The present invention relates to novel imidazole derivatives of formula I as active ingredients which have microbicidal activity, in particular fungicidal activity wherein (I) wherein R is halogen, Cl-C alkyl or Cl-C alkoxyalkyl, R is an optionally substituted aryl, Cl is halogen or OR, R and R are, independently of each other, hydrogen, halogen or OR. R is halogen or Cl-C alkyl, and R is hydrogen, Cl-C alkyl, C-C cycloalkyl, C-C cycloalkylalkyl, Cl-C haloalkyl, C-C alkenyl, C-C haloalkenyl, C-C cycloalkenyl, C-C alkoxyalkyl, C-C dialkylaminoalkyl, C-C haloalkylaminoalkyl or C-C heterocyclylalkyl, or an agrochemically usable salt form thereof, provided that when R is halogen, at least one of R or R is OR, or when R is OR, at least one of R or R is OR or halogen.

**Title:** NOVEL IMIDAZOLE DERIVATIVES HAVING MICROBICIDAL ACTIVITY

**Abstract:** The present invention relates to novel imidazole derivatives of formula I as active ingredients which have microbicidal activity, in particular fungicidal activity wherein (I) wherein R is halogen, Cl-C alkyl or Cl-C alkoxyalkyl, R is an optionally substituted aryl, Cl is halogen or OR, R and R are, independently of each other, hydrogen, halogen or OR. R is halogen or Cl-C alkyl, and R is hydrogen, Cl-C alkyl, C-C cycloalkyl, C-C cycloalkylalkyl, Cl-C haloalkyl, C-C alkenyl, C-C haloalkenyl, C-C cycloalkenyl, C-C alkoxyalkyl, C-C dialkylaminoalkyl, C-C haloalkylaminoalkyl or C-C heterocyclylalkyl, or an agrochemically usable salt form thereof, provided that when R is halogen, at least one of R or R is OR, or when R is OR, at least one of R or R is OR or halogen.
NOVEL IMIDAZOLE DERIVATIVES HAVING MICROBIOCIDAL ACTIVITY

The present invention relates to novel imidazole derivatives as active ingredients which have microbiocidal activity, in particular fungicidal activity. The invention also relates to preparation of these active ingredients, to novel heterocyclic derivatives used as intermediates in the preparation of these active ingredients, to preparation of these novel intermediates, to agrochemical compositions which comprise at least one of the novel active ingredients, to preparation of these compositions and to use of the active ingredients or compositions in agriculture or horticulture for controlling or preventing infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms, preferably fungi.

The present invention provides a compound of formula I:

![Chemical Structure](image)

wherein

R¹ is halogen, d-C₄ alkyl or d-C₄ haloalkyl;
R² is an optionally substituted aryl;
R³ is halogen or OR⁷;
R⁴ and R⁵ are, independently of each other, hydrogen, halogen or OR⁷;
R⁶ is halogen or CrC₄ alkyl; and

R⁷ is hydrogen, Ci-C₆ alkyl, C₃-C₇ cycloalkyl, C₃-Ci₀ cycloalkylalkyl, Ci-C₆ haloalkyl, C₂-C₆ alkenyl, C₂-C₆ haloalkenyl, C₃-C₇ cycloalkenyl, C₂-C₆ alkynyl, C₂-C₆ haloalkynyl, C₂-C₆ alkoxyalkyl, C₃-C₆ dialkylaminoalkyl, C₄-Ci₀ cycloalkylaminoalkyl or C₄-Ci₀ heterocyclylalkyl;

or an agrochemically usable salt form thereof;

provided that

when R³ is halogen, at least one of R⁴ or R⁵ is OR⁷; or
when $R^3$ is $OR^7$, at least one of $R^4$ or $R^5$ is $OR^7$ or halogen.

In the above definition aryl includes aromatic hydrocarbon rings like phenyl, naphthyl, anthracenyl, phenanthrenyl and biphenyl, with phenyl being preferred.

In the above definition, alkyl, alkenyl and alkynyl moieties can be in the form of straight or branched chains, and the alkenyl moieties, where appropriate, can be of either the (E)- or (Z)-configuration. Examples are vinyl, allyl and propargyl. Alkenyl and alkynyl moieties can contain one or more double and/or triple bonds in any combination. It is understood, that allenyl and alkylalkenyl are included in these terms.

In the above definition, $C_2\text{C}_6$ alkyl for example, means that the sum of the carbon atom of the two alkyl parts is between 2 and 6 carbon atoms. As a matter of example, it also applies to $C_3\text{C}_8$ dialkylalkyl or $C_4\text{Cl}_0$ heterocyclalkyl.

The above or below mentioned fused ring, carbocyclic ring, heterocyclic ring and aryl group may be optionally substituted. This means that they may carry one or more identical or different substituents. Normally not more than three substituents are present at the same time. Examples of substituents are: halogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, haloalkenyl, cycloalkenyl, alkynyl, haloalkynyl, alkoxy, haloalkoxy, cycloalkoxy, alkenyloxy, haloalkenyloxy, alkynyl, haloalkynyl, alkylthio, haloalkylthio, cycloalkylthio, alkenylthio, alkynylthio, alkylcarbonyl, haloalkylcarbonyl, cycloalkylcarbonyl, alkenylcarbonyl, alkynylcarbonyl, alkoxyalkyl, cyano, nitro, hydroxy, mercapto, amino, alkylamino, dialkylamino. Typical examples for optionally substituted aryl include 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 4-bromophenyl, m-tolyl, p-tolyl, 3-trifluoromethylphenyl, 3-trifluoromethylphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3-trifluoromethoxyphenyl, 3-trifluoromethoxyphenyl, 3-cyanophenyl, 4-cyanophenyl, 2,4-difluorophenyl, 2,5-
difluorophenyl, 2,6-difluorophenyl, 3,4-difluorophenyl, 2,4-dichlorophenyl, 2,5-
dichlorophenyl, 2,6-dichlorophenyl, 3,4-dichlorophenyl, 3,4-dimethoxyphenyl, 2-chloro-4-fluorophenyl, 2-chloro-5-fluorophenyl, 2-chloro-6-fluorophenyl, 3-chloro-4-fluorophenyl, 3-chloro-6-fluorophenyl, 3-chloro-4-methylphenyl, 3-chloro-4-methoxyphenyl, 4-chloro-2-fluorophenyl, 4-chloro-3-fluorophenyl, 4-chloro-3-methylphenyl, 4-chloro-3-methoxyphenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-4-methylphenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-4-methylphenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-4-methylphenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-4-methylphenyl, 4-fluoro-3-methylphenyl, 3-methoxy-4-methylphenyl, 4-methoxy-3-methylphenyl, 2,6-difluoro-4-methylphenyl, 2,6-difluoro-4-trifluoromethylphenyl, 2,6-difluoro-4-methoxyphenyl, 2,6-difluoro-4-trifluoromethoxyphenyl, 2,6-difluoro-4-cyanophenyl, 2,4,6-
trifluorophenyl, 2,5,6-trifluorophenyl.

In the above definition halogen is fluorine, chlorine, bromine or iodine.

Alkyl on its own or as part of another substituent is, depending upon the number of
carbon atoms mentioned, for example, methyl, ethyl, propyl, butyl, pentyl, hexyl and the
isomers thereof, for example, isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl or tert-
pentyl.

A haloalkyl group may contain one or more identical or different halogen atoms and,
for example, may stand for CH₂Cl, CHCl₂, CCl₃, CH₂F, CHF₂, CF₃, CF₃CH₂, CH₃CF₂, CF₃CF₂
or CCl₃CCl₂.

Cycloalkyl on its own or as part of another substituent is, depending upon the number
of carbon atoms mentioned, for example, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

Alkenyl on its own or as part of another substituent is, depending upon the number of
carbon atoms mentioned, for example, ethenyl, allyl, 1-propenyl, buten-2-yl, buten-3-yl,
penten-1-yl, penten-3-yl, hexen-1-yl or 4-methyl-3-pentenyl.
Alkynyl on its own or as part of another substituent is, depending upon the number of carbon atoms mentioned, for example, ethynyl, propyn-1-yl, propyn-2-yl, butyn-1-yl, butyn-2-yl, 1-methyl-2-butynyl, hexyn-1-yl or 1-ethyl-2-butynyl.

The presence of one or more possible asymmetric carbon atoms in a compound of formula I means that the compounds may occur in optically isomorphic, that means enantiomeric or diastereomeric forms. As a result of the presence of a possible aliphatic C=C double bond, geometric isomerism, that means cis-trans or (E)-(Z) isomerism may also occur. Also atropisomers may occur as a result of restricted rotation about a single bond.

Formula I is intended to include all those possible isomeric forms and mixtures thereof. The present invention intends to include all those possible isomeric forms and mixtures thereof for a compound of formula I.

In each case, the compounds of formula I according to the invention are in free form or in an agronomically usable salt form.

In a first embodiment, compounds of formula I according to the invention have R₁ which is halogen or d-C₃ alkyl.

In a second embodiment, compounds of formula I according to the invention have R₂ which is an optionally substituted phenyl.

In a third embodiment, compounds of formula I according to the invention have R₃ which is fluoro, chloro, bromo or OR⁷.

In a fourth embodiment, compounds of formula I according to the invention have R₄ and R₅ which are, independently of each other, hydrogen, chloro, fluoro, bromo or OR⁷.

In a fifth embodiment, compounds of formula I according to the invention have R₆ which is chloro, fluoro, bromo or d-C₃ alkyl.
In a sixth embodiment, compounds of formula I according to the invention have R\(^7\) which is hydrogen, CrC\(_5\) alkyl, C\(_3\)-C\(_6\) cycloalkyl, C\(_3\)-C\(_9\) cycloalkylalkyl, CrC\(_5\) haloalkyl, C\(_2\)-C\(_5\) alkenyl, C\(_2\)-C\(_5\) haloalkenyl, C\(_3\)-C\(_6\) cycloalkenyl, C\(_2\)-C\(_5\) alkynyl, C\(_2\)-C\(_5\) haloalkynyl, C\(_2\)-C\(_5\) alkyloxyalkyl, C\(_3\)-C\(_7\) dialkylaminoalkyl, C\(_4\)-C\(_9\) cycloalkylaminoalkyl or C\(_4\)-C\(_9\) heterocyclylalkyl.

Preferred subgroups of compounds of formula I according to the invention are those wherein

R\(^1\) is chloro, fluoro or C\(_i\)-C\(_j\) alkyl;

R\(^2\) is 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 4-bromophenyl, m-tolyl, p-tolyl, 3-methoxyphenyl, 4-methoxyphenyl, 3-cyanophenyl, 4-cyanophenyl, 3,4-difluorophenyl, 3,4-dichlorophenyl, 3-chloro-4-fluorophenyl, 4-chloro-3-fluorophenyl, 3-fluoro-4-methoxyphenyl, 2-fluorophenyl, 2-chlorophenyl, 2-bromophenyl, 2-methoxyphenyl, o-tolyl or 4-chloro-2-fluorophenyl;

R\(^3\) is chloro, fluoro or OR\(^7\);

R\(^4\) and R\(^5\) are, independently of each other, hydrogen, chloro, fluoro or OR\(^7\);

R\(^6\) is chloro or methyl; and

R\(^7\) is hydrogen, C\(_r\) C\(_3\) alkyl, C\(_3\)-C\(_6\) cycloalkylalkyl, C\(_2\)-C\(_5\) alkenyl, C\(_2\)-C\(_4\) alkynyl, C\(_2\)-C\(_4\) alkyloxyalkyl, C\(_3\)-C\(_6\) dialkylaminoalkyl, C\(_4\)-C\(_8\) cycloalkylaminoalkyl or C\(_4\)-C\(_8\) heterocyclylalkyl.

More preferred subgroups of compounds of formula I according to the invention are those wherein

R\(^1\) is chloro, methyl or ethyl;

R\(^2\) is 4-chlorophenyl;

R\(^3\) is fluoro or OR\(^7\);

R\(^4\) is fluoro or OR\(^7\);

R\(^5\) is hydrogen or fluoro;

R\(^6\) is chloro; and

R\(^7\) is methyl, ethyl, propargyl, 1-pyrrolidinylethyl, dimethylaminopropyl or C\(_3\)-C\(_5\) allenyl.

Preferred individual compounds are:
2,4-dichloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1H-imidazole,
2,4-dichloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1H-imidazole,
5 4-chloro-1-(4-chloro-phenyl)-5-(4-ethoxy-2,6-difluoro-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-propoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-[2,6-difluoro-4-(2-methoxy-ethoxy)-phenyl]-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-prop-2-ynyloxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1-p-tolyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole,
10 4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-prop-2-ynyloxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1-p-tolyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,4-difluoro-6-methoxy-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole,
15 4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-(2-pyrrolidin-1-yl-ethoxy)-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-prop-2-ynyloxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-prop-2-ynyloxy-phenyl)-2-methyl-1H-imidazole,
20 4-chloro-1-(4-chloro-phenyl)-5-(2-ethoxy-4,6-difluoro-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2-ethoxy-4,6-difluoro-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole.

The compounds of formula 1.1, wherein R² and R⁷ are as defined for compound of
formula 1, and R¹ is C⁴alkyl, can be obtained by reaction of a compound of formula II,
wherein R² is as defined for compound of formula I, and R¹ is C⁴alkyl, with a reagent of
formula NaOR⁷, wherein R⁷ is as defined for compound of formula I.
The compounds of formula 1.2, wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined for compound of formula I, and R<sup>1</sup> is CrC<sub>4</sub>alkyl or Ci-C<sub>4</sub>haloalkyl, can be obtained by reaction of a compound of formula III, wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined for compound of formula I, and R<sup>1</sup> is CrC<sub>4</sub>alkyl or Ci-C<sub>4</sub>haloalkyl, with N-chlorosuccinimide or molecular chlorine.

The compounds of formula III, wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined for compound of formula I, and R<sup>1</sup> is Ci-C<sub>4</sub>alkyl, can be obtained by transformation of a compound of formula IV, wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined for compound of formula I, with a reagent of formula (R<sup>1</sup>)<sub>3</sub>Al, wherein R<sup>1</sup> is Ci-C<sub>4</sub>alkyl, preferably methyl, in the presence of a transition metal catalyst.

The compounds of formula III, wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined for compound of formula I, and R<sup>1</sup> is Ci-C<sub>4</sub>alkyl or CrC<sub>4</sub>haloalkyl, can alternatively be obtained by
transformation of a compound of formula V, wherein \( R^2, R^3, R^4 \) and \( R^5 \) are as defined for compound of formula I, with a strong base, e.g. lithium di-isopropylamide, followed by a reagent of formula \( R^1\text{Hal} \), wherein \( R^1 \) is \( \text{CrC}_4 \text{alkyl} \) or \( \text{Ci-C}_4 \text{haloalkyl} \), and \( \text{Hal} \) is halogen, preferably bromine or iodine.

The compounds of formula I, wherein \( R^2, R^3, R^4 \) and \( R^5 \) are as defined for compound of formula I, and \( R^1 \) and \( R^6 \) are Halogen, preferably chlorine or bromine, can be obtained by reaction of a compound of formula V, wherein \( R^2, R^3, R^4 \) and \( R^5 \) are as defined for compound of formula I, with at least 2 equivalents of N-chlorosuccinimide, N-bromosuccinimide, molecular chlorine or bromine.

The compounds of formula IV, wherein \( R^2, R^3, R^4 \) and \( R^5 \) are as defined for compound of formula I, can be obtained by transformation of a compound of formula V, wherein \( R^2, R^3, R^4 \) and \( R^5 \) are as defined for compound of formula I, with N-bromosuccinimide.
The compounds of formula VI and VII, wherein R² and R⁷ are as defined for compound of formula I, can be obtained by reaction of a compound of formula VIII, wherein R² is as defined for compound of formula I, with a reagent of formula NaOR⁷, wherein R⁷ is as defined for compound of formula I.

![Chemical structure of compounds VI, VII, and VIII]

The compounds of formula V, wherein R², R³, R⁴ and R⁵ are as defined for compound of formula I, can be obtained by reaction of a compound of formula IX, wherein R², R³, R⁴ and R⁵ are as defined for compound of formula I, with toluenesulfonylmethyl isocyanide in the presence of a base, e.g. anhydrous potassium carbonate, as already described in Journal of Medicinal Chemistry 2003, 46, 3463.

![Chemical structure of compounds V, IX, and VIII]

The compounds of formula IX, wherein R², R³, R⁴ and R⁵ are as defined for compound of formula I, can be obtained by reaction of an aldehyde of formula X, wherein R³, R⁴ and R⁵ are as defined for compound of formula I, with an amine of formula XI, wherein R² is as defined for compound of formula I, as already described in Journal of Medicinal Chemistry 2003, 46, 3463.
Surprisingly, it has now been found that the novel compounds of formula I have, for practical purposes, a very advantageous level of biological activity for protecting plants against diseases that are caused by fungi as well as by bacteria and viruses.

The compounds of formula I can be used in the agricultural sector and related fields of use as active ingredients for controlling plant pests or on non-living materials for control of spoilage microorganisms or organisms potentially harmful to man. The novel compounds are distinguished by excellent activity at low rates of application, by being well tolerated by plants and by being environmentally safe. They have very useful curative, preventive and systemic properties and are used for protecting numerous cultivated plants. The compounds of formula I can be used to inhibit or destroy the pests that occur on plants or parts of plants (fruit, blossoms, leaves, stems, tubers, roots) of different crops of useful plants, while at the same time protecting also those parts of the plants that grow later e.g. from phytopathogenic microorganisms.

It is also possible to use compounds of formula I as dressing agents for the treatment of plant propagation material, e.g., seed, such as fruits, tubers or grains, or plant cuttings (for example rice), for the protection against fungal infections as well as against phytopathogenic fungi occurring in the soil. The propagation material can be treated with a composition comprising a compound of formula I before planting: seed, for example, can be dressed before being sown. The active ingredients according to the invention can also be applied to grains (coating), either by impregnating the seeds in a liquid formulation or by coating them with a solid formulation. The composition can also be applied to the planting site when the propagation material is being planted, for example, to the seed furrow during sowing. The invention relates also to such methods of treating plant propagation material and to the plant propagation material so treated.
Furthermore the compounds according to present invention can be used for controlling fungi in related areas, for example in the protection of technical materials, including wood and wood related technical products, in food storage, in hygiene management.

In addition, the invention could be used to protect non-living materials from fungal attack, e.g. lumber, wall boards and paint.

The compounds of formula I are, for example, effective against the phytopathogenic fungi of the following classes: Fungi imperfecti (e.g. Alternaria spp.), Basidiomycetes (e.g. Corticium spp., Ceratobasidium spp., Waitea spp., Thanatephorus spp., Rhizoctonia spp., Hemileia spp., Puccinia spp., Phakopsora spp., Ustilago spp., Tilletia spp.), Ascomycetes (e.g. Venturia spp., Blumeria spp., Erysiphe spp., Podosphaera spp., Uncinula spp., Monilinia spp., Sclerotinia spp., Colletotrichum spp., Glomerella spp., Fusarium spp., Gibberella spp., Monographella spp., Phaeosphaeria spp., Mycosphaerella spp., Cercospora spp., Pyrenophora spp., Rhynchosporium spp., Magnaporthe spp., Gaeumannomyces spp., Oculimacula spp., Ramularia spp., Botryotinia spp.) and Oomycetes (e.g. Phytophthora spp., Pythium spp., Plasmopara spp., Peronospora spp., Pseudoperonospora spp. Bremia spp). Outstanding activity is observed against powdery mildews (e.g. Erysiphe necator) and leaf spots (e.g. Mycosphaerella spp.). Furthermore, the novel compounds of formula I are effective against phytopathogenic gram negative and gram positive bacteria (e.g. Xanthomonas spp, Pseudomonas spp, Erwinia amylovora, Ralstonia spp.) and viruses (e.g. tobacco mosaic virus).

Within the scope of present invention, target crops to be protected typically comprise the following species of plants: cereal (wheat, barley, rye, oat, rice, maize, sorghum and related species); beet (sugar beet and fodder beet); pomes, drupes and soft fruit (apples, pears, plums, peaches, almonds, cherries, strawberries, raspberries and blackberries); leguminous plants (beans, lentils, peas, soybeans); oil plants (rape, mustard, poppy, olives,
sunflowers, coconut, castor oil plants, cocoa beans, groundnuts); cucumber plants
(pumpkins, cucumbers, melons); fibre plants (cotton, flax, hemp, jute); citrus fruit (oranges,
lemons, grapefruit, mandarins); vegetables (spinach, lettuce, asparagus, cabbages, carrots,
onions, tomatoes, potatoes, paprika); lauraceae (avocado, cinnamomum, camphor) or
plants such as tobacco, nuts, coffee, eggplants, sugar cane, tea, pepper, vines, hops,
bananas and natural rubber plants, as well as turf and ornamentals.

The useful plants and/or target crops in accordance with the invention include
conventional as well as genetically enhanced or engineered varieties such as, for example,
insect resistant (e.g. Bt. and VIP varieties) as well as disease resistant, herbicide tolerant
(e.g. glyphosate- and glufosinate-resistant maize varieties commercially available under the
trade names RoundupReady® and LibertyLink®) and nematode tolerant varieties. By way
of example, suitable genetically enhanced or engineered crop varieties include the
Stoneville 5599BR cotton and Stoneville 4892BR cotton varieties.

The term "useful plants" and/or "target crops" is to be understood as including also
useful plants that have been rendered tolerant to herbicides like bromoxynil or classes of
herbicides (such as, for example, HPPD inhibitors, ALS inhibitors, for example
primisulfuron, prosulfuron and trifloxysulfuron, EPSPS (5-enol-pyrovyl-shikimate-3-
phosphate-synthase) inhibitors, GS (glutamine synthetase) inhibitors or PPO
(protoporphyrinogen-oxidase) inhibitors) as a result of conventional methods of breeding or
genetic engineering. An example of a crop that has been rendered tolerant to
imidazolinones, e.g. imazamox, by conventional methods of breeding (mutagenesis) is
Clearfield® summer rape (Canola). Examples of crops that have been rendered tolerant to
herbicides or classes of herbicides by genetic engineering methods include glyphosate- and
glufosinate-resistant maize varieties commercially available under the trade names
RoundupReady®, Herculex® and LibertyLink®.

The term "useful plants" and/or "target crops" is to be understood as including also
useful plants which have been so transformed by the use of recombinant DNA techniques
that they are capable of synthesising one or more selectively acting toxins, such as are known, for example, from toxin-producing bacteria, especially those of the genus Bacillus.

The term "useful plants" and/or "target crops" is to be understood as including also useful plants which have been so transformed by the use of recombinant DNA techniques that they are capable of synthesising antipathogenic substances having a selective action, such as, for example, the so-called "pathogenesis-related proteins" (PRPs, see e.g. EP-A-O 392 225). Examples of such antipathogenic substances and transgenic plants capable of synthesising such antipathogenic substances are known, for example, from EP-A-O 392 225, WO 95/33818, and EP-A-O 353 191. The methods of producing such transgenic plants are generally known to the person skilled in the art and are described, for example, in the publications mentioned above.

The term "locus" of a useful plant as used herein is intended to embrace the place on which the useful plants are growing, where the plant propagation materials of the useful plants are sown or where the plant propagation materials of the useful plants will be placed into the soil. An example for such a locus is a field, on which crop plants are growing.

The term "plant propagation material" is understood to denote generative parts of the plant, such as seeds, which can be used for the multiplication of the latter, and vegetative material, such as cuttings or tubers, for example potatoes. There may be mentioned for example seeds (in the strict sense), roots, fruits, tubers, bulbs, rhizomes and parts of plants. Germinated plants and young plants which are to be transplanted after germination or after emergence from the soil, may also be mentioned. These young plants may be protected before transplantation by a total or partial treatment by immersion. Preferably "plant propagation material" is understood to denote seeds.

The compounds of formula I are used in unmodified form or, preferably, together with the adjuvants conventionally employed in the art of formulation. To this end they are conveniently formulated in known manner to emulsifiable concentrates, coatable pastes, directly sprayable or dilutable solutions or suspensions, dilute emulsions, wettable powders, soluble
powders, dusts, granulates, and also encapsulations e.g. in polymeric substances. As with the type of the compositions, the methods of application, such as spraying, atomising, dusting, scattering, coating or pouring, are chosen in accordance with the intended objectives and the prevailing circumstances. The compositions may also contain further adjuvants such as stabilizers, antifoams, viscosity regulators, binders or tackifiers as well as fertilizers, micronutrient donors or other formulations for obtaining special effects.

Suitable carriers and adjuvants can be solid or liquid and are substances useful in formulation technology, e.g. natural or regenerated mineral substances, solvents, dispersants, wetting agents, tackifiers, thickeners, binders or fertilizers. Such carriers are for example described in WO 97/33890.

The compounds of formula I are normally used in the form of compositions and can be applied to the crop area or plant to be treated, simultaneously or in succession with further compounds. These further compounds can be e.g. fertilizers or micronutrient donors or other preparations, which influence the growth of plants. They can also be selective herbicides or non-selective herbicides as well as insecticides, fungicides, bactericides, nematicides, molluscicides or mixtures of several of these preparations, if desired together with further carriers, surfactants or application promoting adjuvants customarily employed in the art of formulation.

The compounds of formula I are normally used in the form of fungicidal compositions for controlling or protecting against phytopathogenic microorganisms, comprising as active ingredient at least one compound of formula I, in free form or in agrochemically usable salt form, and at least one of the above-mentioned adjuvants.

Said fungicidal compositions for controlling or protecting against phytopathogenic microorganisms, comprising as active ingredient at least one compound of formula I or at least one preferred individual compound as above-defined, in free form or in agrochemically usable salt form, and at least one of the above-mentioned adjuvants can be mixed with
other fungicides, resulting in some cases in unexpected synergistic activities. Mixing components which are particularly preferred are:

Azoles, such as azaconazole, BAY 14120, bitertanol, bromuconazole, cyproconazole, difenoconazole, diniconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imazalil, imibenconazole, ipconazole, metconazole, myclobutanil, pefurazoate, penconazole, prothioconazole, pyrifenox, prochloraz, propiconazole, simeconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, triflumizole, triticonazole;

Pyrimidinyl carbinoles, such as ancymidol, fenarimol, nuarimol;

2-amino-pyrimidines, such as bupirimate, dimethirimol, ethirimol;

Morpholines, such as dodemorph, fenpropidine, fenpropimorph, spiroxamine, tridemorph;

Anilinopyrimidines, such as cyprodinil, mepanipyrim, pyrimethanil;

Pyrroles, such as fenpiclonil, fludioxonil;

Phenylamides, such as benalaxyl, furalaxyl, metalaxyl, R-metalaxyl, ofurace, oxadixyl;

Benzimidazoles, such as benomyl, carbendazim, debacarb, fuberidazole, thiaben-dazole;

Dicarboximides, such as chlозolinate, dichlozoline, iprodione, myclozoline, procymidine, vinclozozoline;

Carboxamides, such as boscalid, carboxin, fenfuram, flutolanil, mepronil, oxycarboxin, pentyopyrad, thifluzamide; guanidines, such as guazatine, dodine, iminoctadine;

Strobilurines, such as azoxystrobin, dimoxystrobin, enestroburin, fluoxastrobin, kresoxim-methyl, metominostrobin, trifloxystrobin, orysastrobin, picioxystrobin, pyraclostrobin;

Dithiocarbamates, such as ferbam, mancozeb, maneub, metiram, propineb, thiram, zineb, ziram;

N-halomethylthiotetrahydrophthalimides, such as captafol, captan, dichlofluanid, fluoromides, folpet, tolyfluanid;

Cu-compounds, such as Bordeaux mixture, copper hydroxide, copper oxychloride, copper sulfate, cuprous oxide, mancopper, oxine-copper;

Nitrophenol-derivatives, such as dinocap, nitrothal-isopropyl;
Organo-phosphorus-derivatives, such as edifenphos, iprobenphos, isoprothiolane, phosdiphen, pyrazophos, tolclofos-methyl;

Triazolopyrimidine derivatives which are known and may be prepared by methods as described in WO98/46607, such as 5-chloro-7-(4-methyl-piperidin-1-yl)-6-(2,4,6-trifluorophenyl)-[1,2,4]triazolo[1,5-a]pyrimidine (formula T.1);

Carboxamide derivatives which are known and may be prepared by methods as described in WO04/035589 and in WO06/37632, such as 3-difluoromethyl-1-methyl-1H-pyrazole-4-carboxylic acid (9-isopropyl-1,2,3,4-tetrahydro-1,4-methano-naphthalen-5-yl)-amide (formula U.1); or

N^S^-dichloro- 5-fluoro-1 J^-biphenyl^-yO-S^difluoromethyO-i-methyl-1H-pyrazole^-carboxamide (compound F-13)
Benzamide derivatives which are known and may be prepared by methods as described in WO 2004/016088, such as N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl}-2-trifluoromethylbenzamide, which is also known under the name fluopyram (formula V.1):

![Chemical structure of V.1]

and

Various others, such as acibenzolar-S-methyl, anilazine, benthiavalicarb, blasticidin-S, chinomethionate, chloroneb, chlorothalonil, cyflufenamid, cytoxanil, dichlone, diclocymet, diclofop, dicloran, diethofencarb, dimethomorph, flumorph, dithianon, ethaboxam, etridiazole, famoxadone, fenamidone, fenoxanil, fentin, ferimzone, fluazinam, flupicilolide, flusulfamide, fenhexamid, fosetyl-aluminium, hymexazol, iprovalicarb, cyazofamid, kasugamycin, mandipropamid, methasulfocarb, metrafenone, nicobifen, pencuricon, phthalide, polyoxins, probenazole, propamocarb, proquinazid, pyroquilon, quinoxyfen, quintozene, sulfur, tiadinil, triazoxide, tricyclazole, triforine, validamycin, zoxamide and glyphosate.

Another aspect of invention is related to the use of a compound of formula I, of a composition comprising at least one compound of formula I or of a fungicidal mixture comprising at least one compound of formula I in admixture with other fungicides, as described above, for controlling or preventing infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms, preferably fungal organisms.

A further aspect of invention is related to a method of controlling or preventing an infestation of crop plants, harvested food crops or non-living materials by phytopathogenic or spoilage microorganisms or organisms potentially harmful to man, especially fungal
organisms, which comprises the application of a compound of formula I as active ingredient to the plants, to parts of the plants or to the locus thereof, to seeds or to any part of the non-living materials.

Controlling or preventing means reducing the infestation of crop plants or of non-living materials by phytopathogenic or spoilage microorganisms or organisms potentially harmful to man, especially fungal organisms, to such a level that an improvement is demonstrated.

A preferred method of controlling or preventing an infestation of crop plants by phytopathogenic microorganisms, especially fungal organisms, which comprises the application of a compound of formula I, or an agrochemical composition which contains at least one of said compounds, is foliar application. The frequency of application and the rate of application will depend on the risk of infestation by the corresponding pathogen. However, the compounds of formula I can also penetrate the plant through the roots via the soil (systemic action) by drenching the locus of the plant with a liquid formulation, or by applying the compounds in solid form to the soil, e.g. in granular form (soil application). In crops of water rice such granulates can be applied to the flooded rice field. The compounds of formula I may also be applied to seeds (coating) by impregnating the seeds or tubers either with a liquid formulation of the fungicide or coating them with a solid formulation.

A formulation [that is, a composition containing the compound of formula I] and, if desired, a solid or liquid adjuvant or monomers for encapsulating the compound of formula I, is prepared in a known manner, typically by intimately mixing and/or grinding the compound with extenders, for example solvents, solid carriers and, optionally, surface active compounds (surfactants).

The agrochemical formulations will usually contain from 0.1 to 99% by weight, preferably from 0.1 to 95% by weight, of the compound of formula I, 99.9 to 1% by weight, preferably 99.8 to 5% by weight, of a solid or liquid adjuvant, and from 0 to 25% by weight, preferably from 0.1 to 25% by weight, of a surfactant.
Advantageous rates of application are normally from 5g to 2kg of active ingredient (a.i.) per hectare (ha), preferably from 10g to 1kg a.i./ha, most preferably from 20g to 600g a.i./ha. When used as seed drenching agent, convenient dosages are from 10mg to 1g of active substance per kg of seeds.

Whereas it is preferred to formulate commercial products as concentrates, the end user will normally use dilute formulations.

Plant growth regulators (PGRs) are generally any substances or mixtures of substances intended to accelerate or retard the rate of growth or maturation, or otherwise alter the development of plants or their produce.

Plant growth regulators (PGRs) affect growth and differentiation of plants.

More specifically, various plant growth regulators (PGRs) can, for example, reduce plant height, stimulate seed germination, induce flowering, darken leaf coloring, change the rate of plant growth and modify the timing and efficiency of fruiting.

Furthermore, the present invention also relates to compositions comprising the novel imidazole derivatives of the present invention that improve plants, a process which is commonly and hereinafter referred to as "plant health".

For example, advantageous properties that may be mentioned are improved crop characteristics including: emergence, crop yields, protein content, increased vigour, faster maturation, increased speed of seed emergence, improved nitrogen utilization efficiency, improved water use efficiency, improved oil content and/or quality, improved digestibility, faster ripening, improved flavor, improved starch content, more developed root system (improved root growth), improved stress tolerance (e.g. against drought, heat, salt, light, UV, water, cold), reduced ethylene (reduced production and/or inhibition of reception), tillering increase, increase in plant height, bigger leaf blade, less dead basal leaves, stronger tillers, greener leaf color, pigment content, photosynthetic activity, less input needed (such as fertilizers or water), less seeds needed, more productive tillers, earlier flowering, early grain
maturity, less plant verse (lodging), increased shoot growth, enhanced plant vigor, increased plant stand and early and better germination.

Advantageous properties, obtained especially from treading seeds, are e.g. improved germination and field establishment, better vigor, more homogeneous field establishment.

Advantageous properties, obtained especially from foliar and/or in-furrow application are e.g. improved plant growth and plant development, better growth, more tillers, greener leaves, larger leaves, more biomass, better roots, improved stress tolerance of the plants, more grain yield, more biomass harvested, improved quality of the harvest (content of fatty acids, metabolites, oil etc), more marketable products (e.g. improved size), improved process (e.g. longer shelf-life, better extraction of compounds), improved quality of seeds (for being seeded in the following seasons for seed production); or any other advantages familiar to a person skilled in the art.

It is therefore an object of the present invention to provide a method which solves the problems outlined above.

The present invention relates to plant-protecting active ingredients that are imidazole compounds of formula I according to the invention, in particular the individual imidazole compounds described in the above description as being preferred, and mixtures with increased efficacy and to a method of improving the health of plants by applying said compounds and mixtures to the plants or the locus thereof.

The action of the compounds of formula I goes beyond the known fungicidal action. The imidazole compounds of formula I according to the invention, in particular the individual imidazole compounds described in the above description as being preferred compounds exhibit plant health.

The term plant health comprises various sorts of improvements of plants that are not connected to the control of harmful fungi.
In another aspect, the present invention relates to a composition comprising at least one compound of formula \(1\) or of a preferred individual compound as above-defined and/or at least one pharmaceutically acceptable salt thereof, at least one pharmaceutically acceptable carrier and/or at least one pharmaceutically acceptable diluent.

In a further aspect, the present invention also relates to a compound of formula \(1\) or of a preferred individual compound as above-defined, or a pharmaceutically acceptable salt thereof for use as a medicament.

In a preferred aspect, the present invention also relates to a compound of formula \(1\) or of a preferred individual compound as above-defined, or a pharmaceutically acceptable salt thereof for the treatment of cancer.

In an additional aspect, the present invention also relates to the use of a compound formula \(1\) or of a preferred individual compound as above-defined, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cancer.

In a particular aspect, the present invention also relates to a method of treating cancer in a subject in need thereof, comprising administering a a compound formula \(1\) or of a preferred individual compound as above-defined to said subject in an amount effective to treat said cancer.

The invention further provides fungicidal or pharmaceutical compositions comprising these compounds \(1\) and/or their agriculturally or pharmaceutically acceptable salts and suitable carriers.

Suitable pharmaceutically acceptable carriers are described below.

The imidazole compounds of formula \(1\) according to the invention, in particular the imidazoles of formula \(1\) according to the invention described in the above description as being preferred, and/or their pharmaceutically acceptable salts are suitable for the
treatment, inhibitor or control of growth and/or propagation of tumor cells and the disorders associated therewith.

Accordingly, they are suitable for cancer therapy in warmblooded vertebrates, for example mammals and birds, in particular man, but also other mammals, in particular useful and domestic animals, such as dogs, cats, pigs, ruminants (cattle, sheep, goats, bison, etc.), horses and birds, such as chicken, turkey, ducks, geese, guineafowl and the like.

The imidazoles of formula I according to the invention, in particular the imidazoles of formula I according to the invention described in the above description as being preferred, and/or their pharmaceutically acceptable salts are suitable for the therapy of cancer or cancerous disorders of the following organs: breast, lung, intestine, prostate, skin (melanoma), kidney, bladder, mouth, larynx, oesophagus, stomach, ovaries, pancreas, liver and brain.

In addition to the imidazole compounds of formula I according to the invention and/or its pharmaceutically acceptable salt, the pharmaceutical compositions according to the invention comprise at least optionally a suitable carrier.

"Pharmaceutically acceptable" means 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 human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

Suitable carriers are, for example, solvents, carriers, excipients, binders and the like customarily used for pharmaceutical formulations, which are described below in an exemplary manner for individual types of administration.

"Pharmaceutically acceptable carrier" as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting the subject agent from one organ, or portion of the body, to another organ, or portion of the body. Each carrier
must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically-acceptable carriers include:

- sugars, such as lactose, glucose and sucrose;
- starches, such as corn starch and potato starch;
- cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate;
- powdered tragacanth;
- malt;
- gelatin;
- talc;
- excipients, such as cocoa butter and suppository waxes;
- oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil;
- glycols, such as propylene glycol;
- polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol;
- esters, such as ethyl oleate and ethyl laurate;
- agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide;
- alginic acid;
- pyrogen-free water;
- isotonic saline;
- Ringer's solution;
- ethyl alcohol;
- phosphate buffer solutions; and
- other non-toxic compatible substances employed in pharmaceutical formulations.

The imidazole compounds of formula I according to the invention, in particular the individual imidazole compounds described in the above description as being preferred (the active compound), can be administered in a customary manner, for example orally, intravenously, intramuscularly or subcutaneously.
For oral administration, the active compound can be mixed, for example, with an inert diluent or with an edible carrier; it can be embedded into a hard or soft gelatin capsule, it can be compressed to tablets or it can be mixed directly with the food/feed.

The active compound can be mixed with excipients and administered in the form of indigestible tablets, buccal tablets, pastilles, pills, capsules, suspensions, potions, syrups and the like.

Such preparations should contain at least 0.1 % of active compound.

The composition of the preparation may, of course, vary.

It usually comprises from 2 to 60% by weight of active compound, based on the total weight of the preparation in question (dosage unit).

Preferred preparations of the imidazole compounds of formula I according to the invention, in particular the individual imidazole compounds described in the above description as being preferred, comprise from 10 to 1000 mg of active compound per oral dosage unit.

The tablets, pastilles, pills, capsules and the like may furthermore comprise the following components: binders, such as tragant, gum arabic, corn starch or gelatin, excipients, such as dicalcium phosphate, disintegrants, such as corn starch, potato starch, alginic acid and the like, glidants, such as magnesium stearate, sweeteners, such as sucrose, lactose or saccharin, and/or flavors, such as peppermint, vanilla and the like.

Capsules may furthermore comprise a liquid carrier.

Other substances which modify the properties of the dosage unit may also be used.

For example, tablets, pills and capsules may be coated with schellack, sugar or mixtures thereof.

In addition to the active compound, syrups or potions may also comprise sugar (or other sweeteners), methyl- or propylparaben as preservative, a colorant and/or a flavor.
The components of the active compound preparations must, of course, be pharmaceutically pure and nontoxic at the quantities employed.

Furthermore, the active compounds can be formulated as preparations with a controlled release of active compound, for example as delayed-release preparations. The active compounds can also be administered parenterally or intraperitoneal.

Solutions or suspensions of the active compounds or their salts can be prepared with water using suitable wetting agents, such as hydroxypropylcellulose.

Dispersions can also be prepared using glycerol, liquid polyethylene glycols and mixtures thereof in oils.

Frequently, these preparations furthermore comprise a preservative to prevent the growth of microorganisms.

Preparations intended for injections comprise sterile aqueous solutions and dispersions and also sterile powders for preparing sterile solutions and dispersions.

The preparation has to be sufficiently liquid for injection.

It has to be stable under the preparation and storage conditions and it has to be protected against contamination by microorganisms.

The carrier may be a solvent or a dispersion medium, for example, water, ethanol, a polyol (for example glycerol, propylene glycol or liquid polyethylene glycol), a mixture thereof and/or a vegetable oil.

Pharmaceutical compositions of this invention suitable for parenteral administration comprise a compound of formula I in combination with one or more pharmaceutically-acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain antioxidants, buffers, bacteriostats, solutes
which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

Examples of suitable aqueous and nonaqueous carriers which may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants. These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and other antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

The pharmaceutical compositions of the present invention may be given by any suitable means of administration including orally, parenterally, topically, transdermal, rectally, etc. They are of course given by forms suitable for each administration route. For example, they are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, etc. administration by injection, infusion or inhalation; topical by lotion or ointment; and rectal by suppositories. Topical or parenteral administration is preferred.

The following non-limiting examples illustrate the above-described invention in more detail.

Example 1: This example illustrates the preparation of 4-Chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1 H-imidazole (Compound No. I.b.006)
a) Preparation of (4-Chloro-phenyl)-[1-(2,4,6-trifluoro-phenyl)-meth-(E)-ylidene]-amine

4-Chloro-aniline (20.36g) and 2,4,6-trifluoro-benzaldehyde (25.55g) are dissolved in toluene (780 ml). Subsequently, the mixture is stirred for 4 days at reflux in a Dean-Stark apparatus. The reaction mixture is evaporated under reduced pressure, to obtain 43.84 g of (4-Chloro-phenyl)-[1-(2,4,6-trifluoro-phenyl)-meth-(E)-ylidene]-amine. 1H NMR (300Mhz, CDCl₃) 8.49ppm, 1H, s; 7.28ppm, 2H, d, J=8.6Hz; 7.08ppm, 2H, d, J=8.6Hz; 6.77ppm, 2H, t, J=8.7Hz.

b) Preparation 1-(4-Chloro-phenyl)-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole

33.6 g of (4-Chloro-phenyl)-[1-(2,4,6-trifluoro-phenyl)-meth-(E)-ylidene]-amine are dissolved in 456 ml of N,N-dimethyl-formamide and 375 ml of 1,2-dimethoxy-ethane. 36.49 g of toluenesulfonylmethyl isocyanide and 34.44 g of anhydrous potassium carbonate are added, and the resulting reaction mixture is heated at 100°C for 120 minutes. After cooling down, the mixture is filtrated, the solvents evaporated, the resulting solid is adsorbed on Isolute® HM-N and purified by chromatography column on silica gel, using a mixture of heptane / t-butyl-methyl-ether 3:1 and 2:1 as successive eluents to obtain 19.94 g of 1-(4-Chloro-phenyl)-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole. 1H NMR (300Mhz, CDCl₃) 7.72ppm, 1H, s; 7.28ppm, 2H, d, J=8.6Hz; 7.22ppm, 1H, s; 7.02ppm, 2H, d, J=8.7Hz; 6.59ppm, 2H, t, J=7.3Hz.

c) Preparation of 2-Bromo-1-(4-chloro-phenyl)-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole

A mixture of 2 g of 1-(4-Chloro-phenyl)-5-(2, 4,6-trifluoro-phenyl)-1 H-imidazole, 1.21 g of N-bromosuccinimide and 21 ml of chloroform is heated for 4 h to 80°C. Subsequently, the mixture is cooled to room temperature, Isolute® HM-N is added to the reaction mixture and the chloroform is evaporated. The crude mixture is purified by chromatography column on silica gel, using a mixture of heptane / ethyl acetate 4:1 as eluent to obtain 1.096 g of 2-Bromo-1-(4-chloro-phenyl)-5-(2, 4,6-trifluoro-phenyl)-1 H-imidazole as a pale yellow-orange solid. 1H NMR (300Mhz, CDCl₃) 7.29ppm, 2H, d, J=8.6Hz; 7.14ppm, 1H, s; 7.05ppm, 2H, d, J=8.5Hz; 6.55ppm, 2H, t, J=7.2Hz.
d) Preparation of 1-(4-Chloro-phenyl)-2-methyl-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole
2-Bromo-1-(4-chloro-phenyl)-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole (3.1 g) is dissolved in
162 ml of tetrahydrofurane. To this solution, 0.13 g of tetrakis(triphenylphosphine) Palladium
is added, before refluxing the resulting mixture for 10 minutes. After this time, the oil bath is
removed and, immediately, 12 ml of a 2M solution of (trimethyl) aluminium in toluene are
added slowly. The reaction mixture is refluxed for 7 hours before being cooled down to 0°C.
5 ml of methanol are added dropwise (gas evolution) and after five minutes, Isolute® HM-N is
added and the solvents removed under reduced pressure. The residue is purified by
chromatography on silica gel, using a mixture of heptane / ethyl acetate 1 : 1 as eluent, to
deliver 1.61 g of 1-(4-Chloro-phenyl)-2-methyl-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole as a
white solid. 1H NMR (300Mhz, CDCl₃) 7.28ppm, 2H, d, J=8.6Hz; 7.13ppm, 1H, s; 7.07ppm,
2H, d, J=8.5Hz; 6.56ppm, 2H, t, J=7.4Hz; 2.31ppm, 3H, s.

e) Preparation of 4-Chloro-1-(4-chloro-phenyl)-2-methyl-5-(2,4,6-trifluoro-phenyl)-1 H-
imidazole
A mixture of 1.61 g of 1-(4-Chloro-phenyl)-2-methyl-5-(2,4,6-trifluoro-phenyl)-1 H-imidazole,
0.83 g of N-chlorosuccinimide and 32 ml of chloroform is heated for 16 h to 80 °C.
Subsequently, the mixture is cooled to room temperature, Isolute® HM-N is added to the
reaction mixture and the chloroform is evaporated. The crude mixture is purified by
chromatography column on silica gel, using a mixture of heptane / ethyl acetate 4:1 as
eluent to obtain 1.01 g of 4-Chloro-1-(4-chloro-phenyl)-2-methyl-5-(2,4,6-trifluoro-phenyl)-
1H-imidazole as a white solid. 1H NMR (300Mhz, CDCl₃) 7.36ppm, 2H, d, J=8.6Hz;
7.07ppm, 2H, d, J=8.5Hz; 6.63ppm, 2H, t, J=7.3Hz; 2.30ppm, 3H, s.

f) Preparation of 4-Chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-2-
methyl-1 H-imidazole (Compound No.1.b.006)
A mixture of 0.4 g of 4-Chloro-1-(4-chloro-phenyl)-2-methyl-5-(2,4,6-trifluoro-phenyl)-1 H-
imidazole, 0.48 ml of a sodium methoxide solution (0.18M in methanol) and 5 ml of
methanol is stirred for 16 hours at room temperature. The reaction mixture is then poured
onto ice-cold acidified water. The aqueous solution is extracted twice with ethyl acetate; the
combined organic layers are washed with brine, then dried over sodium sulfate, filtrated and concentrated under reduced pressure, to obtain 0.304 g of 4-Chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1 H-imidazole (Compound No.1.d.006). \(^1\)H NMR (300Mhz, CDCl\(_3\)) 7.34ppm, 2H, d, J=9.06Hz; 7.07ppm, 2H, d, J=8.58Hz; 6.38ppm, 2H, d, J=9.06Hz; 3.76ppm, 3H, s; 2.29ppm, 3H, s.

Example 2: This example illustrates the preparation of 2,4-Dichloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1 H-imidazole (Compound No.1.d.005)

a) Preparation of 1-(4-Chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1 H-imidazole
A mixture of 0.4 g of 1-(4-Chloro-phenyl)-5-(2, 4,6-trifluoro-phenyl)-1 H-imidazole, 0.48 ml of a sodium methoxide solution (0.18M in methanol) and 5 ml of methanol is stirred for 16 hours at room temperature. The reaction mixture is then poured onto ice-cold acidified water. The aqueous solution is extracted twice with ethyl acetate; the combined organic layers are washed with brine, then dried over sodium sulfate, filtrated and concentrated under reduced pressure. The crude mixture is purified by chromatography column on silica gel, using a mixture of heptane / ethyl acetate 6:4 as eluent to obtain 0.087 g of 1-(4-Chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1 H-imidazole. \(^1\)H NMR (300Mhz, CDCl\(_3\)) 7.77ppm, 1H, s; 7.31 ppm, 2H, d, J=8.7Hz; 7.2ppm, 1H, s; 7.06ppm, 2H, d, J=8.6Hz; 6.47ppm, 1H, dt, J=2.42 and 8.95Hz; 6.35ppm, 1H, td, J=1.84 and 9.6Hz; 3.51 ppm, 3H, s.

b) Preparation of 2,4-Dichloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1H-imidazole (Compound No.1.d.005)
A mixture of 0.087 g of 1-(4-Chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1 H-imidazole, 0.074 g of N-chlorosuccinimide and 1.7 ml of chloroform is heated for 16 h to 80 °C. Subsequently, the mixture is cooled to room temperature, Isolute® HM-N is added to the reaction mixture and the chloroform is evaporated. The crude mixture is purified by chromatography column on silica gel, using a mixture of heptane / ethyl acetate 19 : 1 as eluent to obtain 0.077 g of 2,4-Dichloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1 H-imidazole (Compound No.1.d.005). \(^1\)H NMR (300Mhz, CDCl\(_3\)) 7.38ppm, 2H, d,
J=8.07Hz; 7.12ppm, 2H, d, J=8.68Hz; 6.47ppm, 1H, dt, J=2.41 and 9.01 Hz; 6.35ppm, 1H, td, J=1.84 and 10.4Hz; 3.51 ppm, 3H, s.

Table 1 below illustrates examples of individual compounds of formula I according to the invention.

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
</tr>
</thead>
<tbody>
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<td>001</td>
<td>CH₃</td>
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<td>Cl</td>
</tr>
<tr>
<td>002</td>
<td>CH₃</td>
<td>4-fluorophenyl</td>
<td>Cl</td>
</tr>
<tr>
<td>003</td>
<td>CH₃</td>
<td>3-chlorophenyl</td>
<td>Cl</td>
</tr>
<tr>
<td>004</td>
<td>CH₃</td>
<td>4-chlorophenyl</td>
<td>CH₃</td>
</tr>
<tr>
<td>005</td>
<td>Cl</td>
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<td>Cl</td>
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<td>007</td>
<td>CH₃</td>
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<td>008</td>
<td>CH₃</td>
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<td>Cl</td>
</tr>
<tr>
<td>009</td>
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<td>Cl</td>
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<tr>
<td>010</td>
<td>CH₃</td>
<td>p-tolyl</td>
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</tr>
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<td>011</td>
<td>CH₃</td>
<td>3-methoxyphenyl</td>
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<tr>
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<td>4-methoxyphenyl</td>
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<td>018</td>
<td>CH₃</td>
<td>4-chloro-3-fluorophenyl</td>
<td>Cl</td>
</tr>
<tr>
<td>019</td>
<td>CH₃</td>
<td>3-fluoro-4-methoxyphenyl</td>
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</tr>
<tr>
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</tr>
<tr>
<td>021</td>
<td>CH₃</td>
<td>2-chlorophenyl</td>
<td>Cl</td>
</tr>
</tbody>
</table>
a) 26 compounds of formula (I.a):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

b) 26 compounds of formula (I.b):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

c) 26 compounds of formula (I.c):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

d) 26 compounds of formula (I.d):

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>$R^6$</th>
</tr>
</thead>
<tbody>
<tr>
<td>022</td>
<td>CH$_3$</td>
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<tr>
<td>023</td>
<td>CH$_3$</td>
<td>2-methoxyphenyl</td>
<td>Cl</td>
</tr>
<tr>
<td>024</td>
<td>CH$_3$</td>
<td>o-tolyl</td>
<td>Cl</td>
</tr>
<tr>
<td>025</td>
<td>CH$_3$</td>
<td>4-chloro-2-fluorophenyl</td>
<td>Cl</td>
</tr>
<tr>
<td>026</td>
<td>CH$_2$CH$_3$</td>
<td>4-chlorophenyl</td>
<td>Cl</td>
</tr>
</tbody>
</table>
wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

e) 26 compounds of formula (l.e):

```latex
\text{(l.e)}
```

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

f) 26 compounds of formula (l.f):

```latex
\text{(l.f)}
```

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

g) 26 compounds of formula (l.g):

```latex
\text{(l.g)}
```

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

h) 26 compounds of formula (l.h):
wherein $R_1$, $R_2$ and $R_6$ are as defined in Table 1.

i) 26 compounds of formula (l.i):

wherein $R_1$, $R_2$ and $R_6$ are as defined in Table 1.

j) 26 compounds of formula (l.j):

wherein $R_1$, $R_2$ and $R_6$ are as defined in Table 1.
k) 26 compounds of formula (I.k):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

l) 26 compounds of formula (I.l):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

m) 26 compounds of formula (I.m):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

n) 26 compounds of formula (I.n):

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.
o) 26 compounds of formula (l.o):

wherein \( R^1 \), \( R^2 \) and \( R^6 \) are as defined in Table 1.

p) 26 compounds of formula (l.p):

wherein \( R^1 \), \( R^2 \) and \( R^6 \) are as defined in Table 1.

q) 26 compounds of formula (l.q):

wherein \( R^1 \), \( R^2 \) and \( R^6 \) are as defined in Table 1.

r) 26 compounds of formula (l.r):

wherein \( R^1 \), \( R^2 \) and \( R^6 \) are as defined in Table 1.
s) 26 compounds of formula (I.s):

![Chemical Structure](image)

wherein $R^1$, $R^2$ and $R^6$ are as defined in Table 1.

Throughout this description, temperatures are given in degrees Celsius, "m.p." means melting point, "NMR" means nuclear magnetic resonance spectrum; and "%" is percent by weight, unless corresponding concentrations are indicated in other units.

The following abbreviations are used throughout this description:

- m.p. = melting point
- br = Broad
- s = singlet
- $dd$ = doublet of doublets
- d = doublet
- $dt$ = doublet of triplets
- t = triplet
- q = Quartet
- m = multiplet
- ppm = parts per million

Table 2 shows selected NMR data (unless otherwise stated, no attempt is made to list all characterising data in all cases) for compounds of Table 1.

Table 2: Selected NMR data for compounds of Table 1

<table>
<thead>
<tr>
<th>Compound Number</th>
<th>$^1$H-NMR data (ppm/number of H's/multiplicity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>l.a.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.26ppm, 2H, d, J=8.8Hz; 7.07ppm, 1H, t, J=8.5Hz; 6.97ppm, 2H, d, J=8.5Hz; 6.59ppm, 1H, dd, J=2.4 and 8.7Hz; 6.42ppm, 1H, dd, J=2.5 and 11.5Hz; 3.70ppm,</td>
</tr>
<tr>
<td>Compound Number</td>
<td>$^1$H-NMR data (ppm/number of H's/multiplicity)</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>l.b.004</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.24ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.6Hz; 6.97ppm, 2H, d, J=8.57Hz; 6.30ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=9.11Hz; 3.69ppm, 3H, s; 2.22ppm, 3H,</td>
</tr>
<tr>
<td></td>
<td>s; 2.06, 3H, s.</td>
</tr>
<tr>
<td>l.b.005</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.36ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.63Hz; 7.12ppm, 2H, d, J=8.55Hz; 6.41ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=9.03Hz; 3.78ppm, 3H, s.</td>
</tr>
<tr>
<td>l.b.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.7Hz; 7.07ppm, 2H, d, J=8.58Hz; 6.38ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=9.06Hz; 3.76ppm, 3H, s; 2.29ppm, 3H,</td>
</tr>
<tr>
<td></td>
<td>s.</td>
</tr>
<tr>
<td>l.b.012</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 6.98ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.9Hz; 6.78ppm, 2H, d, J=8.9Hz; 6.31ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=9.1Hz; 3.73ppm, 3H, s; 3.68ppm, 3H, s;</td>
</tr>
<tr>
<td></td>
<td>2.19ppm, 3H, s.</td>
</tr>
<tr>
<td>l.d.005</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.38ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.07Hz; 7.12ppm, 2H, d, J=8.68Hz; 6.47ppm,</td>
</tr>
<tr>
<td></td>
<td>1H, dt, J=2.41 and 9.01Hz; 6.35ppm, 1H, td,</td>
</tr>
<tr>
<td></td>
<td>J=1.84 and 10.4Hz; 3.51ppm, 3H, s.</td>
</tr>
<tr>
<td>l.g.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.65Hz; 7.07ppm, 2H, d, J=8.61Hz; 6.36ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=9.17Hz; 3.96ppm, 2H, q, J=6.99Hz;</td>
</tr>
<tr>
<td></td>
<td>2.28ppm, 3H, s; 1.39ppm, 3H, t, J=6.98Hz.</td>
</tr>
<tr>
<td>l.h.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.67Hz; 7.07ppm, 2H, d, J=8.6Hz; 6.49ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=8.81Hz; 4.64ppm, 2H, d, J=2.44Hz;</td>
</tr>
<tr>
<td></td>
<td>2.57ppm, 1H, t, J=2.36Hz; 2.29ppm, 3H, s.</td>
</tr>
<tr>
<td>l.i.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td>Compound Number</td>
<td>¹H-NMR data (ppm/number of H's/multiplicity)</td>
</tr>
<tr>
<td>-----------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>lj.006</td>
<td>¹H NMR (300Mhz, CDCl₃) 7.34ppm, 2H, d, J=8.6Hz; 7.07ppm, 2H, d, J=8.62Hz; 6.41ppm, 2H, d, J=9.09Hz; 3.99ppm, 2H, t, J=5.61Hz; 2.71ppm, 2H, t, J=5.64Hz; 2.32ppm, 6H, s; 2.29ppm, 3H, s.</td>
</tr>
<tr>
<td>lk.005</td>
<td>¹H NMR (300Mhz, CDCl₃) 7.34ppm, 2H, d, J=8.6Hz; 7.05ppm, 2H, d, J=8.6Hz; 6.34ppm, 2H, d, J=9.12Hz; 3.89ppm, 2H, t, J=6.4Hz; 2.33ppm, 2H, t, J=7.1Hz; 2.16ppm, 6H, s; 1.97ppm, quintet, 2H, J=7Hz.</td>
</tr>
<tr>
<td>lk.008</td>
<td>¹H NMR (300Mhz, CDCl₃) 7.29ppm, 2H, d, J=8.63Hz; 7.07ppm, 2H, d, J=8.6Hz; 6.39ppm, 2H, d, J=9.14Hz; 3.95ppm, 2H, t, J=6.36Hz; 2.41ppm, 2H, t, J=7.17Hz; 2.28ppm, 3H, s; 2.23ppm, 6H, s; 1.92ppm, quintet, 2H, J=7.04Hz.</td>
</tr>
<tr>
<td>ll.006</td>
<td>¹H NMR (300Mhz, CDCl₃) 7.34ppm, 2H, d, J=8.6Hz; 7.07ppm, 2H, d, J=8.6Hz; 6.38ppm, 2H, d, J=9.16Hz; 3.73ppm, 2H, d, J=6.97Hz; 2.28ppm, 3H, s; 1.25ppm, 1H, m; 0.65ppm, 2H, q, J=5ppm, 2H, q, J=4.78Hz.</td>
</tr>
<tr>
<td>lm.006</td>
<td>¹H NMR (300Mhz, D₂O-DMSO) 10.71ppm, 1H, bs; 7.51ppm, 2H, d, J=8.63Hz; 7.26ppm, 2H, d, J=8.6Hz; 6.45ppm, 2H, d, J=9.43Hz; 2.21ppm, 3H, s.</td>
</tr>
<tr>
<td>ln.006</td>
<td>¹H NMR (300Mhz, CDCl₃) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td>Compound Number</td>
<td>$^1$H-NMR data (ppm/number of H's/multiplicity)</td>
</tr>
<tr>
<td>-----------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>l.o.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.6Hz; 7.07ppm, 2H, d, J=8.6Hz; 6.40ppm,</td>
</tr>
<tr>
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<td>2H, d, J=9.1Hz; 4.03ppm, 2H, t, J=5.84Hz;</td>
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<tr>
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<td>2.87ppm, 2H, t, J=5.82Hz; 2.6ppm, 4H, m;</td>
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<tr>
<td></td>
<td>2.28ppm, 3H, s; 1.80ppm, 4H, m.</td>
</tr>
<tr>
<td>l.p.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.35ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.7Hz; 7.07ppm, 2H, d, J=8.6Hz; 6.71ppm,</td>
</tr>
<tr>
<td></td>
<td>1H, t, J=5.88Hz; 6.56ppm, 2H, d, J=8.47Hz;</td>
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<tr>
<td></td>
<td>5.48ppm, 2H, d, J=5.92Hz; 2.29ppm, 3H, s.</td>
</tr>
<tr>
<td>l.q.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.34ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.6Hz; 7.07ppm, 2H, d, J=8.6Hz; 6.39ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, d, J=9.12Hz; 3.95ppm, 2H, t, J=6.31Hz;</td>
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<tr>
<td></td>
<td>2.47ppm, 10H, m; 2.29ppm, 3H, s; 2.28ppm, 3H,</td>
</tr>
<tr>
<td></td>
<td>s; 1.93ppm, 2H, quintet, J=7.18Hz.</td>
</tr>
<tr>
<td>l.e.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.23ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.6Hz; 6.97ppm, 2H, d, J=8.6Hz; 6.13ppm,</td>
</tr>
<tr>
<td></td>
<td>1H, d, J=10.8Hz; 6.06ppm, 1H, s; 3.69ppm, 3H,</td>
</tr>
<tr>
<td></td>
<td>s; 3.52ppm, 3H, s; 2.22ppm, 3H, s.</td>
</tr>
<tr>
<td>l.s.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.2ppm, 2H, d,</td>
</tr>
<tr>
<td></td>
<td>J=8.7Hz; 6.94ppm, 2H, d, J=8.67Hz; 5.93ppm,</td>
</tr>
<tr>
<td></td>
<td>2H, s; 3.71ppm, 3H, s; 3.56ppm, 6H, s; 2.22ppm, 3H, s.</td>
</tr>
<tr>
<td>l.d.006</td>
<td>$^1$H NMR (300Mhz, CDCl$_3$) 7.25ppm, 2H, d,</td>
</tr>
<tr>
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<td>J=8.7Hz; 6.97ppm, 2H, d, J=8.6Hz; 6.35ppm,</td>
</tr>
<tr>
<td></td>
<td>1H, dt, J=2.3, 8.91Hz; 6.26ppm, 1H, dt, J=2,</td>
</tr>
<tr>
<td></td>
<td>10.48Hz; 3.56ppm, 3H, s; 2.22ppm, 3H, s.</td>
</tr>
</tbody>
</table>
The compounds according to the present invention can be prepared according to the above-mentioned reaction schemes, in which, unless otherwise stated, the definition of each variable is as defined above for a compound of formula (I).

**Biological examples**

*Alternaria solani* / tomato / preventative (*Alternaria* on tomato)

4-week old tomato plants cv. Roter Gnom are treated with the formulated test compound in a spray chamber. The test plants are inoculated by spraying them with a spore suspension two days after application. The inoculated test plants are incubated at 22/18° C (day/night) and 95% rh in a greenhouse and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (5 - 7 days after application).

Compounds l.a.006, l.b.005, l.b.006, l.b.012, l.d.006, l.g.006, l.h.006, l.i.006, l.j.006, l.k.005, l.k.006, l.n.006, l.p.006 and l.q.006 according to the invention at 200 ppm inhibit fungal infestation in this test to at least 80 %, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80 %.

*Botryotinia fuckeliana* (*Botrytis cinerea*) / tomato / preventative (*Botrytis* on tomato)

4-week old tomato plants cv. Roter Gnom are treated with the formulated test compound in a spray chamber. The test plants are inoculated by spraying them with a spore suspension two days after application. The inoculated test plants are incubated at 20° C and 95% rh in
a greenhouse and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (5 - 6 days after application).

5 Compounds l.a.006, l.b.006, l.b.012, l.d.006, l.g.006, l.i.006, l.k.005, l.k.006, l.p.006 according to the invention at 200 ppm inhibit fungal infestation in this test to at least 80 %, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80 %.

10 *Erysiphe necator (Ucinula necator)* / grape / preventative (Powdery mildew on grape)

5-week old grape seedlings cv. Gutedel are treated with the formulated test compound in a spray chamber. The test plants are inoculated by shaking plants infected with grape powdery mildew above them 1 day after application. The inoculated test plants are incubated at 24/22° C (day/night) and 70% rh under a light regime of 14/10 h (light/dark) and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (7 - 9 days after application).

Compounds l.a.006, l.b.005, l.b.006, l.b.012, l.b.026, l.d.006, l.g.006, l.h.006, l.i.006, l.j.006, l.k.006, l.m.006, l.p.006 and l.q.006 according to the invention at 200 ppm inhibit fungal infestation in this test to at least 80 %, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80 %.

*Mycosphaerella arachidis (Cercospora arachidicola) / peanut / curative*

3-week old peanut plants cv. Georgia Green are inoculated by spraying them with a spore suspension on their lower leaf surface. After an incubation period of 2 days at 23° C and 100% rh, the inoculated plants are treated with the formulated test compound in a spray chamber. After an additional incubation period of 1 day under a plastic hood at 23° C and 100% rh, the test plants are kept at 23° C / 20° C (day/night) and 70% rh in a greenhouse. The percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (10 - 12 days after application).
Compounds l.b.005, l.b.006, l.b.012, l.i.006 and l.j.006 according to the invention at 200 ppm inhibit fungal infestation in this test to at least 80 %, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80 %.

*Mycosphaerella graminicola (Septoria tritici) /wheat / preventative (Septoria tritici leaf spot on wheat)*

2-week old wheat plants cv. Riband are treated with the formulated test compound in a spray chamber. The test plants are inoculated by spraying a spore suspension on them one day after application. After an incubation period of 1 day at 22°C/21 °C (day/night) and 95% rh, the test plants are kept at 22°C/21°C (day/night) and 70% rh in a greenhouse. The percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (16 - 19 days after application).

Compounds l.b.005, l.b.006, l.i.006, l.j.006, l.k.005 and l.n.006 according to the invention at 200 ppm inhibit fungal infestation in this test to at least 80 %, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80 %.

*Puccinia recondita /wheat / preventative (Brown rust on wheat)*

2-week old wheat plants cv. Arina are treated with the formulated test compound in a spray chamber. The test plants are inoculated by spraying them with a spore suspension one day after application. After an incubation period of 1 day at 20° C and 95% rh, the test plants are kept at 20° C / 18° C (day/night) and 60% rh in a greenhouse. The percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (12 - 14 days after application).

Compounds l.a.006, l.b.005, l.b.006, **l.b.012**, l.g.006, l.h.006, l.j.006, l.l.006, l.m.006, l.p.006 and l.q.006 according to the invention at 200 ppm inhibit fungal infestation in this
test to at least 80%, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80%.

*Pyrenophora teres (Helminthosporium teres)* / barley / preventative (Net blotch on barley)

1-week old barley plants cv. Regina are treated with the formulated test compound in a spray chamber. The test plants are inoculated by spraying them with a spore suspension 2 days after application. The inoculated test plants are incubated at 20°C and 95% rh and the percentage leaf area covered by disease is assessed when an appropriate level of disease appears on untreated check plants (5 - 7 days after application).

Compounds l.b.006, l.h.006, l.i.006, l.j.006, l.k.005, l.k.006, l.l.006, l.n.006 and l.q.006 according to the invention at 200 ppm inhibit fungal infestation in this test to at least 80%, while under the same conditions untreated control plants are infected by the phytopathogenic fungi to over 80%.
What is claimed is:

1. A compound of formula I:

   \[
   \begin{array}{c}
   \text{R}^1 \\
   \hline
   \text{R}^2 \\
   \hline
   \text{R}^3 \\
   \hline
   \text{R}^4 \\
   \hline
   \text{R}^5 \\
   \hline
   \text{R}^6 \\
   \hline
   \end{array}
   \]

   \( \text{(I)} \)

   wherein
   - \( \text{R}^1 \) is halogen, d-C\(_4\) alkyl or d-C\(_4\) haloalkyl;
   - \( \text{R}^2 \) is an optionally substituted aryl;
   - \( \text{R}^3 \) is halogen or OR\( \text{R}^7 \);
   - \( \text{R}^4 \) and \( \text{R}^5 \) are, independently of each other, hydrogen, halogen or OR\( \text{R}^7 \);
   - \( \text{R}^6 \) is halogen or CrC\(_4\) alkyl; and
   - \( \text{R}^7 \) is hydrogen, CrC\(_6\) alkyl, C\(_3\)\,-C\(_7\) cycloalkyl, C\(_3\)\,-C\(_10\) cycloalkylalkyl, CrC\(_6\) haloalkyl, C\(_2\)\,-C\(_6\) alkenyl, C\(_2\)\,-C\(_6\) haloalkenyl, C\(_3\)\,-C\(_7\) cycloalkenyl, C\(_2\)\,-C\(_6\) alkynyl, C\(_2\)\,-C\(_6\) haloalkynyl, C\(_2\)\,-C\(_6\) alkyloxyalkyl, C\(_3\)\,-C\(_6\) dialkylaminoalkyl, C\(_4\)\,-C\(_10\) cycloalkylaminoalkyl or C\(_4\)\,-C\(_10\) heterocyclylalkyl;
   - or an agrochemically usable salt form thereof; provided that
     - when \( \text{R}^3 \) is halogen, at least one of \( \text{R}^4 \) or \( \text{R}^5 \) is OR\( \text{R}^7 \); or
     - when \( \text{R}^3 \) is OR\( \text{R}^7 \), at least one of \( \text{R}^4 \) or \( \text{R}^5 \) is OR\( \text{R}^7 \) or halogen.

2. The compound according to claim 1 wherein \( \text{R}^1 \) is halogen or C\(_1\)\,-C\(_3\) alkyl.

3. The compound according to either claims 1 or 2 wherein \( \text{R}^2 \) is an optionally substituted phenyl.

4. The compound according to any one of claims 1 to 3 wherein \( \text{R}^3 \) is fluoro, chloro, bromo or OR\( \text{R}^7 \).
5. The compound according to any one of claims 1 to 4 wherein R^4 and R^5, independently of each other, are hydrogen, chloro, fluoro, bromo or OR^7.

6. The compound according to any one of claims 1 to 5 wherein R^6 is chloro, fluoro, bromo or CrC_3 alkyl; and

7. The compound according to any one of claims 1 to 6 wherein R^7 is hydrogen, CrC_5 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylalkyl, CrC_5 haloalkyl, C_2-C_5 alkenyl, C_2-C_5 haloalkenyl, C_3-C_6 cycloalkenyl, C_2-C_6 alkynyl, C_2-C_6 haloalkynyl, C_2-C_6 alkyloxoyalkyl, C_5-C_7 dialkylaminoalkyl, C_4-C_9 cycloalkylaminoalkyl or C_4-C_9 heterocyclylalkyl.

8. The compound according to any one of claims 1 to 7 wherein
R^1 is chloro, fluoro or Ci-C_2 alkyl;
R^2 is 3-fluorophenyl, 4-fluorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 4-bromophenyl, m-tolyl, p-tolyl, 3-methoxyphenyl, 4-methoxyphenyl, 3-cyanophenyl, 4-cyanophenyl, 3,4-difluorophenyl, 3,4-dichlorophenyl, 3-chloro-4-fluorophenyl, 4-chloro-3-fluorophenyl, 3-fluoro-4-methoxyphenyl, 2-fluoro-phenyl, 2-chlorophenyl, 2-bromophenyl, 2-methoxyphenyl, o-tolyl or 4-chloro-2-fluorophenyl;
R^3 is chloro, fluoro or OR^7;
R^4 and R^5 are, independently of each other, hydrogen, chloro, fluoro or OR^7;
R^6 is chloro or methyl; and
R^7 is hydrogen, Ci-C_3 alkyl, C_3-C_6 cycloalkylalkyl, C_2-C_5 alkenyl, C_2-C_4 alkynyl, C_2-C_4 alkyloxoyalkyl, C_3-C_6 dialkylaminoalkyl, C_4-C_9 cycloalkylaminoalkyl or C_4-C_9 heterocyclylalkyl.

9. The compound according to any one of claims 1 to 8 wherein
R^1 is chloro, methyl or ethyl;
R^2 is 4-chlorophenyl;
R^3 is fluoro or OR^7;
R^4 is fluoro or OR^7;
R^5 is hydrogen or fluoro;
R^6 is chloro; and
R^7 is methyl, ethyl, propargyl, 1-pyrrolidinylethyl, dimethylaminopropyl or C_3-C_5 allenyl.

10. A compound selected from

5 2,4-dichloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1H-imidazole,
2,4-dichloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(4-ethoxy-2,6-difluoro-phenyl)-2-methyl-1H-imidazole,
10 4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-propoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-[2,6-difluoro-4-(2-methoxy-ethoxy)-phenyl]-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-prop-2-ynyloxy-phenyl)-2-methyl-1H-imidazole,
15 4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-2-methyl-1-p-tolyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,6-difluoro-4-methoxy-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole,
4-chloro-5-(2,4-difluoro-6-methoxy-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-(2-pyrrolidin-1-yl-ethoxy)-phenyl)-2-methyl-1H-imidazole,
20 4-chloro-1-(4-chloro-phenyl)-5-(2,4-difluoro-6-methoxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2,6-difluoro-4-propa-1,2-dienyloxy-phenyl)-2-methyl-1H-imidazole,
4-chloro-1-(4-chloro-phenyl)-5-(2-ethoxy-4,6-difluoro-phenyl)-2-methyl-1H-imidazole,
25 4-chloro-5-(2-ethoxy-4,6-difluoro-phenyl)-1-(4-ethynyl-phenyl)-2-methyl-1H-imidazole.

11. A process for the preparation of a compound of formula 1.1,
wherein $R^2$ and $R^7$ are as defined for compound of formula I, and $R^1$ is Cl-C$_4$alkyl or d-C$_4$haloalkyl, which comprises reacting a compound of formula II,

$\text{(I.1)}$

$\text{(II)}$

wherein $R^2$ is as defined for compound of formula I, and $R^1$ is Cl-C$_4$alkyl or CrC$_4$haloalkyl, with a reagent of formula NaOR$^7$, wherein $R^7$ is as defined for compound of formula I.

12. A process for the preparation of a compound of formula 12,

$\text{(I.2)}$

wherein $R^2$, $R^3$, $R^4$ and $R^5$ are as defined for compound of formula I, and $R^1$ is CrC$_4$alkyl or CrC$_4$haloalkyl, which comprises reacting a compound of formula III,

$\text{(III)}$

wherein $R^2$, $R^3$, $R^4$ and $R^5$ are as defined for compound of formula I, and $R^1$ is CrC$_4$alkyl or CrC$_4$haloalkyl, with N-chlorosuccinimide or molecular chlorine.
13. A process for the preparation of a compound of formula III,

\[
\text{R}^1 \text{N}^2 \text{R}^3 \text{R}^4 \text{R}^5
\]

wherein \( \text{R}^2, \text{R}^3, \text{R}^4 \) and \( \text{R}^5 \) are as defined for compound of formula I, and \( \text{R}^1 \) is \( \text{CrC}_4 \text{alkyl} \), which comprises reacting a compound of formula IV,

\[
\text{Br} \text{N}^2 \text{R}^3 \text{R}^4 \text{R}^5
\]

wherein \( \text{R}^2, \text{R}^3, \text{R}^4 \) and \( \text{R}^5 \) are as defined for compound of formula I, with a reagent of formula \((\text{R}^1)_3 \text{Al}\), wherein \( \text{R}^1 \) is \( \text{CrC}_4 \text{alkyl} \), in the presence of a transition metal catalyst.

14. A fungicidal composition for controlling or protecting against phytopathogenic microorganisms, comprising as active ingredient at least one compound as defined in any one of claims 1 to 10, in free form or in agrochemically usable salt form, and at least one adjuvant.

15. The composition according to claim 14, which comprises at least one additional fungicidally active compound, preferably selected from the group consisting of azoles, pyrimidinyl carbinoles, 2-amino-pyrimidines, morpholines, anilinopyrimidines, pyrroles, phenylamides, benzimidazoles, dicarboximides, carboxamides, strobilurines, dithiocarbamates, N-halomethylthiotetrahydrophthalimides, copper-compounds, nitrophenols, organo-phosphorus-derivatives, pyridazines, triazolopyrimidines, carboxamides or benzamides.
16. The use of a compound as defined in any one of claims 1 to 10 for controlling or preventing infestation of plants, harvested food crops, seeds or non-living materials by phytopathogenic microorganisms.

17. A method of controlling or preventing an infestation of crop plants, harvested food crops or non-living materials by phytopathogenic or spoilage microorganisms or organisms potentially harmful to man, which comprises the application of a compound as defined in any one of claims 1 to 10, as active ingredient to the plants, to parts of the plants or to the locus thereof, to seeds or to any part of the non-living materials.

18. The method according to claim 17, wherein the phytopathogenic microorganisms are fungal organisms.

19. A composition comprising at least one compound as defined in any one of claims 1 to 10 and / or at least one pharmaceutically acceptable salt thereof, at least one pharmaceutically acceptable carrier and / or at least one pharmaceutically acceptable diluent.

20. A compound as defined in any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof for use as a medicament.

21. A compound as defined in any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof for the treatment of cancer.

22. Use of a compound as defined in any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cancer.

23. A method of treating cancer in a subject in need thereof, comprising administering a compound as defined in any one of claims 1 to 10 to said subject in an amount effective to treat said cancer.
INTERNATIONAL SEARCH REPORT

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X Special categories of cited documents

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'X4' document member of the same patent family

Date of the actual completion of the international search

17 June 2009

Date of mailing of the international search report

24/06/2009

Name and mailing address of the ISA/Authorized officer

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Fax (+31-70) 340-3016

Usuel i, Ambrogio
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