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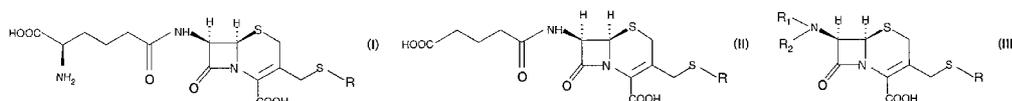
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(54) Title: A PROCESS FOR PREPARING CEPHALOSPORIN DERIVATIVES



(57) Abstract: An enzymatic process for preparing 3-thiolated 7-aminocephalosporanic acid derivatives comprises the steps of enzymatically converting a 3-thiolated cephalosporin C of the formula (I), to form a 3-thiolated-glutaryl-7-ACA of the formula (II) and enzymatically converting a compound of formula (II) to form a 3-thiolated-7-ACA of the formula (III) wherein R is a heterocyclic group comprising at least one nitrogen atom and R₁ And R₂ are both hydrogen atoms or one of them is a hydrogen atom and the other is an acyl donor.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12P35/02 C07D501/18 C12P35/06 C07D501/04 C07D501/36
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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BEILSTEIN Data, EPO-Internal, BIOSIS, PAJ, 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. |
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| X | <p>JUSTIZ OH ET AL: "One-pot chemoenzymatic synthesis of 3'-funcionalized cephalosporines (cefazolin) by three consecutive biotransformations in fully aqueous medium" JOURNAL OF ORGANIC CHEMISTRY, vol. 62, no. 26, 1997, pages 9099-9106, XP002177920 cited in the application schemes 4, 5 page 9103, right-hand column, last paragraph -page 9104, left-hand column, paragraph 2 page 9105, right-hand column, last paragraph</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p> | 1-23 |



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Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | <p>"The Merck Index on CD-ROM, Version 12:2" 1997, MERCK & CO INC., WHITEHOUSE STATION, NJ, USA XP002177921 Cefazolin (Entry 1967), Ceftriaxone (entry 2001), Cefotiamе (entry 1985), Cefatrizine (entry 1965), Cefamandole (entry 1964), Cefoperazone (entry 1981), Cefazedone (entry 1966)</p> <p style="text-align: center;">---</p> | 20 |
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| X | <p>page 3, line 13 - line 16; claim 1 claims 1,10</p> <p style="text-align: center;">---</p> | 20 |
| X | <p>DE 20 56 983 A (CIBA-GEIGY AG) 9 June 1971 (1971-06-09) example 2</p> <p style="text-align: center;">---</p> | 20-22, 39,40 |
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| Y | <p>EP 0 436 355 A (FUJISAWA PHARMACEUTICAL CO.) 10 July 1991 (1991-07-10) claim 1</p> <p style="text-align: center;">---</p> | 1-23 |
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| Y | <p>EP 0 492 495 A (HOECHST AG) 1 July 1992 (1992-07-01) claims 1-6</p> <p style="text-align: center;">---</p> | 1-38 |
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| Y | <p>WO 00 78989 A (ANTIBIOTICOS, S.A.U.) 28 December 2000 (2000-12-28) claims 1-37</p> <p style="text-align: center;">---</p> | 1-23 |
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| Y | GB 1 385 685 A (GLAXO LABORATORIES LTD.) 26 February 1975 (1975-02-26) claims 1-40 --- | 1-38 |
| Y | J. E. BALDWIN ET AL.: "Cleavage of the 5-amino-5-carboxy-2-oxapentanoyl side chain from enzymatically synthesised penicillins and cephalosporins" BIOORG. MED. CHEM. LETT., vol. 5, no. 21, 1995, pages 2507-2512, XP002207185 cited in the application * Schemes 2 and 4 * --- | 1-19 |
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| X | CHEMICAL ABSTRACTS, vol. 80, no. 13, 1 April 1974 (1974-04-01) Columbus, Ohio, US; abstract no. 70820t, page 348; XP002207187 abstract & JP 48 075587 A (FUJISAWA PHARMACEUTICAL CO., LTD.) 11 October 1973 (1973-10-11) --- | 39,40 |
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| X | DE 26 26 026 A (MERCK PATENT GMBH) 22 December 1977 (1977-12-22) claim 1 --- | 39,40 |
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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| X | DE 25 27 291 A (F. HOFFMANN-LA ROCHE & CO AG) 8 January 1976 (1976-01-08) * Compounds of formula IV * | 20 |
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| X | DE 22 37 082 A (TAKEDA CHEMICAL INDUSTRIES LTD.) 8 February 1973 (1973-02-08) * Compound of formula IIa * column 8; claim 1 --- | 20 |
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| X | DE 21 37 386 A (TAKEDA CHEMICAL INDUSTRIES, LTD.) 31 May 1972 (1972-05-31) claims 1,4,10,11 ----- | 20,39 |