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H-1144 Hungary (HU). NÉMETH, Norbert [HU/HU]; Bartók B. út 92-94, H-1113 Budapest (HU). SZYLÁGYI, János [HU/HU]; Reviczky Ezredes utca 8., H-1033 Hungary (HU).
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- (30) Priority Data:  
P 9901559 11 May 1999 (11.05.1999) HU
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- (75) Inventors/Applicants (for US only): LUKÁCS, Gyula [HU/HU]; Bronz u. 5, H-1163 Budapest (HU). SIMIG, Gyula [HU/HU]; Hollósy Simon u. 25, H-1126 Budapest (HU). MEZEI, Tibor [HU/HU]; Borz u. 4, H-1221 Budapest (HU). BUDAI, Zoltán [HU/HU]; Lukács u. 3, H-1023 Budapest (HU). PORCS-MAKKAY, Márta [HU/HU]; Lukács Gy. u. 21, H-1039 Budapest (HU). KRASZNAI, György [HU/HU]; XIII u. 38, H-1172 Budapest (HU). NAGY, Kálmán [HU/HU]; Túrlista u. 2/a, H-1025 Budapest (HU). VERECZKEYNÉ DONÁTH, Györgyi [HU/HU]; San Marco u. 52, H-1034 Budapest (HU). SZABÓ, Tibor [HU/HU]; Szentmihályi u. 24/c,
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(54) Title: PROCESS FOR PREPARING (1R,2S,4R) -(2'-[N,N-DIMETHYLAMINO] -ETHOXY)] -2-[PHENYL] -1,7,7-TRI- [METHYL] -BICYCLO [2.2.1] HEPTANE AND PHARMACEUTICALLY ACCEPTABLE ACID ADDITION SALTS THEREOF

(57) Abstract: The invention relates to a process for preparing (1R,2S,4R) -(2'-[N,N-dimethylamino] -ethoxy)] -2-[phenyl] -1,7,7-tri- [methyl] -bicyclo [2.2.1] heptane and pharmaceutically acceptable acid addition salts thereof with higher yields and higher grades of purity.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/HU 00/00043

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07C213/02 C07C217/12				
According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b>				
Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07C				
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, EMBASE, BIOSIS, WPI Data, BEILSTEIN Data				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	GB 2 065 122 A (EGYT GYOGYSZERVEGYESZETI GYAR) 24 June 1981 (1981-06-24) examples 15,20 & HU 179 164 B 28 August 1982 (1982-08-28) cited in the application --- -/--	1		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.				
<input checked="" type="checkbox"/> Patent family members are listed in annex.				
° Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> <li>*A* document defining the general state of the art which is not considered to be of particular relevance</li> <li>*E* earlier document but published on or after the international filing date</li> <li>*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)</li> <li>*O* document referring to an oral disclosure, use, exhibition or other means</li> <li>*P* document published prior to the international filing date but later than the priority date claimed</li> </ul> </td> <td style="width: 50%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> <li>*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</li> <li>*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</li> <li>*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.</li> <li>*&amp;* document member of the same patent family</li> </ul> </td> </tr> </table>			<ul style="list-style-type: none"> <li>*A* document defining the general state of the art which is not considered to be of particular relevance</li> <li>*E* earlier document but published on or after the international filing date</li> <li>*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)</li> <li>*O* document referring to an oral disclosure, use, exhibition or other means</li> <li>*P* document published prior to the international filing date but later than the priority date claimed</li> </ul>	<ul style="list-style-type: none"> <li>*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</li> <li>*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</li> <li>*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.</li> <li>*&amp;* document member of the same patent family</li> </ul>
<ul style="list-style-type: none"> <li>*A* document defining the general state of the art which is not considered to be of particular relevance</li> <li>*E* earlier document but published on or after the international filing date</li> <li>*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)</li> <li>*O* document referring to an oral disclosure, use, exhibition or other means</li> <li>*P* document published prior to the international filing date but later than the priority date claimed</li> </ul>	<ul style="list-style-type: none"> <li>*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</li> <li>*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</li> <li>*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.</li> <li>*&amp;* document member of the same patent family</li> </ul>			
Date of the actual completion of the international search	Date of mailing of the international search report			
21 December 2000	15/01/2001			
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  Sánchez García, J.M.			

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## INTERNATIONAL SEARCH REPORT

Interr. 1al Application No

PCT/HU 00/00043

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>CHEMICAL ABSTRACTS, vol. 118, no. 23, 7 June 1993 (1993-06-07) Columbus, Ohio, US; abstract no. 234291, BUDAI, ZOLTAN ET AL: "Process for producing (1R,2S)-(-)-2-phenyl-'2'- (dimethylamino)ethoxy)-1,7,7-trimethylbicy clo[2.2.1]heptane" XP002156197 abstract &amp; HU 60 996 A (EGIS GYOGYSZERGYAR, HUNG.) 30 November 1992 (1992-11-30) cited in the application -----</p>	1

# INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/HU 00/00043

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2065122    A	24-06-1981	HU 179164 B	28-08-1982
		AT 374449 B	25-04-1984
		AT 601380 A	15-09-1983
		AU 539173 B	13-09-1984
		AU 6529380 A	18-06-1981
		BE 886579 A	10-06-1981
		CA 1155115 A	11-10-1983
		CH 649986 A	28-06-1985
		CS 216544 B	26-11-1982
		DD 155320 A	02-06-1982
		DE 3047142 A	10-09-1981
		DK 528980 A, B,	15-06-1981
		ES 497717 D	16-11-1981
		ES 8200857 A	16-02-1982
		FI 803858 A, B,	15-06-1981
		FR 2471968 A	26-06-1981
		GR 72509 A	16-11-1983
		IE 51733 B	18-03-1987
		IL 61685 A	31-10-1984
		IT 1209377 B	16-07-1989
		JP 1467011 C	30-11-1988
		JP 56123953 A	29-09-1981
		JP 63014703 B	01-04-1988
		NL 8006722 A, B	16-07-1981
		NO 803764 A, B,	15-06-1981
		PL 228392 A	07-08-1981
		SE 451132 B	07-09-1987
		SE 8008680 A	15-06-1981
		SU 1253425 A	23-08-1986
		US 4342762 A	03-08-1982
		YU 311180 A	31-10-1983
HU 60996    A		NONE	