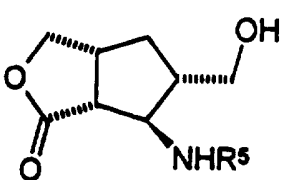




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C07D 471/18, 307/93, C07C 67/347 // (C07D 471/18, 221:00, 221:00, 209:00)</p>	<p>A3</p>	<p>(11) International Publication Number: WO 96/00729</p> <p>(43) International Publication Date: 11 January 1996 (11.01.96)</p>
<p>(21) International Application Number: PCT/US95/06599</p> <p>(22) International Filing Date: 12 June 1995 (12.06.95)</p> <p>(30) Priority Data: 08/269,412 30 June 1994 (30.06.94) US</p> <p>(60) Parent Application or Grant (63) Related by Continuation US 08/269,412 (CON) Filed on 30 June 1994 (30.06.94)</p> <p>(71) Applicant (for all designated States except US): G.D. SEARLE & CO. [US/US]; Corporate Patent Dept., P.O. Box 5110, Chicago, IL 60680-5110 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): BECKER, Daniel, Paul [US/US]; 1800 Maplewood Lane, Glenview, IL 60025 (US). FLYNN, Daniel, Lee [US/US]; 17 North Bristol Court, Mundelein, IL 60060 (US). MOORMANN, Alan, Edward [US/US]; 9450 Latrobe, Skokie, IL 60077 (US). VIL-LAMIL, Clara, Ines [CO/US]; 813 Long Road, Glenview, IL 60025 (US).</p>	<p>(74) Agents: KOVACEVIC, Cynthia, S. et al.; G.D. Searle & Co., Corporate Patent Dept., P.O. Box 5110, Chicago, IL 60680-5110 (US).</p> <p>(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 15 February 1996 (15.02.96)</p>	
<p>(54) Title: PROCESS FOR THE PREPARATION OF AZANORADAMANTANE BENZAMIDES</p>		
<p>(57) Abstract</p> <p>A process for the preparation of a γ-lactone of formula (I) which can be used to produce a single enantiomer of aminoazanoradamantane which is coupled to aromatic acid moieties to produce compounds useful as 5-HT agonists or antagonists.</p>	<div style="text-align: right;">  <p>(I)</p> </div>	

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 95/06599

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D471/18 C07D307/93 C07C67/347 //(C07D471/18,221:00,
221:00,209:00)

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 6 C07D 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TETRAHEDRON LETTERS, vol.33, no.48, , OXFORD GB pages 7283 - 7286 D. L. FLYNN ET AL. 'Use of Atom-Transfer Radical Cyclizations as an Efficient Entry into a New "Serotonergic" Azanoradamantane' see the whole document ---	1-17, 19-21
A	ANGEWANDTE CHEMIE INTERNATIONAL EDITION., vol.17, no.12, , WEINHEIM DE pages 939 - 940 J. NEUMEISTER ET AL. 'Ozone Cleavage of Olefins with Formation of Ester Fragments' see the whole document ---	1-17, 19-21
	-/--	



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

2

Date of the actual completion of the international search	Date of mailing of the international search report
28 September 1995	18.01.96
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 Paisdor, B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 95/06599

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Week 9209, Derwent Publications Ltd., London, GB; AN 92-069451 & JP,A,4 013 663 (SUMITOMO SEIYAKU KK) 17 January 1992 cited in the application see abstract ---	1-17, 19-21
A	EP,A,0 454 121 (G.D. SEARLE & CO.) 30 October 1991 cited in the application see page 6 - page 7; claims; examples ---	1-17, 19-21
A	ANGEWANDTE CHEMIE, vol.102, no.9, , WEINHEIM DE pages 1079 - 1081 G. HELMCHEN ET AL. 'Bausteine zur Synthese von enantiomerenreinen Jasmonoiden: Synthese von (+)-Methylepijasmonat' cited in the application see the whole document -----	1-17, 19-21

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 95/06599

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:

For further information please see Form PCT/ISA/206 mailed 18.10.95

Please see attached 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.:

1-17, 19-21

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/

The separate groups of invention are:

- A. 1) Claims 1 - 13, and 19 disclose a process for the preparation of benzamide aminoazanoradamantane derivatives (cf. eg. formula of Claim 12)
 - 2) Claims 14 - 17 disclose intermediates in a novel process according to the preceding claims
 - 3) Claims 20 and 21 disclose processes for the preparation of homologues of the aminoazanoradamantane derivatives of claim 4
- B. Claim 18 discloses a process for the preparation of known starting materials

- A. Unity of invention can be accepted in the group of invention A, because processes for the preparation of aminoazanoradamantane derivatives (cf. claims 4, 20 and 21) are claimed in which the common inventive concept consists in the oxidative cleavage of 2,3-disubstituted norbornene derivatives and their subsequent cyclization to yield amino- or methanaminoazanoradamantanes. For the intermediates of claims 14 - 17 unity of invention can also be accepted because these intermediates are **key compounds** in a novel process for the formation of the azanoradamantane skeleton.
- B. For the process of claim 18 unity of invention cannot be accepted because it pertains to a further process for the preparation of already known starting compounds or intermediates respectively. Hence, the process leading from the intermediate (or starting product) of claim 18 to the final products of eg. claim 12 is separated by an intermediate which is not new (cf. "Administrative Instructions under the PCT" PCT/GEN/11, Annex B, page 50, item (v)).

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/US 95/06599

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0454121	30-10-91	US-A- 5140023	18-08-92
		AU-B- 630555	29-10-92
		AU-B- 7595191	07-11-91
		FI-B- 94530	15-06-95
		JP-A- 4225979	14-08-92
		NZ-A- 237948	26-05-94
		US-A- 5223613	29-06-93
