

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 February 2003 (27.02.2003)

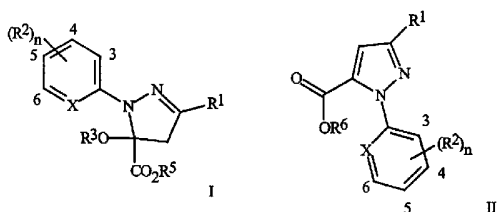
PCT

(10) International Publication Number
WO 03/016282 A3

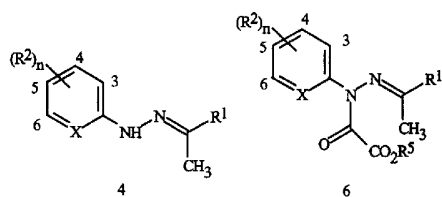
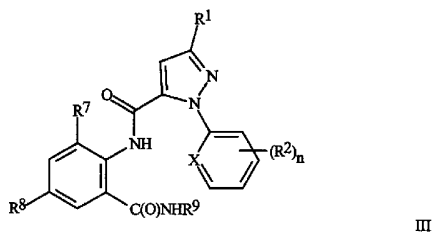
- (51) International Patent Classification⁷: C07D 401/04, A01N 43/56, C07D 231/16, 231/14, 213/77, 231/08
- (21) International Application Number: PCT/US02/25612
- (22) International Filing Date: 13 August 2002 (13.08.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/311,919 13 August 2001 (13.08.2001) US
60/341,894 19 December 2001 (19.12.2001) US
60/369,659 2 April 2002 (02.04.2002) US
- (71) Applicant (for all designated States except US): **E.I. DU PONT DE NEMOURS AND COMPANY** [US/US]; 1007 Market Street, Wilmington, DE 19898 (US).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): **ANNIS, Gary, David** [US/US]; 13 Franklin Road, Landenberg, PA 19350 (US). **LAHM, George, Philip** [US/US]; 148 Fairhill Drive, Wilmington, DE 19808 (US). **SELBY, Thomas, Paul** [US/US]; 116 Hunter Court, Wilmington, DE 19808 (US). **STEVENSON, Thomas, Martin** [US/US]; 103 Iroquois Court, Newark, DE 19702 (US).
- (74) Agent: **HEISER, David, E.**; E.I. du Pont de Nemours and Company, Legal Patent Records Center, 4417 Lancaster Pike, Wilmington, DE 19805 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, 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, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,

[Continued on next page]

(54) Title: SUBSTITUTED 1H-DIHYDROPYRAZOLES, THEIR PREPARATION AND USE



(57) Abstract: This invention provides compounds of Formula (I), methods for their preparation and use for preparing compounds of Formula (II) wherein R_i1?, R_i2?, R_i3?, R_i5?, R_i6?, X and n are as defined in the disclosure. This invention also discloses preparation of compounds of Formula (III) wherein R_i1?, R_i2?, R_i7?, R_i8?, R_i9? and n are as defined in the disclosure. This invention also pertains to certain compounds of Formula 4 and 6 used to prepare compounds of Formula (I), wherein R_i1?, R_i2?, R_i5?, X and n are as defined in the disclosure.





SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, 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, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB,*

GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
 — *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations of inventorship (Rule 4.17(iv)) for US only*
 — *of inventorship (Rule 4.17(iv)) for US only*
 — *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*
 — *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:

24 April 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

In ternational Application No
PCT/US 02/25612

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D401/04 A01N43/56 C07D231/16 C07D231/14 C07D213/77
C07D231/08

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A01N

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------|
| A | NL 9 202 078 A (RIJKSLANDBOUWHOGESCHOOL) 16 June 1994 (1994-06-16) the whole document --- | 1-31 |
| A | EP 0 333 131 A (HOECHST AG) 20 September 1989 (1989-09-20) claim 1; examples 71,191,911,1091 --- | 26 |
| P,A | WO 01 70671 A (DU PONT ;LAHM GEORGE P (US); MYERS BRIAN J (US); SELBY THOMAS P (U) 27 September 2001 (2001-09-27) cited in the application table 9 ----- | 1-31 |

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search: 6 November 2002

Date of mailing of the international search report: 18. 03. 2003

Name and mailing address of the ISA: European Patent Office, P.B. 5818 Patentlaan 2, NL - 2280 HV Rijswijk, Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Authorized officer: DE JONG B.S.

INTERNATIONAL SEARCH REPORT

international application No.
PCT/US 02/25612

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-31

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-31

Compounds of formula I, the use of these compounds for the preparation of known compounds of formula II. The preparation of compounds of formula I and intermediates of formula 4 and 6, which are usefull for this preparation. The preparation of compounds of formula 4 and 6.

2. Claims: 32-35

Compounds of formula II and the use of these compounds for preparing compounds of formula III.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Initial Application No

PCT/US 02/25612

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|--|---|------------------|---|--|
| NL 9202078 | A | 16-06-1994 | NONE | |
| EP 0333131 | A | 20-09-1989 | DE 3808896 A1 AT 96273 T AU 3137389 A AU 634421 B2 AU 8461491 A BR 8901210 A CA 1338071 A1 CN 1035752 A DD 283538 A5 DE 58905988 D1 DK 128689 A EP 0333131 A1 ES 2059596 T3 HU 49785 A2 IL 89620 A JP 1283274 A NZ 228340 A PL 278285 A1 PT 90041 A ,B SU 1836012 A3 US 5945541 A US 5401700 A ZA 8901960 A | 28-09-1989 15-11-1993 21-09-1989 18-02-1993 14-11-1991 31-10-1989 20-02-1996 27-09-1989 17-10-1990 02-12-1993 18-09-1989 20-09-1989 16-11-1994 28-11-1989 29-12-1994 14-11-1989 27-08-1991 13-11-1989 10-11-1989 23-08-1993 31-08-1999 28-03-1995 25-10-1989 |
| WO 0170671 | A | 27-09-2001 | AU 5094601 A BR 0109757 A EP 1265850 A2 WO 0170671 A2 | 03-10-2001 04-02-2003 18-12-2002 27-09-2001 |