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see Notice of 17 April 2008

(54) Title: SYNTHESIS OF TETRACYCLINES AND ANALOGUES THEREOF

(57) Abstract: The tetracycline class of antibiotics has played a major role in the treatment of infectious diseases for the past 50 years. However, the increased use of the tetracyclines in human and veterinary medicine has led to resistance among many organisms previously susceptible to tetracycline antibiotics. The modular synthesis of tetracyclines and tetracycline analogs described provides an efficient and enantioselective route to a variety of tetracycline analogs and polycyclines previously inaccessible via earlier tetracycline syntheses and semi-synthetic methods. These analogs may be used as anti- microbial agents or anti-pro liferative agents in the treatment of diseases of humans or other animals.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/08647

A. CLASSIFICATION OF SUBJECT MATTER IPC: C07C 237/26(2006.01);A61K 31/65(2006.01) USPC: 552/203;514/152 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) U.S. : 552/203;514/152 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 practicable, search terms used) REGISTRY, CAPLUS, EAST		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2005/0282787 A1 (Myers et al.) 22 December 2005 (22.12.2005), see the entire article, especially claims 55, 59 and 60.	1,2,7-10,14,54,55,60-64,67,68 and 74 ----- 3-6,11-13,15-53,56-59,65,66 and 69-73
☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.		
* Special categories of cited documents:		
"A" document defining the general state of the art which is not considered to be of particular relevance	"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	
"E" earlier application or patent published on or after the international filing date	"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	
"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)	"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	
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	
"P" document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 25 February 2008 (25.02.2008)	Date of mailing of the international search report 14 MAR 2008	
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Barbara P. Badio, Ph.D. Telephone No. 571-272-1600	

INTERNATIONAL SEARCH REPORT

International application No.

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Box No. 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:
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.: 226-233
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. 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:
Please See Continuation 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 additional fees, this Authority did not invite payment of any additional fees.
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.: 1-74

- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-74, drawn to compounds, compositions and method of treatment utilizing compounds as defined by claim 1.

Group 2, claim(s) 75-106, drawn to compounds as defined by claim 75 and compositions thereof.

Group 3, claim(s) 107-125 and 226(in part), drawn to compounds as defined by claim 107 and compositions thereof.

Group 4, claim(s) 227-233(in part), drawn to a method of treatment utilizing compounds of Group 4.

Group 5, claim(s) 126-143, drawn to compounds as defined by claim 126 and compositions thereof.

Group 6, claim(s) 144-162, drawn to compounds as defined by claim 144 and compositions thereof.

Group 7, claim(s) 163-178 and 196-211, drawn to compounds as defined by claim 163 and compositions thereof.

Group 8, claim(s) 179-195, drawn to compounds as defined by claim 179 and compositions thereof.

Group 9, claim(s) 212-223, drawn to compounds as defined by claim 211 and compositions thereof.

Group 10, claim(s) 224 and 225, drawn to compounds as defined by claim 224 and compositions thereof.

Group 11, claim(s) 234-252, drawn to a method of synthesizing compounds as defined by claim 233.

The inventions listed as Groups 1-11 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The inventions of Groups 1-11 relate to structurally different compounds and, thus, they do not relate to a single general inventive concept under PCT Rule 13.1.