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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 November 2007 (08.11.2007)

PCT

(10) International Publication Number
WO 2007/126812 A3

(51) International Patent Classification:
C07D 493/04 (2006.01) *C07F 9/02* (2006.01)
C07C 327/42 (2006.01)

(21) International Application Number:
PCT/US2007/007564

(22) International Filing Date: 29 March 2007 (29.03.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/787,126 29 March 2006 (29.03.2006) US

(71) Applicant *(for all designated States except US)*: **GILEAD SCIENCES, INC.** [US/US]; 333 Lakeside Drive, Foster City, CA 94404 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CRAWFORD, Kenneth, R.** [US/US]; 10527 Reeds Landing Circle, Burke, VA 22015 (US). **DOWDY, Eric, D.** [US/US]; 1151 Compass Lane #203, Foster City, CA 94404 (US). **GUTIERREZ, Arnold** [US/US]; 2258 Dry Creek Court, San Jose, CA 95124 (US). **POLNIASZEK, Richard, P.** [US/US]; 112 Monaco Drive, Redwood City, CA 94065 (US). **YU, Richard, Hung Chiu** [US/US]; 2625 35th Avenue, San Francisco, CA 94116 (US).

(74) Agents: **KUTZENCO, Allan, N.** et al.; Gilead Sciences, Inc., 333 Lakeside Drive, Foster City, CA 94404 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

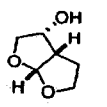
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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*

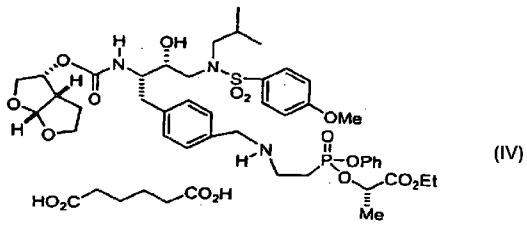
(88) Date of publication of the international search report:
21 December 2007

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.

(54) Title: PROCESS FOR PREPARATION OF HIV PROTEASE INHIBITORS



(O)



(IV)

(57) Abstract: A process for the synthesis of bisfuran intermediates of formula (0) useful for preparing antiviral HIV protease inhibitor compounds is hereby disclosed. Furthermore disclosed is a HIV protease inhibitor of formula (IV) as well as various intermediates thereof.

WO 2007/126812 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/007564

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D493/04 C07C327/42 C07F9/02

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)
C07D C07C C07F

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, WPI Data, 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	WO 02/067239 A (GLAXO GROUP LTD [GB]; DAVIS ROMAN [US]; LOVELACE THOMAS CLAIBORNE [US]) 29 August 2002 (2002-08-29) example 1	1-23
A	WO 2005/042772 A (GILEAD SCIENCES INC [US]; MCDERMOTT MARTIN [US]) 12 May 2005 (2005-05-12) the whole document	1
A	WO 94/26749 A (MERCK & CO INC [US]) 24 November 1994 (1994-11-24) Scheme IV, reaction of cpd. 18 to cpd. 19	1-23
X	US 2004/121316 A1 (BIRKUS GABRIEL [US] ET AL) 24 June 2004 (2004-06-24) p. 464, cpd. GS-3 (3rd structural formula) abstract	24-48

☐ Further documents are listed in the continuation of Box C.

☒ See patent family 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	Date of mailing of the international search report
11 October 2007	25/10/2007

Name and mailing address of the ISA/	Authorized officer
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	Fritz, Martin

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/007564

Box II Observations where certain claims were found unsearchable (Continuation of item 2 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 29-34, 37(part) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.

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 III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

see additional sheet

1. [X] 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.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] 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: 1-23

   Process for the preparation of the intermediate compounds O

   ---

2. claims: 24-48

   Salts of formula (IV), processes for their preparation and uses thereof, intermediates of formulas C, M, and N

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2007/007564

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02067239 A	29-08-2002	AU 2002255473 A1	04-09-2002
		EP 1404680 A2	07-04-2004
		JP 2004519473 T	02-07-2004
		WO 02060905 A2	08-08-2002
WO 2005042772 A	12-05-2005	AU 2004286238 A1	12-05-2005
		AU 2004286239 A1	12-05-2005
		AU 2004290298 A1	26-05-2005
		CA 2543142 A1	12-05-2005
		CA 2543144 A1	12-05-2005
		CA 2543294 A1	26-05-2005
		EP 1680512 A1	19-07-2006
		EP 1678321 A1	12-07-2006
		EP 1678322 A2	12-07-2006
		JP 2007508843 T	12-04-2007
		JP 2007508844 T	12-04-2007
		JP 2007508845 T	12-04-2007
		WO 2005047898 A2	26-05-2005
		WO 2005042773 A1	12-05-2005
WO 9426749 A	24-11-1994	AU 6828894 A	12-12-1994
US 2004121316 A1	24-06-2004	AT 367394 T	15-08-2007
		AU 2003228707 A1	10-11-2003
		AU 2003231765 A1	10-11-2003
		AU 2003231766 A1	10-11-2003
		AU 2003291998 A1	23-11-2004
		BR 0309557 A	01-03-2005
		BR 0309573 A	01-02-2005
		CA 2481261 A1	06-11-2003
		CA 2481285 A1	06-11-2003
		CA 2481449 A1	06-11-2003
		CN 1656109 A	17-08-2005
		CN 1649885 A	03-08-2005
		WO 2004096818 A2	11-11-2004
		EP 1575486 A2	21-09-2005
		EP 1509537 A2	02-03-2005
		EP 1501841 A2	02-02-2005
		EP 1620445 A2	01-02-2006
		HR 20041113 A2	31-08-2005
		HR 20041114 A2	31-08-2005
		IS 7555 A	25-11-2004
		IS 7556 A	25-11-2004
		JP 2005523912 T	11-08-2005
		JP 2006508634 T	16-03-2006
		JP 2005523922 T	11-08-2005
		MX PA04010527 A	13-12-2004
		MX PA04010528 A	27-05-2005
		WO 03090690 A2	06-11-2003
		WO 03091264 A2	06-11-2003
		WO 03090691 A2	06-11-2003
		US 2005209197 A1	22-09-2005
		US 2005197320 A1	08-09-2005
		US 2006128692 A1	15-06-2006
		US 2006115815 A1	01-06-2006
		US 2007010489 A1	11-01-2007
		US 2005239054 A1	27-10-2005