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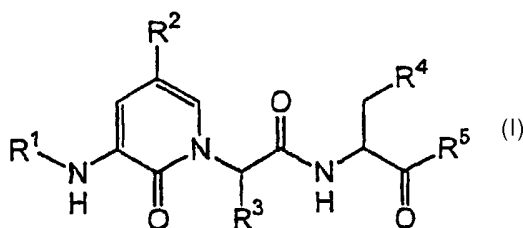
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(54) Title: 3 - [2- (3-AMINO-2-OXO-2H-PYRIDIN-1-YL) - ACETYLAMINO] - 4- OXO-PENTANOIC ACID DERIVATIVES AND THEIR USE AS CASPASE INHIBITORS



(57) Abstract: The present invention provides a compound of formula (I), wherein R¹, R⁶C(O)-, HC(O)-, R⁶SO₂-, R⁶OC(O)-, (R⁶)₂NC(O)-, (R⁶) (H) NC (O)-, R⁶C (O) C (O) -, R⁶-, (R⁶)₂NC (O) C (O)-, R⁶ (H) NC (O) C (O)-, or R⁶OC (O) C (O)-; R² is hydrogen, CF₃, -halo, -OR⁷, -NO₂, -OCF₃, -CN, or R⁸; R³ is hydrogen or (C1-C4) -aliphatic-; R⁴ is -COOH or -COOR⁸; R⁵ is -CH₂F or -CH₂O-2, 3, 5, 6-tetrafluorophenyl. The present invention also provides pharmaceutical compositions and methods using such compositions for treating a caspase-mediated diseases and processes for preparing the compounds of the invention.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/016706

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07D213/74 A61K31/4412 C07D213/75 C07D213/76 C07D213/81 C07D213/82 C07D405/12 C07D417/12		
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 7 C07D A61K		
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, WPI Data, CHEM ABS Data, BEILSTEIN Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/42216 A (BINCH HAYLEY ; GOLEC JULIAN (GB); CHARRIER JEAN DAMIEN (GB); VERTEX PH) 14 June 2001 (2001-06-14) the whole document	1-33, 35
Y	SEMPLÉ G ET AL: "PYRIDONE-BASED PEPTIDOMIMETIC INHIBITORS OF INTERLEUKIN-1beta-CONVERTING ENZYME (ICE)" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 7, no. 10, 20 May 1997 (1997-05-20), pages 1337-1342, XP004136329 ISSN: 0960-894X cited in the application the whole document	1-33, 35
-/--		
<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 : "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		
Date of the actual completion of the international search 27 July 2005		Date of mailing of the international search report 14. 09. 2005
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 Fink, D

INTERNATIONAL SEARCH REPORT

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.
Y	WO 98/16502 A (ALBRECHT HANS P ; WALKER NIGEL (DE); ALLEN HAMISH JOHN (US); HARTER WI) 23 April 1998 (1998-04-23) the whole document	1-33,35
A	WO 00/61542 A (CAI SUI XIONG ; CYTOVIA INC (US); GREEN DOUGLAS R (US); MILLS GORDON B) 19 October 2000 (2000-10-19) the whole document; in particular, page 12, lines 20-29	1-33,35
X	WARNER P ET AL: "NON-PEPTIDIC INHIBITORS OF HUMAN LEUKOCYTE ELASTASE. 1. THE DESIGN AND SYNTHESIS OF PYRIDONE-CONTAINING INHIBITORS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 37, no. 19, 1994, pages 3090-3099, XP000999369 ISSN: 0022-2623 cited in the application page 3092; Scheme 2, steps e and f in the preparation of compound 15	34
X	EP 0 509 769 A (IMPERIAL CHEMICAL INDUSTRIES PLC; ZENECA LIMITED) 21 October 1992 (1992-10-21) page 87, Scheme II, the preparation of the compound XI; and page 89, Scheme IV, the preparation of the compound XXIV page 6, line 29 - line 32 page 7, line 5 - line 6 page 48; example 71d	34
X	EP 0 826 671 A (THE GREEN CROSS CORPORATION; MITSUBISHI PHARMA CORPORATION) 4 March 1998 (1998-03-04) page 20, line 16 - line 23	34
A	US 5 847 135 A (BEMIS ET AL) 8 December 1998 (1998-12-08) cited in the application column 14, line 15 - column 20, line 65 column 126, line 30 - column 128, line 27	1-35

INTERNATIONAL SEARCH REPORT

International application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 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:

Although claims 21-30 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional 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/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-33,35

the compounds of the present claims 1-19, the pharmaceutical composition comprising them (cf., claim 20), the methods of the present claims 21-30 comprising them, and the processes for their preparation (cf., claims 31-33 and 35);

2. claim: 34

the process for the preparation of the intermediate compounds of the present formula (VIII) according to the present claim 34;

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/016706

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