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D E C I S I O N
of 3 February 2000

Case Number: T 0740/95 - 3.3.1

Application Number: 91113705.7

Publication Number: 0471372

IPC: C07D 277/32

Language of the proceedings: EN

Title of invention:
Novel substituted guanidine derivatives, their preparation and use

Applicant:
Takeda Chemical Industries, Ltd.

Opponent:
-

Headword:
Substituted guanidine derivatives/TAKEDA

Relevant legal provisions:
EPC Art. 123(2), 56

Keyword:
"Inventive step (yes) - non-obvious solution"

Decisions cited:
-

Catchword:
-

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Case Number: T 0740/95 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 3 February 2000

Appellant: Takeda Chemical Industries, Ltd.
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Representative: von Kreisler, Alek, Dipl.-Chem.
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 26 April 1995 refusing European patent application No. 91 113 705.7 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. J. Nuss
Members: P. F. Ranguis
S. C. Perryman

Summary of Facts and Submissions

I. The Appeal lies from the Examining Division's decision to refuse the European published patent application No. 0 471 372 (European patent application No. 91 113 705.7) on the ground that the then pending request, namely:

- Claims 1 to 36 for Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK,

- Claims 1 to 35 for Contracting State ES

contained claims which were regarded as offending against Article 56 EPC in the light of the disclosure of three documents:

(1) EP-A-0 376 279

(2) EP-A-0 375 907

(3) US-A-3 878 224.

II. The Examining Division held that the solution to the problem of providing further insecticidal nitroguanidine derivatives having a new type of substituents was obvious since documents (1) or (2) showed that the variations of different substituents attached to the nitroguanidine moiety did not impair the insecticide properties of the compounds. In addition, it was considered that document (3) taught that the groups

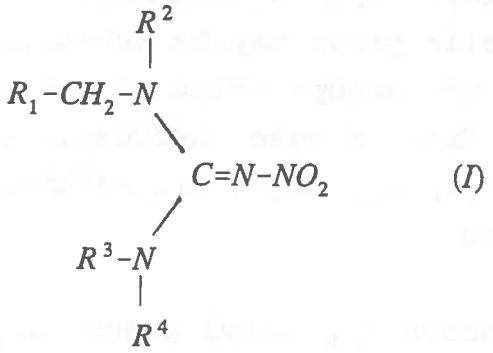
$-CH_2-CH_3$ and $-S-CH_3$ were bioisosteric groups, suggesting therefore to the man skilled in the art to replace one by the other.

III. Together with the statement of Grounds of appeal, the Appellant filed a new set of claims 1 to 35 for the Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK and a new set of claims 1 to 34 for the Contracting State ES. An amended specification was also submitted to accord with the amended sets of claims.

IV. In response to a communication of the Board attached to the summons to oral proceedings, the Appellant filed on 7 January 2000 new amended claims 1 to 35 for the Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK and new amended claims 1 to 40 for the Contracting State ES, those claims therefore superseding the claims filed with the statement of Grounds of Appeal previously mentioned. The Appellant also submitted new amended pages 2c, 3, 48, 53 and 88 of the description. He also submitted a report concerning additional experimental data related to the comparison between compound 19 of the claimed invention and compounds n° 22, 23, 25 and 27 of document (1).

V. At the oral proceedings, the Appellant filed new amended claims 1 to 35 for the Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK and new amended claims 1 to 39 for the Contracting State ES, those claims therefore superseding the claims filed with the letter of 7 January 2000 previously mentioned (see point IV). The independent claims 1 and 22 of the set of claims for the Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK are to be found in the Annex. The essential features of the independent claims 1, 22, 25, 26, 27, 28 relevant for the present decision appear from the following:

Independent Claim 1 relates to a compound of formula:



(I)

wherein R^1 is a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different,

and are selected from C_{1-15} alkyl group, C_{3-10} cycloalkyl group, C_{2-10} alkenyl group, C_{2-10} alkynyl group, C_{3-10} cycloalkenyl group, C_{6-10} aryl group, C_{7-10} aralkyl group, phenethyl group, nitro, hydroxy, mercapto, oxo, thioxo, cyano, carbamoyl, carboxyl, C_{1-4} alkoxycarbonyl, sulfo, halogen, C_{1-4} alkoxy group, C_{6-10} aryloxy group, C_{1-4} alkylthio group, C_{6-10} arylthio group, C_{1-4} alkylsulfinyl group, C_{6-10} arylsulfinyl group, C_{1-4} alkylsulfonyl group, C_{6-10} arylsulfonyl group, amino, C_{2-6} acylamino group, mono- or di-C_{1-4} alkylamino group, C_{3-6} cycloalkylamino group, C_{6-10} arylamino group, C_{2-4} acyl group, C_{6-10} arylcarbonyl group and five- to six-membered heterocyclic group each containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen,

and the above C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{6-10} aryl, C_{7-10} aralkyl, C_{6-10} aryloxy , C_{6-10} arylthio, C_{6-10} arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} arylamino or heterocyclic group may be substituted with 1 to 5 substituents groups which may be the same or different selected from halogen, hydroxyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{6-10} aryl, C_{1-4} alkoxy, C_{1-4} alkylthio and phenylthio,

and the above C_{1-15} alkyl group, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{1-4} alkoxy,C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, mono- or di-C_{1-4} alkylamino or C_{3-6} cycloalkylamino may be substituted with 1 to 5 substituent groups which may be the same or different selected from halogen, hydroxyl, C_{1-4} alkoxy and C_{1-4} alkylthio,

R^2 is cyano,

a group of the formula: $-S(O)_n-R^{13}$

wherein n is an integer of 1 or 2 and R^{13} is a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1,

a group of the formula: $-P(=O)R^{14}R^{15}$

wherein R^{14} and R^{15} are each independently hydroxyl; a hydrocarbon group attached through an oxygen atom selected from C_{1-15} alkoxy, C_{3-10} cycloalkoxy, C_{2-10} alkenyloxy , C_{2-10} alkynyloxyl, C_{3-10} cycloalkenyloxy, C_{6-10} aryloxy or C_{7-10} aralkyloxy, this hydrocarbon group optionally having 1 to 5 substituents defined as above for R^1; a heterocyclyloxy group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1;

a group of the formula: $-CO-O-R^6$

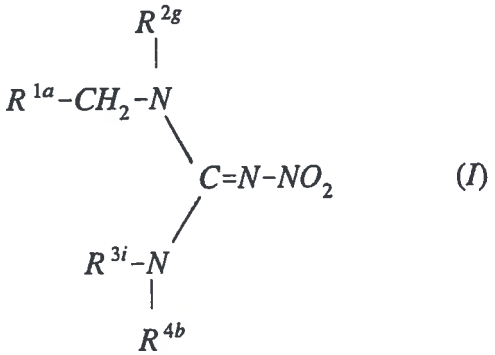
wherein R^6 is a hydrocarbon group consisting of C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; or

a group of the formula: $-CO-NR^7R^8$

wherein R^7 and R^8, which are the same or different, are each independently hydrogen; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl group, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; or R^7 and R^8, taken together with the nitrogen atom to which they are attached are a cyclic amino group which may be substituted with 1 to 4 C_{1-4} alkyl groups.

The definitions given for the groups R^3 and R^4 are not recited as they are not relevant for deciding the present case (those definitions are set out in the Annex).

Independent Claim 22 relates to a compound of formula:



(I)

wherein R^{1a} is pyridyl, halogenopyridyl, thiazolyl, or halogenothiazolyl; R^{2g} is C_7-C_{12} aryloxythiocarbonyl.

The definitions given for the groups R^{3i} and R^{4b} are not recited as they are not relevant for deciding the present case (those definitions are set out in the Annex).

Independent Claim 25 relates to a pesticidal composition comprising an effective amount of the substituted nitroguanidine compound according to any of Claims 1 to 21 or a salt thereof in admixture with an acceptable carrier, vehicle, diluent or excipient.

Independent Claim 26 relates to a pesticidal composition comprising an effective amount of the substituted nitroguanidine compound according to any of Claims 22 to 24 in admixture with an acceptable carrier, vehicle, diluent or excipient.

Independent Claim 27 relates to a use of the substituted nitroguanidine compound according to Claim 1 or 22 or a salt thereof for the manufacture of a pesticidal composition.

Independent Claim 28 relates to a method for controlling a pest which comprises applying an effective amount of the substituted nitroguanidine compound according to Claim 1 or 22 or a salt thereof to prevent said pest.

VI. At the Oral Proceedings the Appellant submitted in essence that the problem to be solved, in view of document (1) i.e. the closest prior art, was to provide further substituted nitroguanidines derivatives which are useful as pesticidal agents.

The general teaching of the document (1) relates to nitroguanidine derivatives useful as insecticidal agents differing from the claimed compounds in that the group R^2 is a hydrogen atom or an optionally substituted hydrocarbon. In addition however, this document discloses three isolated examples of other compounds, namely Example 22, wherein R^1 is 2-chloro-5-pyridyl and R^2 is CHO; Example 23, wherein R^1 is 2-chloro-5-pyridyl and R^2 is COMe; Example 27, wherein R^1 is 2-chloro-5-thiazolyl and R^2 is COMe; for all these three compounds, the group corresponding to NR^3R^4 in the claimed compounds (see formula (I), point V above) being dimethylamino.

The person skilled in the art would have noted that those three compounds were not in line with the general teaching of said document (1). He would not have been motivated to continue any investigation in that other direction due to the fact that the preferred compounds as set out on page 5, lines 28 to 29 are those where R^2 is H or C_1-C_4 alkyl. Furthermore, this general teaching is confirmed by the disclosure of document (2) wherein the corresponding radical again is H or C_1-C_4 alkyl. Additionally, there is no suggestion in the disclosure of document (1) to replace the R^2 group CHO or COMe by the specific groups mentioned in the present claim 1.

One would consider these three compounds as isolated exceptions, which, given the general teaching of document (1) taken in combination with document (2) would not have suggested to the person skilled in the art to consider the claimed compounds.

As for document (3), the Appellant denied that this was relevant, due to the difference of structure of the compounds disclosed and due to their different activity (herbicide versus insecticide). He further pointed out that the Examining Division had based its objection on a meaning for R^2 which had been deleted in the present request, namely the meaning R^2 is $-S-R^{13}$.

VII. The Appellant requested that the decision under appeal be set aside and that the matter be remitted to the Examining Division with the order to grant a patent on the basis of the claims of the present request.

VIII. At the end of the oral proceedings the decision of the Board was given orally.

Reasons for the Decision

1. The appeal is admissible.

2. There are no objections under Article 123(2) EPC to the present sets of claims, for the Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK, on the one hand, and for the Contracting State ES on the other.

In particular, regarding the set for the Contracting States DE, GB, FR, IT, NL, SE, LI, CH, BE, AT, LU, GR and DK:

Claim 1 finds support on page 2, lines 15 to 30; page 14, lines 11 to 14; page 15, line 5 to page 17, line 30; and page 18, lines 1 to 11 of the application as filed;

Claim 22 is supported by the originally filed Claim 21,

Claim 25 is supported by the originally filed Claim 26,

Claim 26 is supported by the originally filed Claim 27,

Claim 27 is supported by the originally filed Claim 30,

Claim 28 is supported by the originally filed Claim 31.

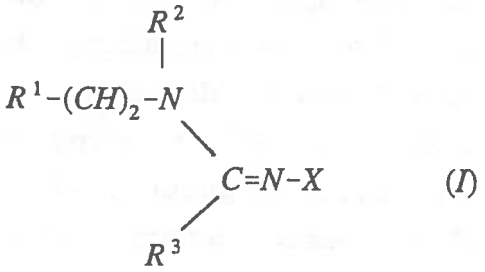
The same finding applies to the set of claims for the Contracting State ES.

3. The present sets of claims are also clear pursuant to Article 84 EPC as the expression "which may be optionally substituted with 1 to 5 substituents" in the refused claims has every time been replaced by a list specifying the said substituents (see point V above).

4. After examination of the cited prior art, including document EP-A-0 302 833 (4) cited in the search report, the Board has reached the conclusion that the claimed subject-matter is novel. Since in the decision under appeal the Examining Division acknowledged the novelty of the subject-matter of the present claims, it is not necessary to give detailed reasons for this finding.

5. It still remains to be decided whether the claimed subject-matter involves an inventive step. In that respect, it is noted that the claimed subject-matter relates to two independent product claims, i.e. claims 1 and 22. However, the subject-matter of both claims is so closely related that the Board will deal with them together.

5.1 The Board considers, in agreement with the Appellant, that the closest prior art to the claimed invention is document (1) which relates to insecticidal guanidine derivatives of formula:



(I)

wherein n is 0 or 1, R^1 is an optionally substituted homocyclic or heterocyclic group, R^2 is a hydrogen atom or an optionally substituted hydrocarbon, R^3 is a primary, secondary or tertiary amino group and X is NO_2 (or CF_3),

The disclosure of the said document also relates in its examples to three isolated compounds where R^2 is something other than a hydrogen atom or an optionally substituted hydrocarbon, namely Example 22 (n is 1, R^1 is 2-chloro-5-pyridyl, **R^2 is CHO**, R^3 is dimethylamino and X is NO_2) ; Example 23 (n is 1, R^1 is 2-chloro-5-pyridyl, **R^2 is COMe**, R^3 is dimethylamino and X is NO_2); Example 27 (n is 1, R^1 is 2-chloro-5-thiazolyl, **R^2 is COMe**, R^3 is dimethylamino and X is NO_2).

The examplified compounds, including numbers 22, 23 and 27, are stated to show an excellent insecticidal effect on Nilaparvata lugens and Spodoptera litura (see page 13, lines 33 to 34 and page 14, lines 23 to 24).

5.2 In the light of this closest state of the art, the technical problem underlying the application is to be seen in providing further nitroguanidine derivatives useful as pesticidal agents.

According to the application in suit, this problem is essentially solved by replacing the groups R^2 of the compounds disclosed in document (1) by other groups R^2 selected from $-S(O)_n-R^{13}$, n being an integer of 1 or 2 (sulfinyl or sulfonyl group), $-P(=O)R^{14}R^{15}$ (phosphonate group), $-CO-OR^6$ (ester group), $-CO-NR^7R^8$ (amide group) as indicated in claim 1 or by a group R^2 which is C_{7-12} aryloxythiocarbonyl as mentioned in claim 22 (see point V above).

In view of the tests results reported in the application in suit for the pests Nilaparvata lugens and Aphis gossypii (compounds N° 1, 2, 6-9, 11, 19, 27, 28, 44-49 and 54) and for Spodoptera litura (compounds N° 1, 2, 6, 7, 9, 19, 45-49 and 54), it is plausible that the compounds as defined in claims 1 and 22 for all the Contracting States other than ES solve the stated technical problem.

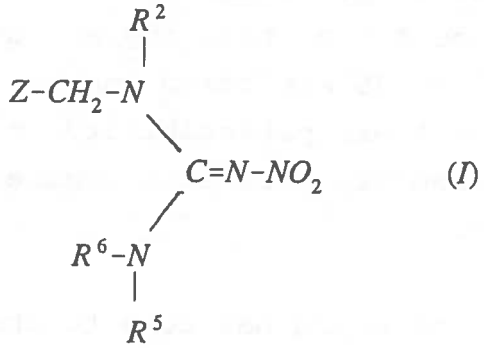
5.3 It remains to be decided whether or not the compounds of claims 1 and 22 of the application in suit involve an inventive step pursuant to Article 56 EPC.

The document (1) actually comprises both a general teaching related to the host of compounds of formula (I) wherein R^2 is H or optionally substituted hydrocarbon and three isolated examples falling outside this general teaching, limited to one compound in which R^2 is CHO (example 22) and two compounds in which R^2 is COMe (examples 23 and 27). In the Board's judgement, while the person skilled in the art might have considered extending the general teaching to other compounds wherein R^2 is either CHO or COMe, the other

groups R^1 and R^3 being one of those mentioned in the general formula (I), for their insecticidal activity, he would not have been directed or incited to look for other groups R^2 such as those presently claimed. There exists thus no pointer toward the groups R^2 mentioned in the present claims 1 and 22.

Moreover, this is consistent with the information in document (1) that the **preferred** compounds are those where R^2 are H or C_1-C_4 alkyl groups, preferably C_1-C_4 alkyl groups (see page 5, lines 28 to 29).

This teaching is confirmed by document (2) which relates, in particular, to insecticidally nitroguanidine compounds of formula:



(I)

wherein R^2 is a hydrogen atom or a C_1-C_4 alkyl group and preferably hydrogen or methyl (see page 4, line 20).

The Board's conclusion is that documents (1) and (2) do not lead to the subject-matter of present claims 1 and 22.

Document (3) discloses herbicidally N-substituted-Δ^1-tetrahydrophtalimides where the substituent R attached to the nitrogen atom may be lower alkyl thio.The Board notes that the claims of the present request no longer cover the possibilities of R^2 being the group $S(O)_n$-R^{13}

with n being 0. Therefore, this document cannot be taken as suggesting the compounds now claimed even if it were legitimate (which the Board doubts) to rely on an argument that the groups $-CH_2-CH_3$ and $-S-CH_3$ are bioisosteric groups (see point II above).

5.4 It follows from the above that the subject-matter of Claims 1 and 22 for the designated Contracting States other than ES is not rendered obvious by document (1), either alone or in combination with documents (2) and (3). The same applies to the dependent Claims 2 to 21 and 23 to 24 relating to specific embodiments of said independent Claims. Independent Claims 25 and 26 relating to pesticidal compositions, independent Claim 27 relating to a use of the substituted nitroguanidine compound for the manufacture of a pesticidal composition, independent Claim 28 relating to a method for controlling a pest, and the process Claims 29 to 35 are based on the same inventive concept and derive their patentability on the same basis as do Claims 1 and 22. This also applies to Claims 1 to 39 for Spain.

5.5 Although the Board has come to the conclusion that the claimed subject-matter complies with the requirements of the Article 52(1) EPC, it was noted that the description has still to be put into conformity with the Claims of the present request. Therefore, having regard to the fact that the function of the Boards of Appeal is primarily to give a judicial decision upon the correctness of the earlier decision taken by the first instance, the Board exercises its discretion under Article 111(1) EPC to remit the case to the first instance in order for the description to be adapted to the allowable claimed subject-matter.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

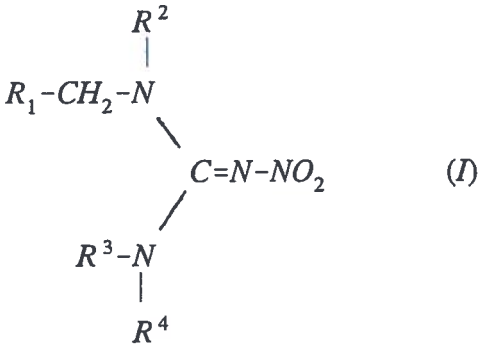
2. The matter is remitted to the first instance with the order to grant a patent in accordance with the appellant's request at the oral proceedings on 3 February 2000 and a description yet to be adapted.

The Registrar: The Chairman:

E. Görgmaier A. Nuss

Annex:

1. A compound of the formula:



(I)

wherein R^1 is a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different,

and are selected from C_{1-15} alkyl group, C_{3-10} cycloalkyl group, C_{2-10} alkenyl group, C_{2-10} alkynyl group, C_{3-10} cycloalkenyl group, C_{6-10} aryl group, C_{7-10} aralkyl group, phenethyl group, nitro, hydroxy, mercapto, oxo, thioxo, cyano, carbamoyl, carboxyl, C_{1-4} alkoxycarbonyl, sulfo, halogen, C_{1-4} alkoxy group, C_{6-10} aryloxy group, C_{1-4} alkylthio group, C_{6-10} arylthio group, C_{1-4} alkylsulfinyl group, C_{6-10} arylsulfinyl group, C_{1-4} alkylsulfonyl group, C_{6-10} arylsulfonyl group, amino, C_{2-6} acylamino group, mono- or di-C_{1-4} alkylamino group, C_{3-6} cycloalkylamino group, C_{6-10} arylamino group, C_{2-4} acyl group, C_{6-10} arylcarbonyl group and five- to six-membered heterocyclic group each containing 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen,

arylsulfinyl, C_{6-10} arylsulfonyl, C_{6-10} arylamino or heterocyclic group may be substituted with 1 to 5 substituent groups which may be the same or different selected from halogen, hydroxyl, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{6-10} aryl, C_{1-4} alkoxy, C_{1-4} alkylthio and phenylthio,

and the above C_{1-15} alkyl group, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{1-4} alkoxy,C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, mono- or di-C_{1-4} alkylamino or C_{3-6} cycloalkylamino may be substituted with 1 to 5 substituents groups which may be the same or different selected from halogen, hydroxyl, C_{1-4} alkoxy and C_{1-4} alkylthio,

R^2 is cyano,

a group of the formula: $-S(O)_n-R^{13}$

wherein n is an integer of 1 or 2 and R^{13} is a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1,

a group of the formula: $-P(=O)R^{14}R^{15}$

wherein R^{14} and R^{15} are each independently hydroxyl; a hydrocarbon group attached through an oxygen atom selected from C_{1-15} alkoxy, C_{3-10} cycloalkoxy, C_{2-10} alkenyloxy , C_{2-10} alkynyloxy, C_{3-10} cycloalkenyloxy, C_{6-10}

aryloxy or C_{7-10} aralkyloxy, this hydrocarbon group optionally having 1 to 5 substituents defined as above for R^1; a heterocyclyloxy group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1;

a group of the formula: $-CO-R^6$

wherein R^6 is a hydrocarbon group consisting of C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; or

a group of the formula: $-CO-NR^7R^8$

wherein R^7 and R^8, which are the same or different, are each independently hydrogen; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl group, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituent defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may be optionally substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; or R^7 and R^8, taken together with the nitrogen atom to which they are attached are a cyclic amino group which may be substituted with 1 to 4 C_{1-4} alkyl groups;

R^3 is hydrogen,

cyano,

a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1 (except for one substituted with an oxo group at the binding site),

a group of the formula: $-S(O)_n-R^{13}$

wherein n is an integer of 0, 1 or 2 and R^{13} is a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected

from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1,

a group of the formula: $-P(=O)R^{14}R^{15}$

wherein R^{14} and R^{15} are each independently hydroxyl; a hydrocarbon group attached through an oxygen atom selected from C_{1-15} alkoxy, C_{3-10} cycloalkoxy, C_{2-10} alkenyloxy , C_{2-10} alkynyloxy, C_{3-10} cycloalkenyloxy, C_{6-10} aryloxy or C_{7-10} aralkyloxy, this hydrocarbon group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclyloxy group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl group, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1,

a group of the formula: $-CO-R^9$

wherein R^9 is a hydrogen; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents

defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1,

a group of the formula: $-CO-O-R^{10}$

wherein R^{10} is a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituent defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are defined as above for R^1,

a group of the formula: $-CO-NR^{11}R^{12}$

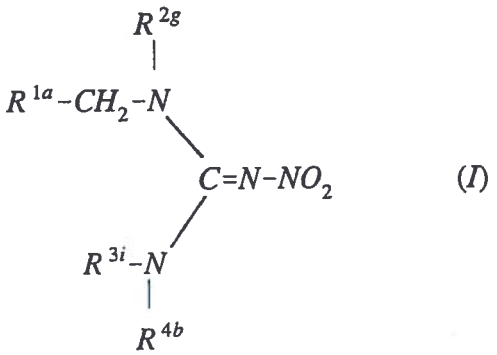
wherein R^{11} and R^{12}, which are the same or different, are each independently hydrogen; a hydrocarbon group selected from C_{1-15} alkyl, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{3-10} cycloalkenyl, C_{6-10} aryl or C_{7-10} aralkyl, this group optionally having 1 to 5 substituents defined as above for R^1; or a heterocyclic group having a single or fused ring with 5 to 8 ring members in each ring and having from one to five heteroatoms in each ring independently selected from oxygen, nitrogen and sulfur, wherein said heterocyclic group may optionally be substituted with 1 to 5 substituents which may be the same or different and are

defined as above for R^1; or R^{11} and R^{12}, taken together with the nitrogen atom to which they are attached are a cyclic amino group which may be substituted with 1 to 4 C_{1-4} alkyl groups; and

R^4 is hydrogen or a C_{1-4} alkyl group;

or a salt thereof.

22. A compound of formula:



(I)

wherein R^{1a} is pyridyl, halogenopyridyl, thiazolyl, or halogenothiazolyl, R^{2g} is C_7-C_{12} aryloxythiocarbonyl, R^{3i} is hydrogen, C_{1-4} alkyl, C_{7-12} arylcarbonyl, C_{7-12} aryloxycarbonyl, C_{8-13} aralkoxycarbonyl, C_{2-7} alkylaminocarbonyl, di-C_{1-4} alkylaminocarbonyl, alicyclic aminocarbonyl, or C_{1-4} alkylsulfonyl, and R^{4b} is hydrogen or C_{1-4} alkyl; or a salt thereof.