

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 December 2003 (24.12.2003)

PCT

(10) International Publication Number
WO 2003/106456 A3

(51) International Patent Classification⁷: **C07D 451/04**,
451/14, A61K 31/46, A61P 3/10, C07D 277/06, 207/06,
207/16, 263/04, 263/06

(74) Agent: **SANOFI-SYNTHELABO**; c/o György Mihályi
and Katalin Mármarosí, Tó u. 1-5, H-1045 Budapest (HU).

(21) International Application Number:
PCT/HU2003/000041

(22) International Filing Date: 11 June 2003 (11.06.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
P0202001 14 June 2002 (14.06.2002) HU

(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, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,
SE, SG, 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, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **SANOFI-
SYNTHELABO** [FR/FR]; 174 avenue de France, F-75013
Paris (FR).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **ARÁNYI, Péter**
[HU/HU]; Bimbó út 216/226, H-1026 Budapest (HU).
BALÁZS, László [HU/HU]; Madách u.15., H-2120
Dunakeszi (HU). **BATA, Imre** [HU/HU]; Frankel
Leó út 7, H-1027 Budapest (HU). **BÁTORI, Sándor**
[HU/HU]; Rákóczi F. u. 268/A, H-1214 Budapest (HU).
BORONKAY, Éva [HU/HU]; Cibakháza u. 42, H-1162
Budapest (HU). **KAPUI, Zoltán** [HU/HU]; Etele u. 56/a,
H-1115 Budapest (HU). **SUSÁN, Edit** [HU/HU]; Hargita
u. 21, H-2120 Dunakeszi (HU). **SZABÓ, Tibor** [HU/HU];
Alkotás u. 25, H-1123 Budapest (HU). **T. NAGY, Lajos**
[HU/HU]; István u. 47., H-1078 Budapest (HU). **UR-
BÁN-SZABÓ, Katalin** [HU/HU]; Szent László u. 158,
H-1131 Budapest (HU). **VARGA, Márton** [HU/HU];
Barátság u. 9, H-2120 Dunakeszi (HU).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

Published:

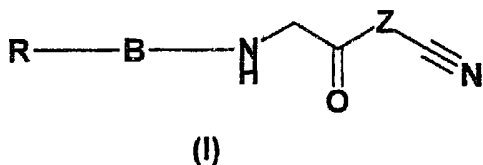
— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

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

4 March 2004

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

(54) Title: AZABICYCLO-OCTANE AND NONANE DERIVATIVES WITH DDP-IV INHIBITING ACTIVITY



(57) Abstract: The present invention relates to the novel compounds of the general formula (I) possessing DPP-IV inhibitory activity. These compounds contain tropane (B) building blocks.

WO 2003/106456 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/HU 03/00041

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D451/04 C07D451/14 A61K31/46 A61P3/10 C07D277/06
C07D207/06 C07D207/16 C07D263/04 C07D263/06

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 A61K A61P

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, BEILSTEIN Data, CHEM ABS Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 19998 A (CIBA GEIGY AG ;VILLHAUER EDWIN BERNARD (US)) 14 May 1998 (1998-05-14) claim 1	1-14
Y	WO 01 34594 A (JACKSON PAUL ;STEINER JOSEPH (US); GUILFORD PHARM INC (US)) 17 May 2001 (2001-05-17) claim 4; examples 44,93	1-14
Y	EP 1 323 710 A (TANABE SEIYAKU CO) 2 July 2003 (2003-07-02) claim 1	1-14
Y	WO 01 96295 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); VILLHAUER EDWIN BE) 20 December 2001 (2001-12-20) claim 1	1-14
	----- -/-	



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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

8 September 2003

Date of mailing of the international search report

13. 01. 2004

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

Steendijk, M.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/HU 03/00041

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 273 778 A (HADLEY MICHAEL S ET AL) 16 June 1981 (1981-06-16) columns 13-17 -----	1-14
P, Y	WO 03 002553 A (HAFFNER CURT DALE ;MCDUGALD DARRYL LYNN (US); SMITHKLINE BEECHAM) 9 January 2003 (2003-01-09) claim 20 -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/HU 03/00041

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.:

1-14

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: 1-14

Compounds of formula I, their preparation and their application as DPP-IV inhibitors

2. claims: 15,16

Intermediates of formulae II and V (R-B-NH₂, R-B-NH-Y)

3. claims: 17-20

Intermediates of formulae VII, VIII, IX and III (proline "Z" analogues)

INTERNATIONAL SEARCH REPORT

International Application No

PCT/HU 03/00041

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9819998	A	14-05-1998	AU 726186 B2	02-11-2000
			AU 5318498 A	29-05-1998
			BR 9714130 A	29-02-2000
			CN 1236361 A	24-11-1999
			CZ 9901615 A3	11-08-1999
			WO 9819998 A2	14-05-1998
			EP 0937040 A2	25-08-1999
			HU 0000323 A2	28-08-2000
			ID 18331 A	26-03-1998
			JP 3217380 B2	09-10-2001
			JP 2000511559 T	05-09-2000
			KR 2000053081 A	25-08-2000
			NO 992028 A	28-04-1999
			NZ 335146 A	29-11-1999
			PL 332777 A1	11-10-1999
			RU 2180901 C2	27-03-2002
			SK 60899 A3	10-04-2000
			TR 9901004 T2	21-07-1999
			TW 492957 B	01-07-2002
			ZA 9709985 A	07-05-1998
WO 0134594	A	17-05-2001	AU 1916401 A	06-06-2001
			CA 2390231 A1	17-05-2001
			EP 1228061 A1	07-08-2002
			WO 0134594 A1	17-05-2001
EP 1323710	A	02-07-2003	AU 9419601 A	22-04-2002
			CA 2424964 A1	18-04-2002
			EP 1323710 A1	02-07-2003
			AU 9419701 A	22-04-2002
			BR 0114436 A	01-07-2003
			CA 2424600 A1	02-04-2003
			EP 1325910 A1	09-07-2003
			WO 0230890 A1	18-04-2002
			WO 0230891 A1	18-04-2002
			JP 2002356471 A	13-12-2002
			JP 2002356472 A	13-12-2002
			NO 20031490 A	02-06-2003
WO 0196295	A	20-12-2001	AU 1359702 A	24-12-2001
			CA 2411778 A1	20-12-2001
			WO 0196295 A2	20-12-2001
			EP 1296974 A2	02-04-2003
US 4273778	A	16-06-1981	AR 225301 A1	15-03-1982
			AT 24320 T	15-01-1987
			AU 527837 B2	24-03-1983
			AU 5425579 A	03-07-1980
			AU 543825 B2	02-05-1985
			AU 9135182 A	10-03-1983
			CA 1218062 A1	17-02-1987
			CA 1220473 A2	14-04-1987
			DE 2966476 D1	12-01-1984
			DE 2967642 D1	29-01-1987
			DE 2967692 D1	14-12-1989
			DK 553979 A	15-08-1980
			EP 0013138 A1	09-07-1980
			EP 0081054 A2	15-06-1983

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/HU 03/00041

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4273778	A	EP 0220339 A1	06-05-1987
		ES 8101072 A1	01-03-1981
		IE 49737 B1	11-12-1985
		IE 49736 B1	11-12-1985
		JP 1706203 C	27-10-1992
		JP 2072178 A	12-03-1990
		JP 3075548 B	02-12-1991
		JP 55092384 A	12-07-1980
		MX 6255 E	15-02-1985
		NZ 192476 A	14-09-1982
		US 4336259 A	22-06-1982
		US 4544660 A	01-10-1985
		US 4599420 A	08-07-1986
		US 4705858 A	10-11-1987
		ZA 7907054 A	31-12-1980
WO 03002553	A	09-01-2003	
		WO 03002530 A2	09-01-2003
		WO 03002553 A2	09-01-2003
		WO 03002531 A2	09-01-2003