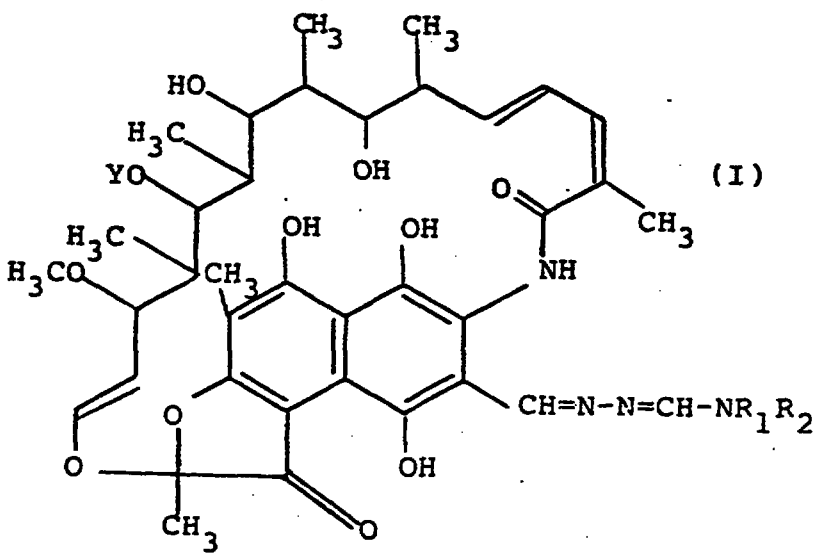
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Azino Methyl-Rifamycins

The invention relates to azino methyl-rifamycins, to methods for their preparation and to pharmaceutical compositions containing them.

The invention provides rifamycin compounds having the general formula (I)

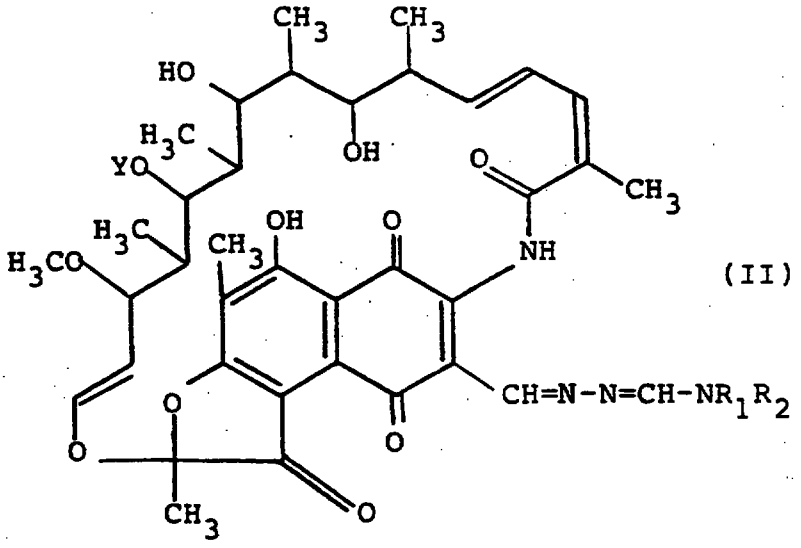


(I)

wherein Y represents a hydrogen atom or an acetyl group and either R_1 represents a linear or branched alkyl group having from 1 to 7 carbon atoms or an alkenyl group having 3 or 4 carbon atoms and R_2 represents a linear or branched alkyl group having from 1 to 7 carbon atoms, a chloroalkyl, hydroxyalkyl or alkoxyalkyl group having from 2 to 4 carbon atoms, an

alkenyl group having 3 or 4 carbon atoms, a cycloalkyl group having from 3 to 7 carbon atoms in the ring, a cycloalkyl-alkyl group having from 3 to 6 carbon atoms in the ring, a phenyl group, an unsubstituted aralkyl group having 7 to 8 carbon atoms or an aralkyl group having 7 or 8 carbon atoms and substituted by one halogen atom in the aryl group, or R_1 and R_2 together with the nitrogen atom to which they are bonded represent a 4-alkyl-1-piperazinyl group, a 4-cycloalkyl-1-piperazinyl group, a morpholino group, or a cyclic moiety having from 5 to 8 carbon atoms, unsubstituted or substituted by one or two methyl group(s).

The invention also provides compounds of the general formula (II)

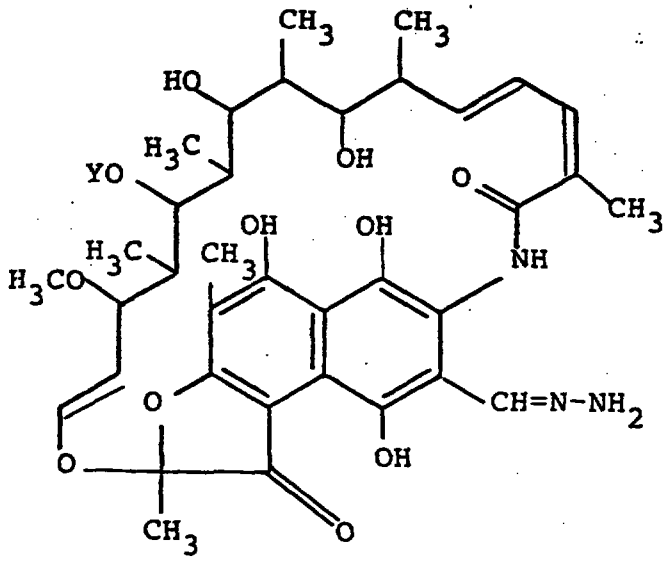


(II)

wherein Y, R_1 and R_2 are as above defined. These compounds of the general formula (II) are oxidation products of the compounds of the general formula (I).

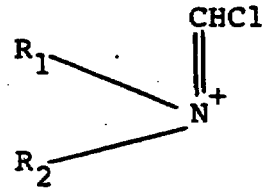
The rifamycin compounds according to the invention have antibacterial activity against Gram-positive and Gram--negative bacteria and against Mycobacterium Tuberculosis. The compounds of the general formula I are orange to red solids, while those of the general formula II are violet or dark black solids. They are generally soluble in most organic solvents, such as chlorinated solvents, alcohols, esters and aromatic hydrocarbons.

The compounds of the general formula I may be prepared by a process comprising reacting a 3-hydrazonomethyl--rifamycin SV of the general formula (III)



(III)

wherein Y represents a hydrogen atom or an acetyl group, in the presence of a tertiary amine and of an aprotic solvent, with a quaternary nitrogen compound of the general formula (IV)



(IV)

wherein R_1 and R_2 are as above defined. This process is within the scope of the invention. The compounds of the general formula III are disclosed in US Patent Specification No. 3,342,810. The compounds of the general formula (IV) are described in British Patent Specification 1293590. The tertiary amine is suitably triethylamine. Several aprotic solvents are suitable, including tetrahydrofuran, dioxan, chloroform, dichloromethane, 1,2-dichloroethane, benzene and toluene.

The compounds of the general formula (II) may be prepared from the corresponding compounds of the general formula (I) by oxidation with manganese dioxide, potassium ferricyanide or with other oxidating agents of common use in this art.

The rifamycin compounds according to the invention may be admixed with a pharmaceutically acceptable carrier or diluent to form a pharmaceutical composition within the scope of the invention. Whether alone or

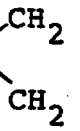
in such a composition, they may be formulated for administration in conventional unit dosage forms.

The invention is illustrated by the following Examples.

Example 1

3-(Piperidinomethylene-azinomethyl)-rifamycin SV

5 g of 3-formyl-rifamycin SV was dissolved in 250 ml of tetrahydrofuran and dropped into a solution of 0.35 ml of hydrazine hydrate in 50 ml of tetrahydrofuran during 15 minutes under stirring and at -20°C. The absence of 3-formyl-rifamycin SV was checked by thin layer chromatography and 2 ml of triethylamine was added keeping the temperature at -20°C. 5 g of 1-chloro-methylene-piperidinium chloride was added portionwise and the mixture was gently warmed to room temperature under stirring. 350 ml of ethyl acetate was added and the resulting solution was washed with water. After drying on anhydrous sodium sulphate the solvent was evaporated off and the crude product was crystallized from methanol and then from acetone. 2.3 g of a red compound of general formula I, wherein Y=$COCH_3$ and NR_1R_2=piperidino, was obtained.

PMR ($CDCl_3$): -0.27 δ [d, CH_3 (34)]; 0.65 δ [d, CH_3(33)]; 0.75 δ [d, CH_3(31)]; 0.99 δ [d, CH_3(32)]; 1.65 δ [s, CH_2 ]; 1.79 δ [s, CH_3(13)]; 2.06 δ [s, CH_3(36)]; 2.10 δ [s, CH_3(30)];

2.23 δ [s, CH_3 (14)]; 3.04 δ [s, CH_3(37)]; 7.73 and 9.03 δ [2s, -CH=N-N=CH-N<]; 11.93 δ [s, -NH-C(=O)-]; 13.27 and 13.87 δ [s, OH-C(1), OH-C(8), OH-C(4)].

MS: 834 (M^+)

The above compound was oxidized with MnO_2 in dichloromethane solution to give the corresponding quinone of formula (II).

MS: 832 (M^+)

Rf: 0.37 in CH_2Cl_2:MeOH 20:1

The 3-(piperidinomethylene-azinomethyl)-rifamycin SV was desacetylated according to Helv. Chim. Acta 56, 2335 (1973) to give the corresponding compound of formula (I) in which Y=H.

MS: 792 (M^+)

Rf: 0.24 in CH_2Cl_2:MeOH 20:1

This last mentioned desacetyl derivative was oxidized with MnO_2 in dichloromethane solution to give the corresponding quinone of formula (II)

MS: 790 (M^+)

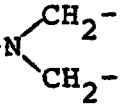
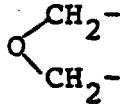
Rf: 0.22 in CH_2Cl_2:MeOH 20:1

Example 2

3-(Morpholinomethylene-azinomethyl)-rifamycin SV

Following the procedure described in Example 1 and reacting 3-formyl-rifamycin SV with 4-chloromethylene--morpholinium chloride a compound of formula I was

obtained wherein Y=$COCH_3$ and NR_1R_2 = morpholino.

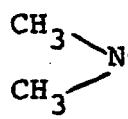
PMR ($CDCl_3$): -0.28 δ [d, CH_3(34)]; 0.65 δ [d, CH_3(33)];
0.76 δ [d, CH_3(31)]; 0.99 δ [d, CH_3(32)];
1.79 δ [s, CH_3(13)]; 2.06 δ [s, CH_3(36)];
2.10 δ [s, CH_3(30)]; 2.23 δ [s, CH_3(14)];
3.04 δ [s, CH_3(37)]; 3.46 δ [m, ];
3.71 δ [m, ]; 7.75 and 9.03 δ [2s,
-CH=N-N=CH-N<]; 11.99 δ [s, -NH-C(=O)-];
13.24, 13.69 and 13.83 δ [3s, OH-C(1),
OH-C(4), OH-C(8)].

MS: 836 (M^+)

EXAMPLE 3

3-(Dimethylaminomethylene-azinomethyl)-rifamycin SV

Following the procedure described in Example 1 and reacting 3-formyl-rifamycin SV with dimethylchloroformiminium chloride a compound of formula I was obtained wherein Y=$COCH_3$ and R_1=R_2=CH_3.

PMR ($CDCl_3$): -0.26 δ [d, CH_3(34)]; 0.68 δ [d, CH_3(33)];
0.77 δ [d, CH_3(31)]; 1.04 δ [d, CH_3(32)];
1.85 δ [s, CH_3(13)]; 2.10 δ [s, CH_3(36)];
2.17 δ [s, CH_3(30)]; 2.27 δ [s, CH_3(14)];
3.03 δ [s, ]; 3.09 δ [s, CH_3(37)];
7.77 and 9.05 δ [2s, -CH=N-N=CH-N<];

11.96 δ [s, -NH-C(=O)-]; 13.29 and 13.92 δ [OH-C(1), OH-C(8), OH-C(4)].

MS: 794 (M^+)

Example 4

3-(N-Perhydroazepinylmethylene-azinomethyl)rifamycin SV

3 g of 3-formyl-rifamycin SV was dissolved in 50 ml of dichloroethane and dropped into a solution of 0.2 ml of hydrazine hydrate in 25 ml of dichloroethane during 15 minutes under stirring and at -20°C. After 15 minutes the resulting solution of 3-hydrazonomethyl-rifamycin SV was allowed to reach +5°C, 1.2 ml of triethylamine and then 3 g of 1-chloromethylene-perhydroazepinium chloride were added. The mixture was stirred for 15 minutes, then was diluted with 100 ml of dichloroethane and washed with water.

After drying on anhydrous sodium sulphate the solvent was evaporated off and the crude product was purified by column chromatograhy on silica gel, using ethyl acetate and methanol as eluents. The pure product thus obtained was crystallized from acetone. 0.70 g of a red compound of general formula I, wherein Y=$COCH_3$ and NR_1R_2=perhydroazepinyl, was obtained.

MS: 848 (M^+).

EXAMPLE 5

3-(Morpholinomethylene-azinomethyl)-rifamycin S

0.25 g of the compound obtained in Example 2 was dissolved in 30 ml of chloroform and 0.20 g of manganese dioxide was added. A stream of air was bubbled through the suspension for 180 minutes, the manganese dioxide was filtered and the solvent was evaporated off. The residue was crystallized from methanol. 0.150 g of a violet compound was obtained.

MS: 834 (M^+)

Example 6

3-(Di-n-propylaminomethylene-azinomethyl)-rifamycin SV

A solution of 3 g of 3-formyl-rifamycin SV in 150 ml of tetrahydrofuran was added to 0.2 ml of hydrazine hydrate dissolved in 50 ml of tetrahydrofuran cooled to -20°C. After 15 minutes the resulting solution of 3-hydrazonomethyl-rifamycin SV was allowed to reach 0°C, and 1.2 ml of triethylamine and then 3 g of di-n-propyl--chloroformiminium chloride were added.

After 15 minutes at room temperature the reaction mixture was diluted with 200 ml of ethyl acetate, washed with a 3% aqueous solution of sodium bicarbonate and then with water. The organic phase was dried over anhydrous sodium sulphate, and the solution was concentrated and then diluted with petroleum ether. 0.8 g of a red compound of general formula I, wherein

Y=$COCH_3$ and R_1=R_2=n-C_3H_7, was obtained.

PMR ($CDCl_3$): -0.25 δ [d, CH_3(34)]; 0.59 δ [d, CH_3(33)]; 0.73 δ [d, CH_3(31)]; 0.98 δ [d, CH_3(32)]; 1.5-1.6 δ [m, $N(CH_2CH_2CH_3)_2$]; 1.78 δ [s, CH_3(13)]; 2.05 δ [s, CH_3(36)]; 2.09 δ [s, CH_3(30)]; 2.21 δ [s, CH_3(14)]; 3.04 δ [s, OCH_3]; 4.91 δ [d, H(25)]; 5.08 δ [dd, H(28)]; 5.80 δ [dd, H(19)]; 6.1-6.8 δ [m, H(17), H(18), H(29)]; 7.78 δ [s, CH=N-N=CH-N]; 9.00 δ [s, CH=N-N=CH-N]; 12.03 and 13.40 δ (s, OH and NH).

MS: 850 (M^+)

Example 7

3-(N-Methyl-n-butylaminomethylene-azinomethyl)-rifamycin SV

Following the procedure described in Example 6, but reacting 3-formyl-rifamycin SV hydrazone with N-methyl N-(n-butyl)-chloroformiminium chloride, a compound of formula I was obtained, wherein Y = $COCH_3$, R_1 = CH_3, and R_2 = n-C_4H_9.

PMR ($CDCl_3$): -0.23 δ [d, CH_3(34)]; 0.64 δ [d, CH_3(33)]; 0.73 δ [d, CH_3(31)]: 0.98 δ [d, CH_3(32)]; 1.44 δ [m, N-$CH_2CH_2CH_2CH_3$]; 1.77 δ [s, CH_3(13)]: 2.04 δ [s, CH_3(36)]; 2.07 δ [s, CH_3(30)]; 2.14 δ [s, CH_3(14)]; 2.93 δ [s, ($N-CH_3$)]; 3.04 δ [s, OCH_3]; 4.7-5.2 δ [m,

H(25), H(28)]; 5.5-6.6 δ [m, H(17), H(18), H(29)]; 7.78 δ [s, CH=N-N=CH-N]; 9.01 δ [s, CH=N-N=CH-N]; 12.03 δ [s, NH].

MS: 836 (M^+)

Example 8

3-(Di-s-butylaminomethylene-azinomethyl)-rifamycin SV

Following the procedure described in Example 6, but reacting 3-formyl-rifamycin SV hydrazone with di-(s-butyl)-chloroformiminium chloride, a compound of formula I was obtained, wherein Y = $COCH_3$, $R_1=R_2=$ s-C_4H_9.

PMR ($CDCl_3$): -0.25 δ [d, CH_3(34)]; 0.64 δ [d, CH_3(33)]; 0.75 δ [d, CH_3(31)]; 1.01 δ [d, CH_3(32)]; 1.21 δ [bd, $NCHCH_3$]; 1.55 δ [t, CH_2CH_3]; 1.78 δ [s, CH_3(13)]; 2.05 δ [s, CH_3(36)]; 2.09 δ [s, CH_3(30)]; 2,22 δ [s, CH_3(14)]; 3.03 δ [s, OCH_3]; 4.20 δ [m, N-CH-)]; 4.91 δ [d, H(25)]; 5.10 δ [dd, H(28)]; 5.38 δ [dd, H(19)]; 6.1-6.8 δ [m, H(17), H(18), H(29)]; 7.89 δ [s, CH=N-N=CH-N]; 8.99 δ [s, CH=N-N=CH-N]; 11.90; 13.25; 13.82 and 14.01 δ [s, NH, three OH].

MS: 878 ($M^{\pm}$)

Example 9

3-(N-Methyl-benzylaminomethylene-azinomethyl)-rifamycin SV

Following the procedure described in Example 6, but reacting 3-formyl-rifamycin SV hydrazone with N-methyl--N-benzyl-chloroformiminium chloride, a compound of formula I was obtained, wherein Y=$COCH_3$, R_1=CH_3 and R_2=$CH_2C_6H_5$.

PMR ($CDCl_3$): -0.23 δ [d, CH_3(34)]; 0.64 δ [d, CH_3(33)]; 0.72 δ [d, CH_3(31)]; 0.96 δ [d, CH_3(32)]; 1.77 δ [s, CH_3(13)]; 2.04 δ [s, CH_3(36)]; 2.11 δ [s, CH_3(14)]; 2.90 δ [s, NCH_3]; 3.02 δ [s, OCH_3]; 4.39 δ [bs, $CH_2C_6H_5$]; 4.7-5.2 δ [m, H'25), H(28)]; 5.5-6.7 δ [m, H(17), H(18), H(29)]; 7.31 δ [m, C_6H_5]; 7.94 δ [s, CH=N-N=CH-N]; 9.03 δ [s, CH=N-N=CH-N]; 12.13 δ [s, NH].

MS: 870 (M^+)

Example 10

3-(Diethylaminomethylene-azinomethyl)-rifamycin SV

A solution of 3 g of 3-formyl-rifamycin SV in 150 ml of tetrahydrofuran was added to 0.2 ml of hydrazine hydrate dissolved in 50 ml of tetrahydrofuran cooled at -20°C. After 15 minutes the resulting solution of 3--hydrazonomethyl-rifamycin SV was allowed to reach 0°C, 3 g of diethyl-chloroformiminium chloride and 3 ml of triethylamine were added and the reaction was complete within 15 minutes. Ethyl acetate (300 ml) was added. The resulting solution was washed with dilute acetic

acid and then with water. The organic phase was dried over anhydrous sodium sulphate. The solvent was evaporated off, the residue was crystallized from ethanol and then from acetone. 1.5 g of a red compound of general formula I was obtained, wherein Y=$COCH_3$, R_1=R_2=CH_2CH_3.

PMR ($CDCl_3$): -0.23 δ [d, CH_3(34)]; 0.66 δ [d, CH_3(33)]; 0.74 δ [d, CH_3(31)]; 0.99 δ [d, CH_3(32)]; 1.21 δ [t, $NCH_2\underline{CH_3}$]; 1.79 δ [s, CH_3(13)]; 2.06 δ [s, CH_3(36)]; 2.10 δ [s, CH_3(30)]; 2.23 δ [s, CH_3(14)]; 3.04 δ [s, OCH_3]; 3.40 δ [m, $N\underline{CH_2}CH_3$]; 4.91 δ [d, H(25)]; 5.17 δ [m, H(28)]; 5.84 δ [dd, H(19)]; 6.1-6.6 δ [m, H(29), H(17), H(18)]; 7.7 δ [s, $\underline{CH}$=N-N=CH-N]; 9.05 δ [s, CH=N-N=$\underline{CH}$-N]; 11.95; 13.26; 13.80 and 13.89 δ [s, NH, three OH].

MS: 822 (M^+).

Example 11

3-(N-Pyrrolidinylmethylene-azinomethyl)-rifamycin SV

Following the procedure described in Example 10, but reacting 3-hydrazonomethyl-rifamycin SV with 1-chloro-methylene-pyrrolidinium chloride a compound of formula I was obtained, wherein Y=$COCH_3$, NR_1R_2=1-pyrrolidinyl.

PMR ($CDCl_3$): -0.27 δ [d, CH_3(34)]; 0.66 δ [d, CH_3(33)]; 0.74δ [d, CH_3(31)]; 0.99 δ [d, CH_3(32)];

1.79 δ [s, CH_3(13)]; 1.96 δ [m, N(-CH_2--CH_2-)]; 2.06 δ [s, CH_3(36)]; 2.10 δ [s, CH_3(30)]; 2.23 δ [s, CH_3(14)]; 3.04 δ [s, OCH_3]; 3.45 δ [m, N($\underline{CH_2}CH_2)_2$]; 4.90 δ [d, H(25)]; 5.07 δ [dd, H(28)]; 5.82 δ [dd, H(19)]; 6.1-6.7 δ [m, H(17), H(18), H(29)]; 7.95 δ [s, $\underline{CH}$=N-N=CH-N]; 9.08 δ [s, CH=N-N=$\underline{CH}$-N]; 11.94; 13.44 and 13.86 δ [s, NH, three OH].

MS: 820 (M^+).

Analogously the following compounds of formula I, wherein Y=$COCH_3$ and R_1 and R_2 have the meanings specified below, were obtained.

$\underline{R_1=R_2=i\text{-}C_3H_7}$

PMR ($CDCl_3$): -0.28 δ [d, CH_3(34)]; 0.66 δ [d, CH_3(33)]; 0.76 δ [d, CH_3(31); 0.98 δ [d, CH_3(32)]; 1.2-1.3 δ [m, $NCH\begin{matrix}\diagup CH_3\\ \diagdown CH_3\end{matrix}$]; 1.78 δ [s, CH_3(13)]; 2.06 δ [s, CH_3(36)]; 2.11 δ [s, CH_3(30)]; 2.22 δ [s, CH_3(14)]; 3.03 δ [s, OCH_3]; 3.45 δ [bd, H(21)]; 3.72 δ [bd, H(27)]; 4.57 δ [m, $NCH\begin{matrix}\diagup CH_3\\ \diagdown CH_3\end{matrix}$]; 4.91 δ [d, H(25)]; 5.10 δ [dd, H(28)]; 5.89 δ [dd, H(19)]; 6.28 δ [d, H(29)]; 6.37 δ [d, H(17)]; 6.55 δ [m, H(18)]; 6.89 δ [s, $\underline{CH}$=N-N=CH-N]; 9.02 δ [s, CH=N-N=$\underline{CH}$-N]; 11.92; 13.28;

13.95 and 14.06 δ [s, NH, three OH].

MS: 850 (M^+)

$\underline{R_1=R_2=n\text{-}C_4H_9}$

PMR ($CDCl_3$): -0.25 δ [d, CH_3(34)]; 0.66 δ [d, CH_3(33)]; 0.74 δ [d, CH_3(31)]; 1.00 δ [d, CH_3(32)]; 1.3-1.5 δ [m, $N(CH_2CH_2CH_2\underline{CH_3})_2$]; 1.79 δ [s, CH_3(13)]; 2.07 δ [s, CH_3(36)]; 2.11 δ [s, CH_3(30)]; 2.24 δ [s, CH_3(14)]; 3.05 δ [s, OCH_3]; 4.91 δ [d, H(25)]; 5.08 δ [dd, H(28)]; 5.82 δ (dd, H(19)]; 6.1-6.8 δ [m, H(17), H(18), H(29)]; 7.77 δ [s, $\underline{CH}$=N-N=CH-N]; 9.03 δ [s, CH=N-N=$\underline{CH}$-N];11.97; 13.28; 13.81 and 13.93 δ [s, NH, three OH]

MS: 878 (M^+)

$\underline{R_1=CH_3,\ R_2=C_6H_5}$

PMR ($CDCl_3$): -0.28 δ [d, CH_3(34)]; 0.58 δ [d, CH_3(33)]; 0.66 δ [d, CH_3(31)]; 0.95 δ [d, CH_3(32)]; 1.80 δ [s, CH_3(13)]; 2.06 δ [s, CH_3(36)]; 2.11 δ [s, CH_3(30)]; 2.23 δ [s, CH_3(14)]; 3.04 δ [s, OCH_3]; 3.43 δ [s, NCH_3]; 3.77 δ [bd, H(27)]; 4.95 δ [bd, H(25)]; 5.14 δ (dd, H(28)]; 5.74 δ [dd, H(19)]; 6.26 δ [d, H(29)];6.34 δ [d, H(17)]; 6.59 δ [bdd, H(18)]; 7.1-7.5 δ [m, NC_6H_5]; 8.37 δ [s, $\underline{CH}$=N-N=CH-N]; 9.17 δ [s, CH=N--N=$\underline{CH}$-N]; 12.07; 13.25; 13.78 and 13.87 δ

[s, NH, three OH].

MS: 856 (M^+)

R_1=CH_3, R_2=C_6H_{11}

MS = 862 (M^+)

Rf = 0.38 (in dichloromethane:methanol, 20:1 by volume).

In a similar manner the following compounds of formula (I) were obtained, only the meanings of the radicals R_1 and R_2 being here specified.

R_1=CH_2CH_3, R_2=CH_2CH_2OH

R_1=CH_2CH_3, R_2=$CH_2CH_2OCH_3$, and

R_1 and R_2 together with the N atom to which they are bonded form a 4-substituted-1-piperazinyl group in which the substituent in position 4 is a methyl, isobutyl or cyclopentyl group.

The activity in vitro of the rifamycin compounds obtained as described in Examples 1,2 and 3 have been tested against some Gram-positive and Gram-negative microorganisms and against Mycobacterium Tuberculosis (serial dilution method). The results are set out in the following Table, wherein the novel compounds are compared with Rifampicin and the figures are the values of the minimal inhibiting concentrations (MIC) given in mcg/ml.

TABLE

Microorganisms	Example 1	Example 2	Example 3	Rifampicin
K.Pneumoniae	10	20	20	10
P.vulgaris	10	20	10	10
E.coli B	10	20	10	10
E.coli ginetta	10	20	10	10
E.coli ClRifR	>200	200	200	>200
P.aeruginosa	5	20	10	10
S.abortivoequina	5	20	10	10
S.aureus 209 P	0.037	0.009	0.018	0.018
S.foecalis	0.6	0.6	0.6	0.6
S.pyogenes	1.25	1.25	2.5	2.5
S.lutea	0.037	0.018	0.037	0.037
S. aureus 209P Rif R	>200	>200	>200	>200
M.tuberculosis H37Rv	0.01	0.02	0.02	0.01

CLAIMS:

1. An azinomethyl-rifamycin having the general formula I or II as herein defined.

2. 3-(Piperidinomethylene-azinomethyl)-rifamycin SV.

3. 3-(Piperidinomethylene-azinomethyl)-rifamycin S.

4. 3-(Piperidinomethylene-azinomethyl)- 25-desacetyl--rifamycin SV.

5. 3-Piperidinomethylene-azinomethyl)-25-desacetyl--rifamycin S.

6. 3-(Morpholinomethylene-azinomethyl)-rifamycin SV.

7. 3-(Dimethylaminomethylene-azinomethyl)-rifamycin SV.

8. 3-(N-Perhydroazepinylmethylene-azinomethyl)--rifamycin SV.

9. 3-(Morpholinomethylene-azinomethyl)-rifamycin S.

10. 3-(Di-n-propylaminomethylene-azinomethyl)--rifamycin SV.

11. 3-(N-Methyl-n-butylaminomethylene-azinomethyl)--rifamycin SV.

12. 3-(Di-s-butylaminomethylene-azinomethyl)-rifamycin SV.

13. 3-(N-Methyl-benzylaminomethylene-azinomethyl)-rifamycin SV.

14. 3-(Diethylaminomethylene-azinomethyl)-rifamycin SV.

15. 3-(N-Pyrrolidinylmethylene-azinomethyl)-rifamycin SV.



16. 3-(Di-isopropylaminomethylene-azinomethyl)-
-rifamycin SV.

17. 3-(Di-n-butylaminomethylene-azinomethyl)-
-rifamycin SV.

18. 3-(N-Methyl-anilinomethylene-azinomethyl)-
-rifamycin SV.

19. 3-(N-Methyl-cyclohexylaminomethylene-azinomethyl)-
-rifamycin SV.

20. 3-(N-Hydroxyethyl-ethylaminomethylene-azinomethyl)-
-rifamycin SV.

21. 3-(N-Methoxyethyl-ethylaminomethylene-azinomethyl)-
-rifamycin SV.

22. 3-[(4-Methyl-N-piperazinyl)-methylene-azinomethyl]-
-rifamycin SV.

23. 3-[(4-Isobutyl-N-piperazinyl)-methylene-azino-
methyl]-rifamycin SV.

24. 3-[(4-Cyclopentyl-N-piperazinyl)-methylene-
-azinomethyl]-rifamycin SV.

25. A process for the preparation an azinomethyl-
-rifamycin SV having the general formula I as herein defined, the process comprising reacting a 3-hydrazono-methyl-rifamycin SV having the general formula III as herein defined with a quaternary nitrogen compound having the general formula IV as herein defined in an aprotic solvent in the presence of a tertiary amine.

26. A process according to claim 25 in which the

tertiary amine is triethylamine.

27. A process according to claim 25 or claim 26 in which the aprotic solvent is tetrahydrofuran, dioxan, chloroform, dichloromethane, 1,2-dichloroethane, benzene or toluene.

28. A process for the preparation of an azinomethyl--rifamycin S having the general formula II as herein defined, the process being as claimed in any of claims 25 to 27 and further comprising oxidising the azino--rifamycin SV having the general formula I as herein defined with manganese dioxide or potassium ferricyanide.

29. A process according to claim 25, the process being substantially as described herein with reference to any of Examples 1 to 4 or 6 to 11.

30. A process according to claim 28, the process being substantially as described herein with reference to Example 1 or Examples 2 and 5.

31. A pharmaceutical composition comprising an azinomethyl-rifamycin having the general formula I or II as herein defined in admixture with a pharmaceutically acceptable diluent or carrier.