PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C07D 263/20, 417/12, 413/10, 413/04, A61K 31/42, C07D 261/04, 307/32, 471/10 // (C07D 471/10, 235:00, 221:00)

A1

(11) International Publication Number: WO 98/54161

(43) International Publication Date: 3 December 1998 (03.12.98)

(21) International Application Number: PCT/US98/09889

(22) International Filing Date: 18 May 1998 (18.05.98)

(30) Priority Data:
60/048,342 30 May 1997 (30.05.97) US

(71) Applicant *(for all designated States except US)*: PHARMACIA & UPJOHN COMPANY [US/US]; 301 Henrietta Street, Kalamazoo, MI 49001 (US).

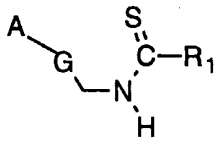
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: HESTER, Jackson, B., Jr. [US/US]; 9219 East ML Avenue, Galesburg, MI 49053 (US). NIDY, Eldon, George [US/US]; 3103 Morgan Street, Kalamazoo, MI 49001 (US). PERRICONE, Salvatore, Charles [US/US]; 7011 Division Avenue, Delton, MI 49046 (US). POEL, Toni–Jo [US/US]; 304 Anderson, Wayland, MI 49348 (US).

(74) Agent: YANG, Lucy, X.; Pharmacia & Upjohn Company, Intellectual Property Legal Services, 301 Henrietta Street, Kalamazoo, MI 49001 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: OXAZOLIDINONE ANTIBACTERIAL AGENTS HAVING A THIOCARBONYL FUNCTIONALITY



(I)

(57) Abstract

The present invention provides compounds of Formula (I) or pharmaceutical acceptable salts thereof wherein A, G and R_1 are as defined in the claims which are antibacterial agents.

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.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

OXAZOLIDINONE ANTIBACTERIAL AGENTS HAVING A THIOCARBONYL FUNCTIONALITY

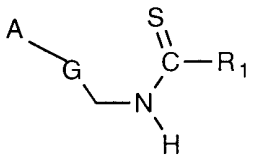
BACKGROUND OF THE INVENTION

The present invention relates to new and useful oxazolidinone compounds and their preparations, and more particularly to oxazolidinone compounds in which the carbonyl functionality of -NH-C(O)-R is converted to a thiocarbonyl functionality, such as a thiourea -NH-C(S)-NH_2, an alkyl thiourea -NH-C(S)-NH-(C_{1-4} alkyl), thioamide -NH-C(S)-(C_{1-4} alkyl) or -NH-C(S)-H.

Replacement of the oxygen atom with a sulfur atom has unexpectedly improved the antimicrobial properties of the compounds. The compounds are useful antimicrobial agents, effective against a number of human and veterinary pathogens, including Gram-positive aerobic bacteria such as multiply-resistant staphylococci and streptococci, Gram-negative organisms such as H. *influenzae* and M. *catarrahlis* as well as anaerobic organisms such as bacteroides and clostridia species, and acid-fast organisms such as *Mycobacterium tuberculosis* and *Mycobacterium avium*. The compounds are particularly useful because they are effective against the latter organisms which are known to be responsible for infection in persons with AIDS.

SUMMARY OF THE INVENTION

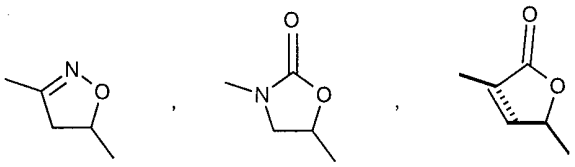
In one aspect the subject invention is a compound of the Formula I



I

or pharmaceutical acceptable salts thereof wherein:

G is



R_1 is

a) H,

b) NH_2,

c) NH-C_{1-4} alkyl,

d) C_{1-4} alkyl,

e) -OC_{1-4} alkyl,

f) -S C_{1-4} alkyl,

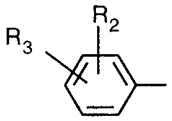
g) C_{1-4} alkyl substituted with 1-3 F, 1-2 Cl, CN or -COOC_{1-4} alkyl,

h) C_{3-6} cycloalkyl,

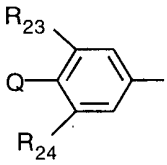
i) $N(C_{1-4}$ alkyl$)_2$ or

j) $N(CH_2)_{2-5}$;

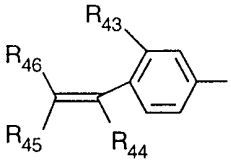
A is

a) 

,

b) 

,

c) 

,

d) a 5-membered heteroaromatic moiety having one to three atoms selected from the group consisting of S, N, and O,

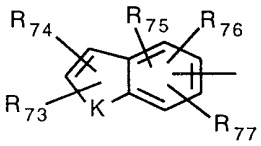
wherein the 5-membered heteroaromatic moiety is bonded via a carbon atom,

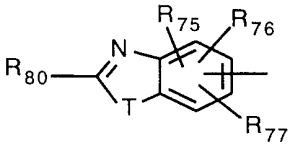
wherein the 5-membered heteroaromatic moiety can additionally have a fused-on benzene or naphthyl ring,

wherein the heteroaromatic moiety is optionally substituted with one to three R_{48},

e) a 6-membered heteroaromatic moiety having at least one nitrogen atom,
wherein the heteroaromatic moiety is bonded via a carbon atom,
wherein the 6-membered heteroaromatic moiety can additionally have a fused-on benzene or naphthyl ring,
wherein the heteroaromatic moiety is optionally substituted with one to three R_{55},

f) a β-carbolin-3-yl, or indolizinyl bonded via the 6-membered ring, optionally substituted with one to three R_{55},

g)  , or

h)  ;

wherein R_2 is

a) H,
b) F,
c) Cl,
d) Br,
e) C_{1-3} alkyl,
f) NO_2, or
g) R_2 and R_3 taken together are -O-$(CH_2)_h$-O-;

R_3 is

a) -S(=O)$_i$ R_4,
b) -S(=O)$_2$-N=S(O)$_j$$R_5$$R_6$,
c) -SC(=O)R_7,
d) -C(=O)R_8,
e) -C(=O)R_9,
f) -C(=O)N$R_{10}$$R_{11}$,

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.