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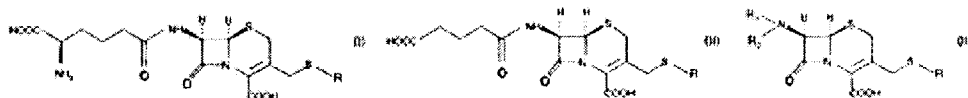
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(54) Title: ENZYMATIC PROCESS FOR PREPARING CEPHALOSPORIN DERIVATIVES

(57) Abstract: An enzymatic process for preparing 3-thiolated 7-aminocephalosporanic acid derivatives comprises the steps of en-
zymatically 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.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

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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)

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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)

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.
X	JUSTIZ OH ET AL: "One-pot chemoenzymatic synthesis of 3'-functionalized 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 --- -/--	1-23



Further documents are listed in the continuation of box C.



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.
X	"The Merck Index on CD-ROM, Version 12:2" 1997, MERCK & CO INC., WHITEHOUSE STATION, NJ, USA XP002177921 Cefazolin (Entry 1967), Ceftriaxone (entry 2001), Cefotiam (entry 1985), Cefatrizine (entry 1965), Cefamandole (entry 1964), Cefoperazone (entry 1981), Cefazedone (entry 1966) ---	20
Y	WO 90 12110 A (BIOPURE CORP) 18 October 1990 (1990-10-18)	1-19
X	page 3, line 13 - line 16; claim 1 claims 1,10 ---	20
X	DE 20 56 983 A (CIBA-GEIGY AG) 9 June 1971 (1971-06-09) example 2 ---	20-22, 39,40
Y	DE 19 53 861 A (FUJISAWA PHARMACEUTICAL CO., LTD.) 6 May 1971 (1971-05-06) claims 1-21 ---	1-23
Y	EP 0 436 355 A (FUJISAWA PHARMACEUTICAL CO.) 10 July 1991 (1991-07-10) claim 1 ---	1-23
Y	EP 0 583 817 A (ASAHI KASEI KOGYO KABUSHIKI KAISHA) 23 February 1994 (1994-02-23) claims 1-12 ---	1-38
Y	EP 0 492 495 A (HOECHST AG) 1 July 1992 (1992-07-01) claims 1-6 ---	1-38
Y	EP 0 517 200 A (MINISTERO DELL'UNIVERSITA' E DELLA RICERCA SCIENTIFICA E TECNOLOGICA) 9 December 1992 (1992-12-09) cited in the application claims 1-10 ---	1-38
Y	WO 00 78989 A (ANTIBIOTICOS, S.A.U.) 28 December 2000 (2000-12-28) claims 1-37 ---	1-23
X	DE 19 39 341 A (GLAXO LABORATORIES LTD.) 5 February 1970 (1970-02-05) claims 1-40; example 13 ---	1-23
Y	PATENT ABSTRACTS OF JAPAN vol. 005, no. 152, 25 September 1981 (1981-09-25) & JP 56 085298 A (ASAHI CHEM. IND. CO.) abstract ---	1-38
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Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PATENT ABSTRACTS OF JAPAN vol. 011, no. 322, 20 October 1987 (1987-10-20) & JP 62 107798 A (ASAHI CHEM. IND. CO.), 19 May 1987 (1987-05-19) abstract ---	1-38
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
Y	EP 0 496 993 A (ANTIBIOTICOS SPA) 5 August 1992 (1992-08-05) claims 1-12 ---	1-23
X	CH 520 709 A (GLAXO LABORATORIES LTD.) 31 March 1972 (1972-03-31) ---	20
Y	claim 1 ---	23
Y	CONLON HUGH D ET AL.: "Two-step immobilized enzyme conversion of cephalosporin C to 7-aminocephalosporanic acid" BIOTECHNOLOGY AND BIOENGINEERING, vol. 46, no. 6, 1995, pages 510-513, XP001093638 tables I-IV ---	1-38
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 1097400,1062954,1061615 XP002211692 abstract & ZA 6 802 695 A (FUJISAWA PHARM. CO.) 1967 --- -/--	39,40

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International Application No

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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	DE 24 42 302 A (BRISTOL-MYERS CO.) 6 March 1975 (1975-03-06) * Compounds of formula II *	20
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	US 3 968 226 A (G. L. DUNN, J. R. E. HOOVER) 6 July 1976 (1976-07-06) example 2 ---	20
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