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**New process for preparing pesticidal intermediates**

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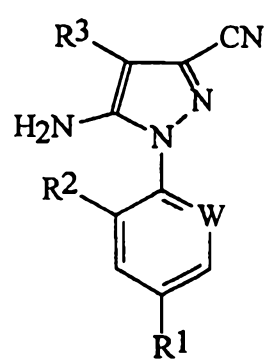
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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (51) International Patent Classification <sup>7</sup> :<br>C07D 231/38  | A2   | (11) International Publication Number: <b>WO 00/46210</b><br>(43) International Publication Date: 10 August 2000 (10.08.00) |
| <p>(21) International Application Number: PCT/EP00/01101</p> <p>(22) International Filing Date: 1 February 2000 (01.02.00)</p> <p>(30) Priority Data:<br/>99/01469 4 February 1999 (04.02.99) FR</p> <p>(71) Applicant (for all designated States except US): AVENTIS CROPS SCIENCE S.A. [FR/FR]; 55, avenue René Cassin, F-69009 Lyon (FR).</p> <p>(72) Inventor; and<br/>(75) Inventor/Applicant (for US only): ANCEL, Jean-Erick [FR/FR]; 14, rue Lucien Begule, F-69230 Saint-Genis-Laval (FR).</p> <p>(74) Agent: RHÔNE-POULENC AGRO; Groupement de Mandataires no. 153, Département Propriété Industrielle, DPI, B.P. 9163, F-69263 Lyon Cedex 09 (FR).</p> | <p>(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b><br/>Without international search report and to be republished upon receipt of that report.</p> |   |
| (54) Title: NEW PROCESS FOR PREPARING PESTICIDAL INTERMEDIATES  |  |   |
| (57) Abstract   |  |   |
| <p>The invention relates to a process for the preparation of a compound of formula (I): wherein W, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are as defined in the description.</p>  |   | (I)   |

New Process For Preparing Pesticidal  
Intermediates

This invention relates to novel processes for preparing pesticides or pesticidal intermediates (particularly 5-amino-1-aryl-3-cyanopyrazole derivatives).

European Patent Publication Nos. 0295117 and 0234119 describe the preparation of pesticidally active phenylpyrazole compounds and of 5-amino-1-aryl-3-cyanopyrazole intermediate compounds used in their synthesis.

Various methods for preparing these compounds are known. The present invention seeks to provide improved or more economical methods for the preparation of pesticides and the intermediate compounds useful in preparing them.

The present invention advantageously provides a convenient process for preparing pesticidally active phenylpyrazole compounds or 5-amino-1-aryl-3-cyanopyrazole pesticidal intermediates, which may be obtained in high yield and high purity.

The present invention also advantageously provides a convenient process for preparing pesticidally active phenylpyrazole compounds of 5-amino-1-aryl-3-cyanopyrazole pesticidal intermediates, which proceeds without the need for a diazotisation step and hence serves to avoid problems associated with diazotisation such as hazards known to occur for such reactions.

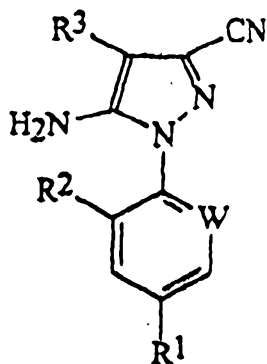
The present invention also advantageously provides a process for preparing pesticidally active phenylpyrazole compounds or 5-amino-1-aryl-3-cyanopyrazole pesticidal intermediates, which is simple to perform, and where one can

employ less expensive starting materials compared to known methods.

The present invention also advantageously provides novel intermediates for the manufacture of pesticidally active compounds.

These and other advantages of the invention will become apparent from the following description, and are achieved in whole or in part by the present invention.

The present invention accordingly provides a process (A) for the preparation of a compound of formula (I):



(I)

wherein W represents nitrogen or  $-CR^4$ ;

R<sup>1</sup> represents halogen, haloalkyl (preferably trifluoromethyl), haloalkoxy (preferably trifluoromethoxy),  $R^5S(O)_n^-$ , or  $-SF_5$ ;

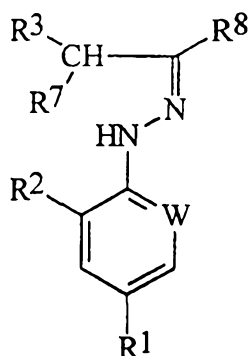
R<sup>2</sup> represents hydrogen or halogen (for example chlorine or bromine);

R<sup>3</sup> represents hydrogen or  $R^6S(O)_m^-$ ;

R<sup>4</sup> represents halogen (for example chlorine or bromine);

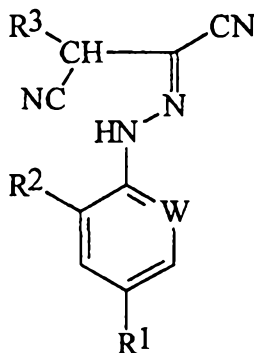
R<sup>5</sup> and R<sup>6</sup> represent alkyl or haloalkyl; and

m and n represent 0, 1 or 2; which process comprises the reaction of a compound of formula (II):



(II)

wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $W$  are as hereinbefore defined,  $R^7$  represents a leaving group (preferably chlorine or bromine) and  $R^8$  represents chlorine or bromine (preferably  $R^7$  and  $R^8$  each represent chlorine), with a cyanide salt. The reaction proceeds via dicyano intermediates of formula (III):



(III)

wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $W$  are as hereinbefore defined, which generally cyclise under the conditions of the reaction, thus providing a simple and convenient process. Optionally the intermediates of formula (III) may be cyclised in the presence of base according to known methods. Compounds of formula (II) and (III) may exist as a mixture of syn and anti isomers.

Unless otherwise specified in the present specification 'alkyl' means straight- or

branched- chain alkyl having from one to six carbon atoms (preferably one to three). Unless otherwise specified 'haloalkyl' and 'haloalkoxy' are straight- or branched- chain alkyl or alkoxy respectively having from one to six carbon atoms (preferably one to three) substituted by one or more halogen atoms selected from fluorine, chlorine or bromine.

Suitable cyanide salts for the above reaction to form compounds of formula (I) include alkali metal cyanides such as potassium, sodium or lithium cyanide, alkaline earth metal cyanides or ammonium cyanide. Potassium cyanide or sodium cyanide are preferred. The reaction is generally conducted in a solvent. Solvents suitable for use include nitriles such as acetonitrile, amides such as N-methylpyrrolidinone, sulphoxides such as dimethylsulphoxide, ethers such as tetrahydrofuran or alcohols such as ethanol. Water may be employed as a co-solvent. The reaction temperature is generally from about  $-20^{\circ}\text{C}$  to the reflux temperature of the solvent, and preferably from about  $0^{\circ}\text{C}$  to about  $20^{\circ}\text{C}$ .

Generally from two to 5 molar equivalents of cyanide and preferably from about two to about three equivalents are employed.

In formulae (I), (II) and (III) and in the formulae depicted hereinafter, preferred values of the symbols are as follows:-

$\text{R}^1$  represents haloalkyl (preferably trifluoromethyl), haloalkoxy (preferably trifluoromethoxy) or  $-\text{SF}_5$ ;

W represents  $-\text{CR}^4$ ;

$\text{R}^2$  and  $\text{R}^4$  represent halogen (preferably chlorine);

R<sup>3</sup> represents a hydrogen atom, or R<sup>6</sup>S(O)<sub>m</sub>-;  
wherein R<sup>6</sup> represents optionally halogenated  
methyl or ethyl (preferably trifluoromethyl);  
and R<sup>7</sup> and R<sup>8</sup> represent chlorine.

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Particularly preferred compounds of formula  
(I) include:

5-amino-3-cyano-1-(2,6-dichloro-4-  
trifluoromethylphenyl)pyrazole;

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5-amino-3-cyano-1-(2,6-dichloro-4-  
trifluoromethylphenyl)-4-  
trifluoromethylthiopyrazole;

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5-amino-3-cyano-1-(2,6-dichloro-4-  
trifluoromethylphenyl)-4-  
trifluoromethylsulphonylpyrazole; and

5-amino-3-cyano-1-(2,6-dichloro-4-  
trifluoromethylphenyl)-4-ethylsulphonylpyrazole.

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The process is particularly useful for  
preparing compounds in which R<sup>3</sup> represents  
hydrogen, and most preferably for 5-amino-3-  
cyano-1-(2,6-dichloro-4-  
trifluoromethylphenyl)pyrazole.

25

In formulae (II) and (III) and in the  
formulae depicted hereinafter, the most  
preferred values of the symbols are as follows:-

R<sup>1</sup> represents trifluoromethyl;

W represents -CR<sup>4</sup>;

R<sup>2</sup>, R<sup>4</sup>, R<sup>7</sup> and R<sup>8</sup> represent chlorine; and

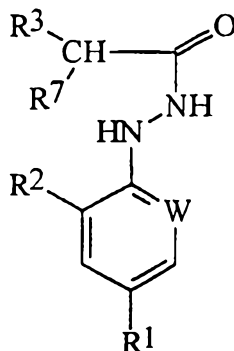
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R<sup>3</sup> represents hydrogen.

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According to a further feature of the present  
invention the above process (A) can be combined  
with additional process steps (B) and (C) as  
defined hereinbelow.

Process step (B); comprises the reaction of a compound of formula (IV):



(IV)

5            wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>7</sup> and W are as hereinbefore defined, with a chlorinating or brominating agent; to give a compound of formula (II) wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>7</sup>, R<sup>8</sup> and W are as hereinbefore defined.

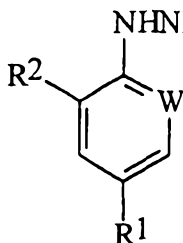
10            Suitable chlorinating agents are thionyl chloride, phosphoryl chloride, phosphorus trichloride, phosphorus pentachloride or a mixture of triphenylphosphine and carbon tetrachloride. Brominating agents which may be  
15            used include thionyl bromide, phosphoryl bromide or a mixture of triphenylphosphine and carbon tetrabromide. Preferably the process is performed using a chlorinating agent. A  
20            preferred chlorinating agent is phosphoryl chloride.

25            Solvents which may be used include ethers, aromatic hydrocarbons such as toluene, aromatic halogenated hydrocarbons such as chlorobenzene, or halogenated hydrocarbons such as dichloroethane.

            The reaction temperature is generally from 0°C to 120°C, preferably from 70°C to 90°C.



Process step (C) comprises the reaction of an arylhydrazine compound of formula (V):



(V)

5            wherein R<sup>1</sup>, R<sup>2</sup> and W are as hereinbefore defined; with a compound of formula (VI):



          wherein R<sup>3</sup> and R<sup>7</sup> are as defined above, and R<sup>9</sup> represents a leaving group preferably a chlorine or bromine atom (generally both R<sup>7</sup> and R<sup>9</sup> represent a chlorine atom); to give a compound of formula (IV) as defined above. The reaction to obtain compounds of formula (IV) is generally performed in a solvent such as halogenated hydrocarbons for example dichloromethane, ethers for example tetrahydrofuran or dioxan, or N,N-dialkylamides for example N,N-dimethylformamide, and at a temperature of from -20° to 50°C, preferably from 0 to 20°C.

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          The above combination of process step (A), preceded by process step (B), preceded by process step (C), represents in certain aspects an improvement over the prior art.

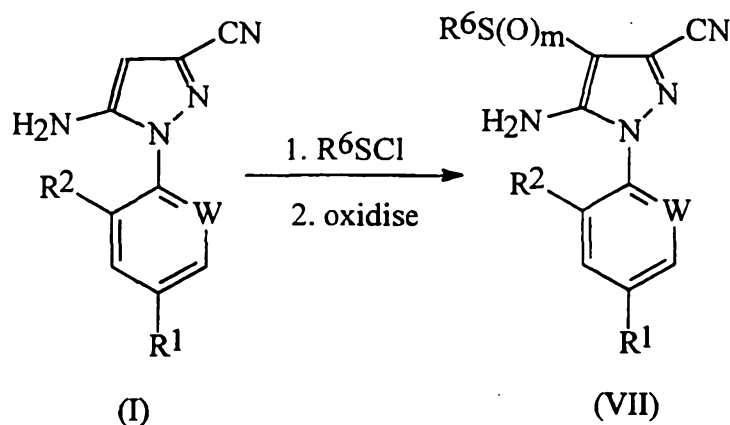
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          Compounds of formula (II) and (IV) above are novel and therefore constitute a further feature of the present invention.

30            Where R<sup>3</sup> is other than hydrogen, compounds of formula (III) are novel.

Compounds of formula (VI) are known.

The intermediate 5-amino-1-aryl-3-cyanopyrazole compounds of formula (I) obtained  
 5 by the process (A) of the invention wherein  $R^3$  represents hydrogen, may be used in the preparation of pesticidally active phenylpyrazole derivatives of formula (VII) according to the following reaction scheme:



10

wherein the symbols used above are as hereinbefore defined.

15

The following non-limiting examples illustrate the invention. NMR spectra are recorded using deuteriochloroform as solvent.

#### Example 1

#### **Preparation of 5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-3-cyanopyrazole**

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A solution of *N'*-(2,6-dichloro-4-trifluoromethylphenyl)-chloroacetohydrazonoyl chloride (1.1g) in ethanol (6ml) was added during 25 minutes to a stirred solution of sodium cyanide (0.475g) in ethanol (6ml) and water (6ml). The temperature rose to 32°C. After 15 minutes an addition of ethanol (4.5ml) and water (3ml) was made and stirred for 15 minutes at 20°C. A further addition of water (3ml) was

made and the mixture filtered. The residue was dissolved in ethanol, concentrated and purified by chromatography on silica gel eluting with dichloromethane to give the title compound (0.55g), obtained in 53% yield.

### Example 2

#### **Preparation of N'-(2,6-dichloro-4-trifluoromethylphenyl)-chloroaceto-hydrazoneyl chloride**

Phosphoryl chloride (500 microlitres, 1.7 equivalents) was added in one portion to a stirred solution of N'-(2,6-dichloro-4-trifluoromethylphenyl)-chloroaceto-hydrazide (1.0g, 3.11 mmol) in toluene (20ml) and heated at 70°C under an argon atmosphere for 20 hours. The cooled mixture was evaporated and the residue extracted with cyclohexane. The extracts were combined and evaporated to give the title compound (0.971g) as an orange oil, NMR 4.4(s,2H), 7.55(s,2H), 7.7(s,1H). The yield was 90%.

### Example 3

#### **Preparation of N'-(2,6-dichloro-4-trifluoromethylphenyl)-chloroaceto-hydrazide**

A solution of chloroacetyl chloride (2.3ml, 1.08 equivalents) in anhydrous dichloromethane (30ml) was added during 30 minutes to a stirred solution of 2,6-dichloro-4-trifluoromethylphenylhydrazine (6.1g, 24.89 mmol) in anhydrous dichloromethane (60ml) maintaining between 5 and 12°C under an argon atmosphere. The mixture was then stirred for 5-12 hours at 20°C. A solution of sodium hydroxide (11.2ml of 10%) and dichloromethane were added

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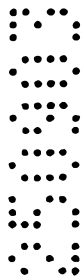
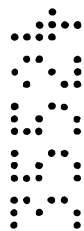
and the organic phase washed (water), dried (magnesium sulphate) and evaporated to give the title compound (7.25g) as a white solid, NMR 4.05 (s, 2H), 6.77 (s, 1H), 7.47 (s, 2H), 8.6 (s, 1H). The yield was 91%.

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The reference to any prior art in this specification is not, and should not be taken as, an acknowledgment or any form of suggestion that that prior art forms part of the common general knowledge in Australia.

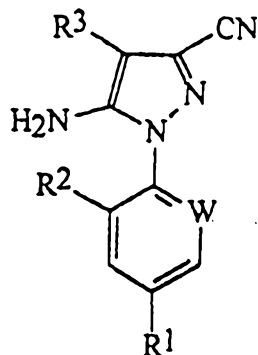
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Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.



THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A process for the preparation of a compound of formula (I):



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(I)

wherein W represents nitrogen or -CR<sup>4</sup>;

R<sup>1</sup> represents halogen, haloalkyl, haloalkoxy, R<sup>5</sup>S(O)<sub>n</sub><sup>-</sup>, or -SF<sub>5</sub>;

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R<sup>2</sup> represents hydrogen or halogen;

R<sup>3</sup> represents hydrogen or R<sup>6</sup>S(O)<sub>m</sub><sup>-</sup>;

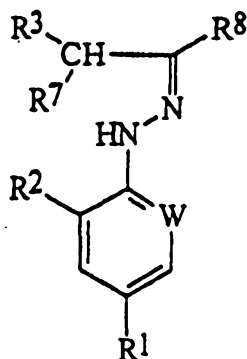
R<sup>4</sup> represents halogen;

R<sup>5</sup> and R<sup>6</sup> represent alkyl or haloalkyl; and

m and n represent 0, 1 or 2; which process

comprises the reaction of a compound of formula

(II):



(II)

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and W are as hereinbefore defined, R<sup>7</sup> represents a leaving group and R<sup>8</sup> represents chlorine or bromine, with a cyanide salt.

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2. A process according to claim 1 in which the cyanide salt is an alkali metal cyanide, an alkaline earth metal cyanide or ammonium cyanide.

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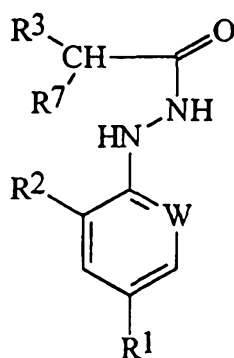
3. A process according to claim 1 or 2 which is conducted in a solvent selected from nitriles, amides, sulphoxides, ethers or alcohols, optionally in the presence of water.

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4. A process according to any one of claims 1 to 3 in which 2 to 5 molar equivalents of cyanide are used.

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5. A process according to any one of claims 1 to 4 in which the compound of formula (II) is prepared by a process which comprises the reaction of a compound of formula (IV):

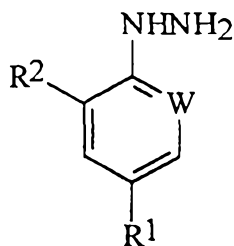


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(IV)

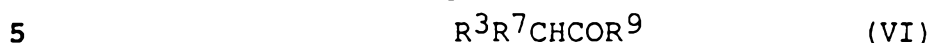
wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>7</sup> and W are as defined in claim 1, with a chlorinating or brominating agent; and the compound of formula (IV) is prepared by a process which comprises the reaction of a compound of formula (V):

25



(V)

wherein R<sup>1</sup>, R<sup>2</sup> and W are as defined in claim 1, with a compound of formula (VI):



wherein R<sup>3</sup> and R<sup>7</sup> are as defined in claim 1 and R<sup>9</sup> represents a leaving group.

6. A process according to claim 5 in which  
 10 a chlorinating agent is used for the preparation of the compound of formula (II) from the compound of formula (IV), and is selected from thionyl chloride, phosphoryl chloride, phosphorus trichloride, phosphorus pentachloride  
 15 and a mixture of triphenylphosphine and carbon tetrachloride.

7. A process according to any one of the preceding claims wherein:

20 R<sup>1</sup> represents trifluoromethyl, trifluoromethoxy or -SF<sub>5</sub>;

W represents -CR<sup>4</sup>;

R<sup>2</sup> and R<sup>4</sup> represent chlorine or bromine;

R<sup>3</sup> represents a hydrogen atom, or R<sup>6</sup>S(O)<sub>m</sub>-;

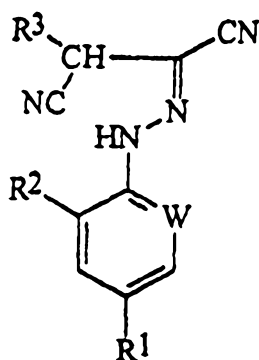
25 wherein R<sup>6</sup> represents optionally halogenated methyl or ethyl; and R<sup>7</sup> and R<sup>8</sup> represent chlorine.

8. A process according to any one of the  
 30 preceding claims wherein:

$R^1$  represents trifluoromethyl;  $W$  represents  $-CR^4$ ;  $R^2$ ,  $R^4$ ,  $R^7$  and  $R^8$  represent chlorine; and  $R^3$  represents hydrogen.

5 9. A compound of formula (II) or (IV) wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^7$ ,  $R^8$  and  $W$  are as defined in claim 1 or claim 5.

10. A compound of formula (III):



(III)

wherein  $R^1$ ,  $R^2$ ,  $R^3$  and  $W$  are as defined in claim 1, with the exclusion of compounds wherein  $R^3$  represents hydrogen.

11. A compound of formula (I) prepared by the process according to claim 1.

12. A process according to claim 1 substantially as hereinbefore described with reference to the examples.

DATED this 15<sup>th</sup> day of September, 2003

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