

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 December 2002 (27.12.2002)

PCT

(10) International Publication Number
WO 02/102793 A3

(51) International Patent Classification⁷: C07D 403/04,
239/96, 471/04, 487/04, 498/08, 487/06, 471/06, 409/04,
495/04, 413/04, 491/04, A61P 31/04 // (C07D 471/04,
221:00, 235:00)

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(21) International Application Number: PCT/IB02/01768

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(22) International Filing Date: 13 May 2002 (13.05.2002)

(25) Filing Language: English

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(26) Publication Language: English

(30) Priority Data:
60/299,249 19 June 2001 (19.06.2001) US

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(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

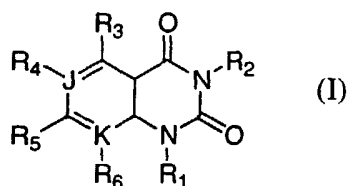
Published:

— with international search report

(88) Date of publication of the international search report:
10 April 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: QUINAZOLINEDIONES AS ANTIBACTERIAL AGENTS



(57) Abstract: The present invention provides compounds of formula (I): wherein R₁-R₆ and J and K have any of the values defined in the specification, and pharmaceutically acceptable salt thereof, that are useful as antibacterial agents. Also disclosed are pharmaceutical compositions comprising one or more compounds of formula I, processes for preparing compounds of formula I, and intermediates useful for preparing compounds of formula I.



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INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/IB 02/01768

A. CLASSIFICATION OF SUBJECT MATTER		
IPC 7	C07D403/04	C07D239/96 C07D471/04 C07D487/04 C07D498/06 C07D487/06 C07D471/06 C07D409/04 C07D495/04 C07D413/04 C07D491/04 A61P31/04 //(C07D471/04,221:00,235:00),
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		
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, 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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<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	"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 document but 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	Date of mailing of the international search report	
29 November 2002	10. 01. 03	
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 Herz, C	

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 02/01768

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 (C07D487/04, 209:00, 235:00), (C07D495/04, 221:00, 333:00)

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)

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.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 157768 XP002210835 abstract & CHATTERJEE, ANAND: J. SCI. IND. RES., vol. 17B, 1958, page 63 --- -/--	1

 Further documents are listed in the continuation of box C. 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

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"O" document referring to an oral disclosure, use, exhibition or other means

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"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

29 November 2002

Date of mailing of the international search report

10. 01. 03

Name and mailing address of the ISA

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Herz, C

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/IB 02/01768

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	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 1198342 & 1174334 XP002210837 abstract & K. GROHE, H. HEITZER: JUSTUS LIEBIGS ANN. CHEM., 1974, pages 2066-2073, ---	2
X	R. BARONNET ET AL.: "Synthèse et pharmacodynamie de dialkylamino-3 1H,3H quinazolinediones-2,4 et de dérivés" EUR. J. MED. CHEM., vol. 18, no. 3, 1983, pages 241-247, XP000985490 cited in the application table I ---	1,6-10
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Y	CHEMICAL ABSTRACTS, vol. 118, no. 23, 7 June 1993 (1993-06-07) Columbus, Ohio, US; abstract no. 233993w, H. A. ABDEL-HAMID ET AL.: "Synthesis of some biologically active heterocycles. Reactions of the hydrazide of 2'-thienoylanthranilic acid and its 3,5-dibromo derivative" page 996; XP002210829 abstract & PHOSPHORUS, SULFUR SILICON RELAT. ELEM., vol. 72, no. 1-4, 1992, pages 237-247, ---	1-12
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Y	CHEMICAL ABSTRACTS, vol. 127, no. 2, 14 July 1997 (1997-07-14) Columbus, Ohio, US; abstract no. 17901h, A. K. YADAV ET AL.: "Synthesis of some novel nucleosides of dioxo pyrido'2,3-d!pyrimidines" page 586; XP002210831 abstract & INDIAN J. HETEROCYCL. CHEM., vol. 6, no. 3, 1997, pages 237-238, ---	1-12
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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.
Y	CHEMICAL ABSTRACTS, vol. 128, no. 4, 26 January 1998 (1998-01-26) Columbus, Ohio, US; abstract no. 34737x, E. H. EL-TAMANY ET AL.: "Synthesis and antimicrobial activities of some quinazolinone derivatives" page 565; XP002210832 abstract & EGYPT. J. CHEM., vol. 40, no. 5, 1997, pages 339-351, ---	1-12
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P,X	WO 01 79206 A (SUMITOMO PHARMACEUTICALS CO.) 25 October 2001 (2001-10-25) claim 1 ---	4-12
E	JP 2002 284699 A (SUMITOMO PHARMACEUTICAL CO.) 3 October 2002 (2002-10-03) * Compounds of formula 3 * ---	4-12
X	F. ISHIKAWA ET AL.: "Cyclic Guanidines. 17. Novel (N-Substituted amino)imidazo[2,1-b]quinazolin-2-ones: Water-Soluble Platelet Aggregation Inhibitors" J. MED. CHEM., vol. 28, no. 10, 1985, pages 1387-1393, XP009000843 table VII ---	1
X	DE 24 46 543 A (HOECHST AG) 15 April 1976 (1976-04-15) example 54 ---	1
X	EP 0 382 687 A (ISTITUTO DE ANGELI S.P.A.) 16 August 1990 (1990-08-16) claim 1 ---	1
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 02/01768

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 26 14 148 A (HENKEL & CIE.) 20 October 1977 (1977-10-20) claim 1 ---	1
X	JP 50 148368 A (HISAMITSU PHARMACEUTICAL CO., LTD.) 27 November 1975 (1975-11-27) * Compounds of formula I * ---	1
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X	EP 0 789 020 A (SUMITOMO CHEMICAL CO., LTD.) 13 August 1997 (1997-08-13) * Compounds of formula II * ---	1
X	PATENT ABSTRACTS OF JAPAN vol. 1997, no. 12, 25 December 1997 (1997-12-25) & JP 09 208543 A (ONO PHARMACEUTICAL CO., LTD.), 12 August 1997 (1997-08-12) abstract ---	1
X	WO 97 24335 A (FUJI CHEMICAL INDUSTRY CO., LTD.) 10 July 1997 (1997-07-10) claims 1-11 ---	1
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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.
X	DATABASE CROSSFIRE BEILSTEIN 'Online! Beilstein Institut zur Förderung der Chemischen Wissenschaften, Frankfurt am Main, DE; Database accession no. 329145, 233007 XP002222384 abstract & HELLER: J. PRAKT. CHEM. <2>, vol. 111, 1925, page 19 ----	1
X	M. GÜTSCHOW: "Novel Heterocycles Derived from Substituted Aroylthioureas: Synthesis of 3,1-Benzothiazin-4-ones, Thieno'3,2-d!'1,3!thiazin-4-ones and 1,2,4-Thiadiazolo'2,3-a!'3,1!benzothiazin- 5-ones" J. HETEROCYCL. CHEM., vol. 33, no. 2, 1996, pages 355-360, XP002222380 * Compounds of formula 8 * ----	1
X	M. KHALIFA ET AL.: "Synthesis and Biological Activity of Certain Derivatives of 2,4-Dioxo-1,2,3,4-tetrahydroquinazoline Part 2" EGYPT. J. CHEM., vol. 25, no. 3, 1982, pages 285-291, XP000978530 table I ----	1
X	M. KHALIFA ET AL.: "Synthesis and Biological Activity of Certain Derivatives of 2,4-Dioxo-1,2,3,4-tetrahydroquinazoline" PHARMAZIE, vol. 37, no. 2, 1982, pages 115-117, XP002157063 table 1 ----	1
X	Z. BUDESINSKY ET AL.: "Alkoxy-2,4-quinazolinodiamines" COLLECT. CZECH. CHEM. COMMUN., vol. 41, no. 11, 1976, pages 3405-3414, XP002222381 * Compounds of formula I * ----	1
X	J. BOMPART ET AL.: "Determination of the hydrophobic constants of 1H,3H-quinazoline-2,4-diones" ANNALES PHARMACEUTIQUES FRANCAISES, vol. 46, no. 5, 1988, pages 301-308, XP009001200 tables I,II ----	1
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/01768

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>J. BOMPART ET AL.: "1H,3H-Quinazoline-2,4-diones: synthesis, physicochemical characterization and study of the stabilization of bovine serum albumin against denaturation" ANNALES PHARMACEUTIQUES FRANCAISES, vol. 46, no. 6, 1989, pages 361-370, XP009001198 table I</p>	1
X	<p>----- A. N. OSMAN ET AL.: "Synthesis and biological activity of certain derivatives of 2,4-dioxo-1,2,3,4-tetrahydroquinazoline. I" EGYPT. J. CHEM., vol. 25, no. 2, 1982, pages 159-164, XP009001225 * Compounds of formula II and III * table I</p>	1
X	<p>----- A. N. OSMAN ET AL.: "Synthesis and biological activity of certain derivatives of 2,4-dioxo-1,2,3,4-tetrahydroquinazoline. I" REV. ROUM. CHIM., vol. 27, no. 7, 1982, pages 859-864, XP009001179 * Compounds of formula II and III * -----</p>	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/01768

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.: 1 (part)
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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:

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

Continuation of Box I.2

Claims Nos.: 1 (part)

The initial phase of the search on Claim 1 revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of Claim 1 is impossible. Consequently, the search on Claim 1 has been restricted to compounds wherein R2 is not H.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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, 2, 4-10 (all part)

Compounds of formula I having specific substituents R1 to R6

2. Claims: 1, 3, 4-12 (all part)

Compounds of formula I wherein R5 represents an azaheterocyclic moiety being bound to the quinazolidione via its nitrogen atom

3. Claims: 1, 3, 4-10 (all part)

Compounds of formula I wherein R5 represents a 5-membered thia and/or azaheterocyclic ring

4. Claims: 4-12 (all part)

peri-condensed compounds of formula VIII

5. Claims: 1(part), 11-12

Compounds of formula IX wherein Z = -C=

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 02/01768

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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