



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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|--|---------------------------|---|----|-----------|--------------------------|----|---|
| <p>(51) International Patent Classification⁶ : C07D 211/60, C07B 55/00, C07C 231/24</p> | <p>A3</p> | <p>(11) International Publication Number: WO 96/11173</p> <p>(43) International Publication Date: 18 April 1996 (18.04.96)</p> | | | | | |
| <p>(21) International Application Number: PCT/GB95/02383</p> <p>(22) International Filing Date: 9 October 1995 (09.10.95)</p> <p>(30) Priority Data:</p> <table border="0"> <tr> <td>9420245.4</td> <td>7 October 1994 (07.10.94)</td> <td>GB</td> </tr> <tr> <td>9504924.3</td> <td>10 March 1995 (10.03.95)</td> <td>GB</td> </tr> </table> <p>(71) Applicant (for all designated States except US): CHIRO-SCIENCE LIMITED [GB/GB]; Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): DYER, Ulrich, Conrad [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB). McCAGUE, Raymond [GB/GB]; 5 Mansfield Close, Milton, Cambridgeshire CB4 6EE (GB). WOODS, Martin [GB/GB]; Chiroscience Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4WE (GB).</p> <p>(74) Agent: GILL JENNINGS & EVERY; Broadgate House, 7 Eldon Street, London EC2M 7LH (GB).</p> | 9420245.4 | 7 October 1994 (07.10.94) | GB | 9504924.3 | 10 March 1995 (10.03.95) | GB | <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, UG, 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.</i></p> <p>(88) Date of publication of the international search report: 4 July 1996 (04.07.96)</p> |
| 9420245.4 | 7 October 1994 (07.10.94) | GB | | | | | |
| 9504924.3 | 10 March 1995 (10.03.95) | GB | | | | | |
| <p>(54) Title: RACEMISATION OF PRECURSORS TO LEVOBUPIVACAINE AND ANALOGUES THEREOF</p> | | | | | | | |
| <p>(57) Abstract</p> <p>A process for the preparation of optically-enriched pipecolic acid as a salt with an optically-active acid, comprises asymmetric transformation of pipecolic acid, as a racemic mixture or a mixture enriched in the opposite enantiomer from that desired, with the optically-active acid in a solvent comprising an acid that causes racemisation, in the absence of aldehyde.</p> | | | | | | | |

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 95/02383

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D211/60 C07B55/00 C07C231/24

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 C07B 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 | EP,A,0 175 840 (DEGUSSA) 2 April 1986 see claims; examples --- | 1-10 |
| A | EP,A,0 173 921 (BEECHAM) 12 March 1986 see claims; examples --- | 1-10 |
| A | EP,A,0 137 371 (HOECHST) 17 April 1985 see whole document --- | 1-10 |
| A | FR,A,2 074 022 (DYNAMIT NOBEL AKTIENGESELLSCHAFT) 1 October 1971 see whole document --- | 1-10 |
| | -/-- | |

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

* Special categories of cited documents :

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| <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> | <p>"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</p> <p>"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</p> <p>"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.</p> <p>"&" document member of the same patent family</p> |
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| Date of the actual completion of the international search <p style="text-align: center;">10 April 1996</p> | Date of mailing of the international search report <p style="text-align: center;">26.04.96</p> |
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| 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 <p style="text-align: center;">Helps, I</p> |
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 95/02383

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
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| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, vol. 54, no. 11, November 1981 TOKYO, JP, pages 3286-90, C. HONGO ET. AL. 'Asymmetric Transformation of N-Acyl-DL-Amino Acids.' cited in the application see Table 5, Experimental section --- | 11,12 |
| X | JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 111, no. 16, 2 August 1989 WASHINGTON DC, US, pages 6354-64, H. K. CHENAULT ET. AL. 'Kinetic Resolution of Unnatural and Rarely Occurring Amino Acids: Enantioselective Hydrolysis of N-acyl Amino Acids Catalysed by Acylase I.' see page 6360, column 1, paragraph 1 - paragraph 3; table II ----- | 11,12 |

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB95/ 02383

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:

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.:

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/

1. Claims 1 - 10 Process for the racemisation of an N-acyl amino acid
2. Claims 11 - 14 Mixture of enantiomers of optically active N-acyl amino acid

Claim 11, drawn to a mixture of optical isomers of N-acyl amino acids, does not fall within same inventive concept as Claims 1 - 10 which are drawn to a process of racemisation of N-acyl amino acids. The isomer mixture of claim 11 is merely an optional starting material for the process of claim 1 (see page 2 lines 20 - 34 of description) and the use of said mixture is not limited to the claimed racemisation process.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 95/02383

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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