the invention can be varied within wide limits of from 20 to 77.5% by weight, with amounts in the range of from 25 to 65% by weight and amounts in the range of from 25 to 50% by weight being particularly preferred and very particularly preferred, respectively.
- 20 According to a preferred embodiment, the compositions according to the invention may additionally comprise one or more esters of a dihydric or trihydric alcohol having up to three carbon atoms with organic fatty acids having 6 to 18 carbon atoms. As alcohol component, the esters used according to the invention contain a di- or trihydric alcohol having up to three carbon atoms, such as, for example, ethylene
25 glycol, propylene glycol or glycerol. In general, at least two, preferably all, hydroxyl groups of the alcohol are esterified. The acid components of the esters are fatty acids having 6 to 18 carbon atoms, which may be straight-chain, branched and also mono- or polyunsaturated. It is possible to use mixed esters or else mixtures of various types of esters. Preferred triglycerides are caprylic/capric acid triglycerides and also
30 caprylic/capric/linoleic acid triglycerides. Preference is likewise given to esters of propylene glycol with caprylic and/or capric acid (propylene glycol octanoate decanoate). Particularly preferably, these glycerol or propylene glycol esters of caprylic/capric acid have a viscosity range (20°C) of 0.08 - 1.3 Pa.s, and preferably

0.08 - 0.40 Pa.s. It is also possible to use their polyethylene oxide-, polypropylene oxide- and/or propylene carbonate-modified derivatives having the viscosity range mentioned. Examples which may be mentioned are propylene glycol dicaprylate, propylene glycol octanoate decanoate having a viscosity range of 0.09-0.12 Pa.s, 5 caprylic/capric diglyceryl succinate having a mean viscosity of 0.23 Pa.s, medium-chain caprylic/capric triglycerides having a viscosity of 0.27 - 0.30 Pa.s.

The liquid formulations according to the invention may comprise one or more of the esters mentioned above. Usually, the compositions according to the invention 10 comprise the ester or the ester mixture in proportions of from 0 to 40% by weight, preferably from 1 to 35% by weight, particularly preferably from 1 to 12.5% by weight and very particularly preferably from 2.5 to 7.5% by weight.

If appropriate, customary organic or inorganic antioxidants may be used for 15 stabilizing the formulations mentioned. Suitable inorganic antioxidants are, for example, the sulphites and bisulphites, in particular sodium bisulphite. Preference is given to phenolic antioxidants, such as anisole, butylated hydroxytoluene and hydroxyanisole, and their mixtures with one another. Usually, from 0.01 to 1% by weight, preferably from 0.05% to 0.5%, particularly preferably from 0.075 to 0.2% 20 by weight is used.

The formulation ingredients mentioned, in particular the organic esters, may be stabilized against possible hydrolytic degradation using acidifying agents. Suitable acidifying agents are pharmaceutically acceptable acids, in particular carboxylic 25 acids, such as, for example, succinic acid, tartaric acid, lactic acid or citric acid. Their preferred amount is in the range of from 0 to 0.5% by weight, but preferably from 0 to 0.2% by weight.

Polymeric surfactants based on polymethoxysiloxanes having a low surface tension 30 of < 30 mN/m, preferably < 22 mN/m, can be used as further formulation auxiliaries for improving the spreadability. Such surfactants are known ethoxylated and/or propoxylated, preferably neutral or particularly preferably cationic formulation auxiliaries. An example of a preferred polymeric auxiliary which may be mentioned

is the methoxysilane/ethylene oxide copolymer Belisil Silvet L 77 from Bayer GE Siliconics GmbH. The amount of these formulation auxiliaries may be varied within wide limits in the range of from 0.01 to 1.0% by weight. The preferred range is from 0.2 to 0.4% by weight.

5

If appropriate, the formulations may comprise further pharmaceutically acceptable auxiliaries and additives.

10 In addition to the arylpyrazoles and pyrethroids, the compositions according to the invention may also comprise one or more additional active compounds. Preferred examples of such active compounds for combinations which may be mentioned are: growth inhibitors, such as, for example, chitin biosynthesis inhibitors, such as, for example, benzoylphenylureas (for example triflumuron, lufenuron); phenyloxazolines (for example etoxazole); juvenile hormone analogues (for example
15 methoprene, hydroprene, pyriproxifen) and also mixtures of these active compounds with one another. Their amount may be varied within wide limits in the range of from 0.1 to 7.5% by weight, but preferably from 0.25 to 5.0% by weight, particularly preferably from 0.25 to 2.5% by weight.

20 The formulations according to the invention may also comprise synergists. Synergists in the sense of this application are to be understood as meaning compounds which for their part do not have the desired activity, but which, as mixing partners, increase the activity of the active compounds. Piperonyl butoxide, MGK264, verbutin, S,S,S-tributyl phosphorotrithioate may be mentioned here in an
25 exemplary manner. In the formulations according to the invention, synergists are preferably used for α -cyanopyrethroids, namely in a synergist:pyrethroid ratio of 20-50:1 (see also WO 04/098290). The preferred synergist is MGK264.

30 The compositions according to the invention are environmentally compatible and have a low toxicity which is reduced compared to that of known compositions. Accordingly, they are user-friendly and furthermore distinguished by their easy handling. The compositions have a favourable flashpoint of $> 70^{\circ}\text{C}$ and can therefore

be manufactured in simple plants which do not require additional measures to protect against explosions.

5 Having favourable homeotherm toxicity, the compositions of the invention are suitable for controlling parasitic arthropods, in particular insects and arachnids, very particularly fleas and ticks, encountered on animals, in particular homeotherms, particularly preferably mammals. These animals may be domestic animals and useful animals and also zoo animals, laboratory animals, test animals and pets.

10 The compositions described herein are used in particular against ectoparasites on pets, in particular dogs and cats, and useful animals.

The compositions of the invention are active against all or individual stages of development of the pests and against resistant and normally sensitive pest species.

The pests include:

15 from the order of the Anoplura, for example, Haematopinus spp., Linognathus spp., Solenopotes spp., Pediculus spp., Pthirus spp.;

from the order of the Mallophaga, for example, Trimenopon spp., Menopon spp., Eomenacanthus spp., Menacanthus spp., Trichodectes spp., Felicola spp., Damalinae spp., Bovicola spp.;

20 from the order of the Diptera, suborder Brachycera, for example, Chrysops spp., Tabanus spp., Musca spp., Hydrotaea spp., Muscina spp., Haematobosca spp., Haematobia spp., Stomoxys spp., Fannia spp., Glossina spp., Lucilia spp., Calliphora spp., Auchmeromyia spp., Cordylobia spp., Cochliomyia spp., Chrysomyia spp., Sarcophaga spp., Wohlfartia spp., Gasterophilus spp., Oesteromyia spp., Oedemagena spp., Hypoderma spp., Oestrus spp., Rhinoestrus spp., Melophagus
25 spp., Hippobosca spp..

from the order of the Diptera, suborder Nematocera, for example, Culex spp., Aedes spp., Anopheles spp., Culicoides spp., Phlebotomus spp., Simulium spp..

from the order of the Siphonaptera, for example, Ctenocephalides spp., Echidnophaga spp., Ceratophyllus spp., Pulex spp..

from the order of the Metastigmata, for example, Hyalomma spp., Rhipicephalus spp., Boophilus spp., Amblyomma spp., Haemaphysalis spp., Dermacentor spp.,
5 Ixodes spp., Argas spp., Ornithodoros spp., Otobius spp.;

from the order of the Mesostigmata, for example, Dermanyssus spp., Ornithonyssus spp., Pneumonyssus spp..

from the order of the Prostigmata, for example, Cheyletiella spp., Psorergates spp., Myobia spp., Demodex spp., Neotrombicula spp.;

10 from the order of the Astigmata, for example, Acarus spp., Myocoptes spp., Psoroptes spp., Chorioptes spp., Otodectes spp., Sarcoptes spp., Notoedres spp., Knemidocoptes spp., Neoknemidocoptes spp., Cytodites spp., Laminosioptes spp..

Particular emphasis may be given to the action against fleas (Siphonaptera, for example, Ctenocephalides spp., Echidnophaga spp., Ceratophyllus spp., Pulex spp.),
15 ticks (Hyalomma spp., Rhipicephalus spp., Boophilus spp., Amblyomma spp., Haemaphysalis spp., Dermacentor spp., Ixodes spp., Argas spp., Ornithodoros spp., Otobius spp.) and the Diptera mentioned above (Chrysops spp., Tabanus spp., Musca spp., Hydrotaea spp., Muscina spp., Haematobosca spp., Haematobia spp., Stomoxys spp., Fannia spp., Glossina spp., Lucilia spp., Calliphora spp., Auchmeromyia spp.,
20 Cordylobia spp., Cochliomyia spp., Chrysomyia spp., Sarcophaga spp., Wohlfartia spp., Gasterophilus spp., Oesteromyia spp., Oedemagena spp., Hypoderma spp., Oestrus spp., Rhinoestrus spp., Melophagus spp., Hippobosca spp.).

The useful and breeding animals include mammals, such as, for example, cattle, horses, sheep, pigs, goats, camels, water buffalo, donkeys, rabbits, fallow deer,
25 reindeer, fur-bearing animals, such as, for example, mink, chinchilla, racoon, birds, such as, for example, hens, geese, turkeys, ducks.

The laboratory animals and test animals include mice, rats, guinea pigs, rabbits, golden hamsters, dogs and cats.

The pets include dogs and cats.

Particular emphasis is given to application on cat and dog.

Application can take place both prophylactically and therapeutically.

5 Preferably, the liquid formulations according to the invention are suitable for spot-on, pour-on or spray application, where the spray application may be carried out, for example, using a pump spray or an aerosol spray (pressurized spray). For specific indications, the formulations may also be used after dilution with water as a dip; in this case, the formulation should contain emulsifying additives.

10 The preferred application forms are pump spray, pour-on and spot-on. The spot-on application is very particularly preferred.

The formulations according to the invention are distinguished by their excellent compatibility with customary "single-dose" plastic tubes and by their storage stability in various climate zones. They have low viscosity and can be applied without any problems.

15 The liquid formulations according to the invention can be prepared by mixing appropriate amounts of the components with one another, using, for example, conventional stirring tanks or other suitable instruments. If required by the ingredients, it is also possible to operate under a protective atmosphere or with other methods of excluding oxygen.

20 **Examples:**

Example 1

100 ml of liquid formulation consisting of
10.0 g of 5-amino-4-trifluoromethylsulphonyl-1-(2,6-dichloro-4-trifluoromethyl-
25 phenyl)-3-thiocarbamoylpyrazole
57.30 g of diethylene glycol monoethyl ether
0.10 g of BHT
0.20 g of BHA

- 30.02 g of propylene carbonate
5.00 g of propylene glycol octanoate decanoate
0.24 g of flumethrin
10.36 g of MGK 264
5 0.02 g of citric acid

Example 2

- 100 ml of liquid formulation consisting of
10 10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
0.24 g of flumethrin
0.02 g of citric acid
0.20 g of BHT
15 68.00 g of dipropylene glycol monomethyl ether
13.40 g of propylene carbonate
5.00 g of demineralized water
5.00 g of propylene glycol octanoate decanoate
5.00 g of MGK 264
20

Example 3

- 100 ml of liquid formulation consisting of
10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
25 0.50 g of PPF (pyriproxyfen)
0.24 g of flumethrin
0.02 g of citric acid
0.20 g of BHT
30 67.50 g of dipropylene glycol monomethyl ether
13.40 g of propylene carbonate
5.00 g of demineralized water
5.00 g of propylene glycol octanoate decanoate

5.00 g of MGK 264

Example 4

100 ml of liquid formulation consisting of

- 5 10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
- 0.50 g of PPF (pyriproxyfen)
- 0.24 g of flumethrin
- 0.02 g of citric acid
- 10 0.20 g of BHT
- 60.90 g of diethylene glycol monoethyl ether
- 20.00 g of propylene carbonate
- 5.00 g of demineralized water
- 5.00 g of propylene glycol octanoate decanoate
- 15 5.00 g of MGK 264

Example 5

100 ml of liquid formulation consisting of

- 20 10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
- 45.00 g of permethrin
- 37.90 g of diethylene glycol monoethyl ether
- 0.10 g of BHT
- 25 0.20 g of BHA
- 25.00 g of propylene carbonate
- 5.00 g of propylene glycol octanoate decanoate
- 0.02 g of citric acid

30 Example 6

100 ml of liquid formulation consisting of

- 10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
- 45.00 g of permethrin
- 1.00 g of PPF
- 5 36.90 g of diethylene glycol monoethyl ether
- 0.10 g of BHT
- 0.20 g of BHA
- 25.00 g of propylene carbonate
- 5.00 g of propylene glycol octanoate decanoate
- 10 0.02 g of citric acid

Example 7

- 100 ml of liquid formulation consisting of
- 15 10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
- 45.00 g of permethrin
- 1.00 g of PPF
- 0.25 g of Silvet L 77 from GE Siliconocs GmbH D-51368 Leverkusen
- 20 36.65 g of diethylene glycol monoethyl ether
- 0.10 g of BHT
- 0.20 g of BHA
- 25.00 g of propylene carbonate
- 5.00 g of propylene glycol octanoate decanoate
- 25 0.02 g of citric acid

Example 8

- 10.00 g of 5-amino-4-trifluoromethylsulphanyl-1-(2,6-dichloro-4-trifluoromethyl-phenyl)-3-thiocarbamoylpyrazole
- 30 45.00 g of permethrin
- 1.00 g of PPF
- 0.25 g of Silvet L 77 (from Bayer-GE Silicones GmbH, D-51368 Leverkusen)

- 36.65 g of diethylene glycol monoethyl ether
- 0.10 g of BHT
- 0.20 g of BHA
- 25.00 g of ethylene carbonate
- 5 5.00 g of propylene glycol octanoate decanoate
- 0.02 g of citric acid

Comparative Example 1

- A commercially available 10% fipronil spot-on formulation from Merial Ltd., 3239
10 Satellite Blvd., Duluth, GA 30096-4640, USA.

Comparative Example 2

- A formulation comprising 5-amino-4-trifluoromethylsulphonyl-1-(2,6-dichloro-
4-trifluoromethylphenyl)-3-thiocarbamoylpyrazole, but without added flumethrin or
15 MGK264:

- 100 ml of liquid formulation consisting of
- 10.00 g of 5-amino-4-trifluoromethylsulphonyl-1-(2,6-dichloro-4-trifluoromethyl-
phenyl)-3-thiocarbamoylpyrazole
 - 20 57.7 g of diethylene glycol monoethyl ether
 - 40.0 g of propylene carbonate
 - 5.0 g of propylene glycol octanoate decanoate
 - 0.1 g of butylated hydroxytoluene
 - 0.2 g of butylated hydroxyanisole
- 25

Comparative Example 3

- A formulation comprising flumethrin and MGK264 and PPF, but, instead of the
3-thiocarbamoylpyrazole mentioned in the application, the known insecticide
imidacloprid.

- 30
- 100 ml of liquid formulation consisting of
- 10.00 g of imidacloprid
 - 0.50 g of PPF

- 56.80 g of benzyl alcohol
- 0.10 g of BHT
- 0.20 g of BHA
- 30.02 g of propylene carbonate
- 5 5.00 g of propylene glycol octanoate decanoate
- 0.24 g of flumethrin
- 10.36 g of MGK 264
- 0.02 g of citric acid

10 **Biological examples**

All compounds were metered out exactly by weight to ensure better comparability. To this end, 20 pipettes of the fipronil-containing commercial preparation were emptied into a glass bottle and likewise blinded using a code.

- 15 All samples were applied as a single spot to the neck (cats and smaller dogs) using Eppendorf pipettes (volume up to 0.95 ml). For application volumes of more than 1 ml, the volume was halved and applied to the neck as two spots at a distance of about 10 cm.
- 20 Further laboratory tests for the activity against fleas and ticks according to Example 2 show that the preparations in the abovementioned formulations according to the invention have very good and long-lasting action against ticks and fleas which, in the tests, is consistently superior to the prior art (CE1 - CE3). Furthermore, the preparations in the abovementioned formulations according to the invention are
- 25 distinguished in that they are tolerated by target animal and user, and they are thus highly suitable for controlling fleas and ticks on small animals.

A. Activity against fleas (Ctenocephalides felis) on dogs

- 30 Between days -4 and -1, dogs are infested 1-2 times with about 100 adult unfed Ctenocephalides felis per dog. The fleas are placed on the neck of the animal.
- On day 0, the success of the infestation on the dog is examined by checking the awake animal for fleas. The number of live fleas is noted.

After the fleas have been counted, the animals are treated. The dogs of the control group are not treated. The medicaments to be examined are administered to the animals dermally as a spot-on in an application rate of 0.1-0.15 ml/kg of bodyweight or as a spray in an application rate of 1-1.5 ml/kg of bodyweight. The application is carried out once on day 0. Only animals that are clinically healthy are used.

On days 1 and 2, all dogs are examined for live fleas. The results are noted with the crude data.

On days 7, 14, 21, 28 and 35 and, if appropriate, also on days 42 and 49, all dogs are reinfested with about 100 adult unfed *Ctenocephalides felis* per dog. In each case one day after the reinfestation, all dogs are checked for live fleas. The results are noted with the crude data.

A formulation is considered to be highly effective if, between 24 and 48 hours after reinfestation, an efficacy of > 95% is found, and this action persists for at least 3-4 weeks.

The efficacy is calculated using a modified formula according to Abbott:

$$\text{Efficacy \%} = \frac{\text{number of fleas CG} - \text{number of fleas TG}}{\text{number of fleas CG}} \times 100$$

CG: control group; TG: treatment group

The medicaments of Formulation Example 2, applied as a spot-on at a dosage of 0.15 ml/kg, were found to be highly effective against *Ctenocephalides felis*.

B. Activity against ticks (*Rhipicephalus sanguineus*, *Dermacentor variabilis*) on dogs

Between days -4 and -1, dogs are sedated using 2% Rompun® (Bayer AG, active compound: xylazine hydrochloride) (0.1 ml/kg of bodyweight). Once all dogs have been sedated (after about 10-15 minutes), they are transferred to transport boxes, and 50 *Rhipicephalus sanguineus* or *Dermacentor variabilis* (25♀, 25♂) per dog are applied to the neck of the animal. After about 1½ hours, the animals are retransferred from the transport box into the cage.

On day 0, the success of the infestation on the dog is examined by checking the awake animal for ticks. An intensive search is carried out in the region of the head

and the ears, including the folds of the ears, in the region of the neck, on the lower abdomen, on the lower breast, on the flank and in between the toes and on the limbs. The number of sucking live ticks is noted. Dead ticks are removed.

After the ticks have been counted, the animals are treated. The dogs of the control group are not treated. The medicaments to be examined are administered to the animals dermally as a spot-on at 0.1-0.15 ml/kg of bodyweight or as a spray at 1-1.5 ml/kg of bodyweight. The application is carried out once on day 0. Only animals which are clinically healthy are used.

On day 1 and day 2, all dogs are checked for living and dead sucking ticks. The results are noted with the crude data. On day 2, all living and dead ticks are removed from the dog.

On days 7, 14, 21, 28, 35 and, if appropriate, also on days 42 and 49, all dogs are reinfested with in each case 50 *Rhipicephalus sanguineus* or *Dermacentor variabilis* (25♀, 25♂) per dog. In each case two days after the reinfestation, all dogs are checked for living and dead sucking ticks. The results are noted with the crude data. On the second day after the reinfestation, all living and dead ticks are removed from the dog.

A formulation is considered to be highly effective if, on day 2 and in each case on the second day after reinfestation, an efficacy of > 90% is found, and this action persists for at least 3 weeks.

For calculating the efficacy, a modified formula according to Abbott is used:

$$\text{Efficacy \%} = \frac{\text{number of ticks CG} - \text{number of ticks TG}}{\text{number of ticks CG}} \times 100$$

CG: control group; TG: treatment group

The medicaments according to Formulation Example 2, applied as a spot-on at a dosage of 0.15 ml/kg, were found to be highly effective against *Rhipicephalus sanguineus*.

C. Activity against fleas (*Ctenocephalides felis*) on cats

30

On day -1, cats are infested with about 100 adult unfed *Ctenocephalides felis* per cat. The fleas are placed on the neck of the animal.

On day 0, the success of the infestation on the cat is examined by checking the awake animal for fleas. The number of live fleas is noted.

After the fleas have been counted, the animals are treated. The cats of the control group are not treated. The medicaments to be examined are administered to the
5 animals dermally as a spot-on in an application rate of 0.1-0.15 ml/kg of bodyweight. The application is carried out once on day 0. Only animals that are clinically healthy are used.

On day 2, all cats are examined for live fleas. The results are noted with the crude data.

10 On days 7, 14, 21, 28 and 35 and, if appropriate, also on days 42 and 49, all cats are reinfested with about 100 adult unfed *Ctenocephalides felis* per cat. In each case two days after reinfestation, all cats are checked for live fleas. The results are noted with the crude data.

A formulation is considered to be highly effective if, on day 2 and in each case on
15 the second day after reinfestation, an efficacy of > 95% is found, and this action persists for at least 3-4 weeks.

The efficacy is calculated using a modified formula according to Abbott:

$$\text{Efficacy \%} = \frac{\text{number of fleas CG} - \text{number of fleas TG}}{\text{number of fleas CG}} \times 100$$

CG: control group; TG: treatment group

20

The medicaments of Formulation Example 2, applied as a spot-on at a dosage of 0.15 ml/kg, were found to be highly effective against *Ctenocephalides felis*.

D. Activity against ticks (*Ixodes ricinus*) on cats

25

In each case on day -2, cats are sedated using a mild sedative (acepromazine maleate). Once all cats have been sedated (after about 10-15 minutes), 30-50 *Ixodes ricinus* (15-25♀, 15-25♂) per cat are applied to the neck of the animal.

On day -1, the success of the infestation on the cats is examined by checking the
30 awake animal for ticks. An intensive search is carried out in the region of the head and the ears, in the region of the neck, on the lower abdomen, on the lower breast, on

the flank and on the limbs. The number of sucking live ticks is noted. Dead ticks are removed.

After the ticks have been counted, the animals are divided into groups. Treatment is carried out on day 0. The cats of the control group are not treated. The medicaments
5 to be examined are administered to the animals dermally, as a spot-on at 0.1-0.15 ml/kg of bodyweight. Application is carried out once on day 0. Only animals which are clinically healthy are used.

On day 2, all cats are checked for living and dead sucking ticks. The results are noted with the crude data. All living and dead ticks are removed from the cat.

10 On days 7, 14, 21, 28 and 35 and, if appropriate, also on days 42 and 49, all cats are reinfested with in each case 30-50 *Ixodes ricinus* (15-25♀, 15-25♂) per cat . In each case two days after the reinfestation, all cats are checked for living and dead sucking ticks. The results are noted with the crude data. On the second day after the reinfestation, all living and dead ticks are removed from the cat.

15 A formulation is considered to be highly effective if, on day 2 and in each case on the second day after reinfestation, an efficacy of > 90% is found, and this action persists for at least 3 weeks.

For calculating the efficacy, a modified formula according to Abbott is used:

$$\text{Efficacy \%} = \frac{\text{number of ticks CG} - \text{number of ticks TG}}{\text{number of ticks CG}} \times 100$$

20 CG: control group; TG: treatment group

The medicaments according to Formulation Example 2, applied as a spot-on at a dosage of 0.15 ml/kg, were found to be highly effective against *Ixodes ricinus*.

E. Efficacy against fleas and ticks over 4 to 7 weeks

25

The efficacy of the compositions according to the invention against fleas and ticks was tested over a period of four to seven weeks. The test was carried out according to the description under items A to D.

Table 1a Efficacy of the composition according to Example 2 against fleas on cats

10		Appl. Vol	Parasite	W0	2. infestation day 7		WD	3. infestation day 14		W2	4. infestation day 21		W3	5. infestation day 28		W4	6. infestation day 35		W5
Treatment	ml/kg	D2		D9	D16	D23	D30	D37											
CE 1	0.1		Ctenocephalides felis	97		100		100		100		100		100		99		100	D37
CE 2	0.15		Ctenocephalides felis	99		100		100		100		100		100		100		100	100
Example 2	0.15		Ctenocephalides felis	99		100		100		100		100		100		100		100	99
CE 3	0.1		Ctenocephalides felis	100		100		100		100		100		99		94		74	
1. infestation day -4																			

Table 1b Efficacy of the composition according to Example 2 against ticks on cats

10		Appl. Vol	Parasite	W0		2. infestation day 7		WD		3. infestation day 14		W2		4. infestation day 21		W3		5. infestation day 28		W4		6. infestation day 35		W5
Treatment		ml/kg		D2	D9	D16	D23	D30	D37															
CE 1	0.1		Ixodes ricinus	74	99	96	92	84	72	D30	82	73	100	93	D37	89	68	95	76					
CE 2	0.15		Ixodes ricinus	84	99	92	100	100	100															
Example 2	0.15		Ixodes ricinus	70	100	100	100	100	100															
CE 3	0.1		Ixodes ricinus	71	100	100	100	100	100															
1. infestation day -4																								

5 Appl. Vol = volume applied in ml/kg of bodyweight
“value” % = efficacy in %, calculated via determination of the geometrical mean compared to an untreated control group

Table 2a Efficacy of the composition according to Example 2 against fleas on dogs

				2. infestation day -1				1. infestation day -4																									
D0	Appl. Vol	Parasite	W0	3. infestation day 7					W1		4. infestation day 14		W2		5. infestation day 21		W3		6. infestation day 28		W4		7. infestation day 35		W5		8. infestation day 42		W6		9. infestation day 49		W7
Treatment	ml/kg		D2						D9				D16				D23				D30				D37		D44		D51				
CE 1	0.1		Ctenocephalides felis	100						100				100				99				99				100		62		33			
CE 2	0.15		Ctenocephalides felis	100						100				100				100				100				99		99		76			
Example 2	0.15	Ctenocephalides felis	100						99						100				100				100		100		100		77				
CE 3	0.1	Ctenocephalides felis	100						100												98		74		nd		nd						

Table 2b Efficacy of the composition according to Example 2 against ticks on dogs

1. infestation day -4				2. infestation day -1				D0	Appl. Vol	Parasite		W0		3. infestation day 7				W1		4. infestation day 14				W2		5. infestation day 21				W3		6. infestation day 28				W4		7. infestation day 35				W5		8. infestation day 42				W6		9. infestation day 49				W7	
								Treatment	ml/kg					D2						D9						D16						D23						D30						D37						D44				D51	
CE 1				0.1				Rhipicephalus sanguineus				97						100		100		100		99		100				100		100				99		94				93				65									
CE 2				0.15				Rhipicephalus sanguineus				96						100		100		100		100		100				100		100				100		99				98				74									
Example 2				0.15				Rhipicephalus sanguineus				92						100		100		100		100		100				100		100				100		99				99				88									
CE 3				0.1				Rhipicephalus sanguineus				60						94						99		98				98		98				98		91				nd				nd									

Appl. Vol = volume applied in ml/kg of bodyweight
“value” % = efficacy in %, calculated via determination of the arithmetic mean compared to an untreated control group

Table 3 Efficacy of the composition according to Example 2 against ticks on dogs

1. infestation day -4		2. infestation day 7		3. infestation day 14		4. infestation day 21		5. infestation day 28	
D0	Appl. Vol	Parasite	W0	W1	W2	W3	W4		
Treatment	ml/kg		D2	D9	D16	D23	D30		
CE 1	0.15	Dermacentor variabilis	25	98	99	100	98		
Example 2	0.15	Dermacentor variabilis	55	100	99	100	100		
CE 3	0.1	Dermacentor variabilis	34	89	80	66	87		

Appl. Vol = volume applied in ml/kg of bodyweight

5 “value” % = efficacy in %, calculated via determination of the geometrical mean compared to an untreated control group

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CLAIMS:

1. Composition for controlling parasites on animals, comprising an N-arylpyrazole and a pyrethroid in a formulation comprising:
 - an aliphatic cyclic carbonate;
 - 5 - an aliphatic cyclic or acyclic polyether; and
 - one or more esters of a dihydric or trihydric alcohol having up to three carbon atoms with organic fatty acids having 6 to 18 carbon atoms.
2. Composition according to claim 1, comprising from 1 to 27.5% by weight of the N-arylpyrazole.
- 10 3. Composition according to claim 1, comprising from 5 to 20% by weight of the N-arylpyrazole.
4. Composition according to any one of claims 1 to 3, comprising from 10 to 70% by weight of the aliphatic cyclic carbonate.
5. Composition according to any one of claims 1 to 3, comprising from 12.5 to
15 50% by weight of the aliphatic cyclic carbonate.
6. Composition according to any one of claims 1 to 5, comprising from 20 to 77.5% by weight of the aliphatic cyclic or acyclic polyether.
7. Composition according to any one of claims 1 to 5, comprising from 25 to 65% by weight of the aliphatic cyclic or acyclic polyether.
- 20 8. Composition according to any one of claims 1 to 7, comprising from 1 to 12.5% by weight of the one or more esters of a dihydric or trihydric alcohol.
9. Composition according to any one of claims 1 to 8, wherein the pyrethroid comprises an α -cyanopyrethroid.

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10. Composition according to claim 9, wherein the α -cyanopyrethroid comprises alpha-cypermethrin, cyfluthrin, beta-cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, fenvalerate, flucythrinate, flumethrin or tau-fluvalinate.
11. Composition according to any one of claims 1 to 8, wherein the pyrethroid
5 comprises a type 1 pyrethroid.
12. Composition according to claim 11, wherein the type 1 pyrethroid comprises allethrin, bioallethrin, permethrin, phenothrin, resmethrin, tetramethrin or transfluthrin.
13. Composition according to any one of claims 1 to 8, wherein the pyrethroid comprises a non-ester pyrethroid.
- 10 14. Composition according to claim 13, wherein the non-ester pyrethroid comprises etofenprox, halfenprox, or silafluofen.
15. Composition according to claim 11, comprising from 30 to 60% by weight of the type 1 pyrethroid.
16. Composition according to claim 9, comprising from 0.01 to 5% by weight of
15 the α -cyanopyrethroid.
17. Composition according to claim 13, comprising from 10 to 60% by weight of the non-ester pyrethroid.
18. Use of the composition as defined in any one of claims 1 to 17 for controlling parasites on animals.