



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 239/48, 401/10, 401/12, 401/14, 403/10, 405/10, 405/12, 405/14, 471/04, 215/56, A61K 31/505, 31/535	A3	(11) International Publication Number: WO 96/16046 (43) International Publication Date: 30 May 1996 (30.05.96)		
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top; padding: 5px;"> (21) International Application Number: PCT/EP95/04451 (22) International Filing Date: 13 November 1995 (13.11.95) (30) Priority Data: 3536/94-3 24 November 1994 (24.11.94) CH 2704/95-0 25 September 1995 (25.09.95) CH (71) Applicant (for all designated States except US): F. HOFFMANN-LA ROCHE AG [CH/CH]; 124 Grenzacherstrasse, CH-4002 Basle (CH). (72) Inventors; and (75) Inventors/Applicants (for US only): GUERRY, Philippe [CH/CH]; 2 In den Holeematten, CH-4102 Binningen (CH). JOLIDON, Synèse [CH/CH]; 2 Stutzhalde, CH-4223 Blauen (CH). MASCIADRI, Raffaello [CH/CH]; 228 Klybeckstrasse, CH-4057 Basle (CH). STALDER, Henri [CH/CH]; 40 Friedensgasse, CH-4056 Basle (CH). THEN, Rudolf [DE/DE]; 39 Schutzackerstrasse, D-79576 Weil am Rhein (DE). (74) Agents: GROSSNER, Lutz et al.; P.O. Box 3255, CH-4002 Basle (CH). </td> <td style="width: 50%; vertical-align: top; padding: 5px;"> (81) Designated States: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, LS, MW, SD, SZ, UG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 25 July 1996 (25.07.96) </td> </tr> </table>			(21) International Application Number: PCT/EP95/04451 (22) International Filing Date: 13 November 1995 (13.11.95) (30) Priority Data: 3536/94-3 24 November 1994 (24.11.94) CH 2704/95-0 25 September 1995 (25.09.95) CH (71) Applicant (for all designated States except US): F. HOFFMANN-LA ROCHE AG [CH/CH]; 124 Grenzacherstrasse, CH-4002 Basle (CH). (72) Inventors; and (75) Inventors/Applicants (for US only): GUERRY, Philippe [CH/CH]; 2 In den Holeematten, CH-4102 Binningen (CH). JOLIDON, Synèse [CH/CH]; 2 Stutzhalde, CH-4223 Blauen (CH). MASCIADRI, Raffaello [CH/CH]; 228 Klybeckstrasse, CH-4057 Basle (CH). STALDER, Henri [CH/CH]; 40 Friedensgasse, CH-4056 Basle (CH). THEN, Rudolf [DE/DE]; 39 Schutzackerstrasse, D-79576 Weil am Rhein (DE). (74) Agents: GROSSNER, Lutz et al.; P.O. Box 3255, CH-4002 Basle (CH).	(81) Designated States: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, LS, MW, SD, SZ, UG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 25 July 1996 (25.07.96)
(21) International Application Number: PCT/EP95/04451 (22) International Filing Date: 13 November 1995 (13.11.95) (30) Priority Data: 3536/94-3 24 November 1994 (24.11.94) CH 2704/95-0 25 September 1995 (25.09.95) CH (71) Applicant (for all designated States except US): F. HOFFMANN-LA ROCHE AG [CH/CH]; 124 Grenzacherstrasse, CH-4002 Basle (CH). (72) Inventors; and (75) Inventors/Applicants (for US only): GUERRY, Philippe [CH/CH]; 2 In den Holeematten, CH-4102 Binningen (CH). JOLIDON, Synèse [CH/CH]; 2 Stutzhalde, CH-4223 Blauen (CH). MASCIADRI, Raffaello [CH/CH]; 228 Klybeckstrasse, CH-4057 Basle (CH). STALDER, Henri [CH/CH]; 40 Friedensgasse, CH-4056 Basle (CH). THEN, Rudolf [DE/DE]; 39 Schutzackerstrasse, D-79576 Weil am Rhein (DE). (74) Agents: GROSSNER, Lutz et al.; P.O. Box 3255, CH-4002 Basle (CH).	(81) Designated States: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, LS, MW, SD, SZ, UG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 25 July 1996 (25.07.96)			
(54) Title: NOVEL BENZYL PYRIMIDINES (I) (57) Abstract Substituted 5-benzyl-2,4-diaminopyrimidines of general formula (I) in which R¹ represents lower alkoxy, R² represents bromine or lower alkoxy and R³ represents aryl, heteroaryl or a group -Q-R³⁰, wherein Q signifies ethylene, vinylene or ethynylene and R³⁰ signifies aryl, heteroaryl, lower alkoxy-carbonyl or carbamoyl, as well as readily hydrolyzable esters of carboxylic acids of formula I and pharmaceutically acceptable salts of these compounds can be used in the control or prevention of infectious diseases.				

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TG	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 95/04451

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D239/48 C07D401/10 C07D401/12 C07D401/14 C07D403/10
C07D405/10 C07D405/12 C07D405/14 C07D471/04 C07D215/56
A61K31/505 A61K31/535

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 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ADV. EXP. MED. BIOL., vol. 338, 1993, pages 533-536, XP002002236 THEN, R., L. ET AL.: "Selective Inhibition of Dihydrofolate Reductase from Problem Human Pathogens" see line 5; examples 11-8960; table 1	1,4,10, 24,27-29
Y	in connection with see line 7; examples 11-9016; table 1	1-4
X	WO,A,92 08461 (PROTOS CORPORATION) 29 May 1992 see claim 1	23
Y	see claim 1	1-4,23, 24,27-29

	-/--	

☒ 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
- *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

6 May 1996

Date of mailing of the international search report

23 May 1996

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

Traegler-Goeldel, M

INTERNATIONAL SEARCH REPORT

Intern. Application No

PCT/EP 95/04451

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	J. MED. CHEM., vol. 32, 1989, pages 1949-1958, XP002001960 ROTH, B. ET AL.: "2,4-Diamino-5-benzylpyrimidines as Antibacterial Agents. 13. Some Alkenyl Derivatives with High in Vitro Activity against Anaerobic Organisms" see cpds. 15 and 16, table I ---	23
Y	US,A,4 251 454 (KOMPIS, I. ET AL.) 17 February 1981 see column 1, line 10-29 ---	1-4,22, 24,25, 27-29
Y	US,A,4 515 948 (KOMPIS, I. ET AL) 7 May 1985 see summary and preferred compounds, see example 8 ---	1-4,22, 24,25, 27,28
A	EP,A,0 572 259 (UBE INDUSTRIES, LTD.) 1 December 1993 see claims 1,18 -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 95/04451

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9208461	29-05-92	AU-B- 657348	09-03-95
		AU-B- 2202792	28-04-94
		CA-A- 2095518	15-05-92
		EP-A- 0639075	22-02-95
		JP-T- 7509215	12-10-95

US-A-4251454	17-02-81	CH-A- 605828	13-10-78
		US-A- 4039543	02-08-77
		AT-B- 356117	10-04-80
		AT-B- 344704	10-08-78
		AU-B- 500102	10-05-79
		AU-B- 8643375	12-05-77
		BE-A- 836996	23-06-76
		CA-A- 1059127	24-07-79
		CH-A- 617191	14-05-80
		DE-A- 2558150	01-07-76
		FR-A,B 2295750	23-07-76
		GB-A- 1492140	16-11-77
		JP-A- 51091273	10-08-76
		LU-A- 73971	01-07-77
		NL-A- 7514269	28-06-76
		SE-B- 417607	30-03-81
		SE-A- 7514642	28-06-76

US-A-4515948	07-05-85	CH-A- 591456	15-09-77
		US-A- 4792557	20-12-88
		US-A- 4659818	21-04-87
		AR-A- 207764	29-10-76
		AR-A- 211387	15-12-77
		AT-B- 338797	12-09-77
		AT-B- 351034	15-12-78
		AU-B- 7263174	26-02-76
		BE-A- 819773	11-03-75
		CA-A- 1037476	29-08-78
		DE-A- 2443682	20-03-75
		FR-A,B 2242984	04-04-75
		GB-A- 1484481	01-09-77
		GB-A- 1484482	01-09-77
		GB-A- 1484483	01-09-77
		JP-C- 1322765	27-06-86

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 95/04451

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4515948		JP-A- 50053385	12-05-75
		JP-B- 60042238	20-09-85
		LU-A- 70878	19-08-76
		NL-A- 7411685	14-03-75
		SE-B- 419443	03-08-81
		SE-A- 7411382	13-03-75

EP-A-572259	01-12-93	AU-B- 3981593	02-12-93
		CA-A- 2096998	28-11-93
		CN-A- 1086515	11-05-94
		JP-A- 6116241	26-04-94
		NO-A- 931867	29-11-93
		NZ-A- 247720	27-09-94
		ZA-A- 9303732	15-12-93
