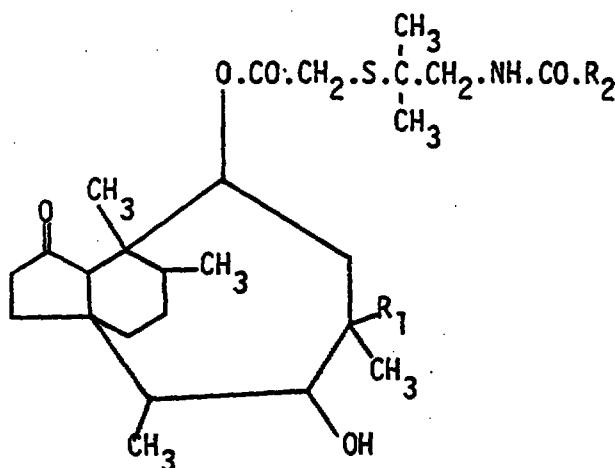


Description

0 153 277

The invention concerns derivatives of 14-O-[(1-amino-2-methyl-propan-2-yl)thioacetyl]-mutilin and -19,20-dihydro-mutilin. In particular it concerns an N-acyl-14-O-[(1-amino-2-methylpropan-2-yl)thioacetyl]-mutilin or -19,20-dihydro-mutilin.

More particularly the invention concerns novel pleuromutilin derivatives of formula I

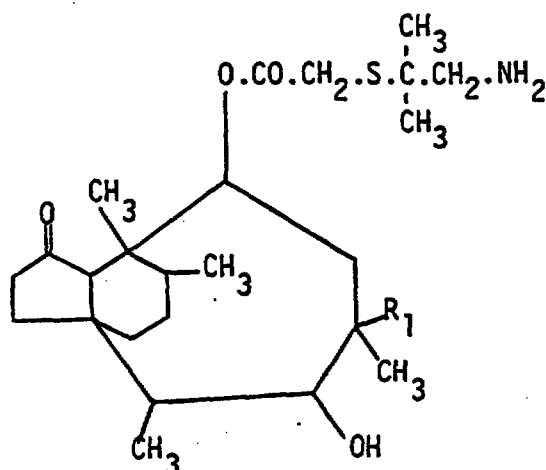


wherein R_1 represents ethyl or vinyl and

R_2 represents a five membered saturated heterocycle or amino-alkyl unsubstituted or substituted in its alkyl moiety by hydroxy,

and their acid addition or quaternary salts, as well as process for their preparation and their use.

The compounds of the invention may be obtained by acylating a compound of formula II



II

wherein R_1 is as defined above, especially with a reactive ester of a compound of formula III



III

whereby R_2' has the same meaning as R_2 above except that any amino groups present therein are protected, and deprotecting any protected amino groups and recovering the compounds thus obtained if desired in the form of their acid addition salts or quaternary salts.

The process according to the invention can be carried out e.g. by dissolving or suspending a compound of formula II and a compound of formula III in a solvent inert under the reaction conditions e.g. in a di(lower)alkylcarboxylic acid amide such as dimethylformamide, and allowing the reaction to proceed at room temperature or at a raised temperature, preferably at room temperature. The subsequent splitting-off of protecting groups can be carried out according to conventional methods, for example by reductive deprotection with Pd/active charcoal and hydrogen or by treatment with trifluoroacetic acid. The final products can be isolated from the reaction mixture and if necessary purified according to conventional methods.

The compounds of formula I can be converted into their acid addition salts and vice versa. Corresponding quaternary salts can be obtained from the compounds of formula I in conventional manner.

The compounds of formula I may contain at least one asymmetric carbon atom and may thus exist in the form of diastereomeric isomers and mixtures thereof which may be separated in conventional manner. Use of optically active starting materials will lead to the corresponding end products. The invention concerns both isomers and mixtures thereof.

The compounds of formula I and their pharmaceutically acceptable acid addition and quaternary salts exhibit interesting biological, in particular chemotherapeutical activity and low toxicity and are therefore indicated for use as medicaments. They display an inhibitory activity against bacteria as determined in tests in vitro with the series dilution test using various bacterial strains e.g. *Staph. aureus*, *Staph. epidermidis*, *Strept. pyogenes*, *Strept. pneumoniae*, *E. coli*, *Klebsiella pneumoniae*, *Haemophilus* spp., *Leptospira* spp., *Erysipelothrix rhusiopathiae* and obligatory anaerobes, e.g. *Bacteroides fragilis* from a concentration of ca. 0.008 to 25 µg/ml. In particular an inhibitory activity was also found against *Mycoplasmas* and *Chlamydia* which exhibits itself from a concentration of ca. 0.008 to 0.5 µg/ml. The chemotherapeutic activity of the compounds was established through tests on mice, using various bacterial strains, and on hens, using mycoplasma strains. This inhibitory activity was observed from a concentration of ca. 12 to 50 mg/kg of body weight. The compounds according to the invention are therefore indicated for use as anti-bacterially active antibiotics.

In addition the above mentioned compounds display an anti-parasitic activity, in particular against coccidia as well as a growth promoting activity. To establish the activity against coccidia testing took place in vivo on the hen. The activities can be confirmed in these animal tests at dosages of 20-150 mg/kg of feed depending upon the period of application. The growth promoting

properties were established in hen and pig in a dosage range of 10-50 mg/kg feed. The compounds of formula I are therefore indicated for use as veterinary agents in particular for the chemotherapeutic treatment of coccidiosis in fowl as well as growth promoters in the animal species mentioned.

The compounds of formula I may be administered orally, locally or parentally. For the preparation of the corresponding compositions for administration the compounds of formula I may be administered in the form of water soluble, physiologically acceptable salts alone or in suitable composition form together with anorganic or organic, pharmaceutically inert additives. They are for example used in the form of components of capsules, injectable and instillable preparations containing an amount of active compounds sufficient to attain an optimal level in blood, such as e.g. ca. 50-500 mg per capsule. The compounds of the invention are further excellent additives for feed mixtures (as premix) or for drink water as well as diluents for artificial insemination and for egg-dipping techniques.

For these applications the dosage to be used varies according to the compound used and the modes of administration and treatment. Satisfactory results are generally obtained for use as anti-bacterially active and antianaerobic antibiotic with a daily dosage of about 10 to 300 mg/kg body weight. For larger mammals satisfactory results are obtained upon administration of a daily dosage of about 1 to 3 g. These amounts may be given two to four times daily in correspondingly smaller amounts or in retard form. The compounds of formula I may be used in free base form or in the form of pharmaceutically acceptable acid addition salts, whereby such salts exhibit the same order of activity as the corresponding free base forms. Examples of suitable acid addition salts are the hydrochloride, the hydrogen fumarate, the fumarate, and the naphthalin-1,5-sulphonate.

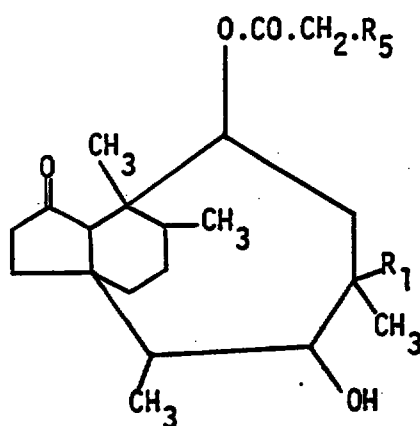
As inert carrier or additives for the preparation of corresponding galenical compositions may be used; sweetening agents,

aromas, dyestuffs, conserving agents, filling or, respectively, carrier agents, e.g. diluents, such as calcium carbonate, sodium carbonate, lactose, polyvinylpyrrolidone, mannitol or talc, granulating and conserving agents such as starch or alginic acid, binding agents such as starch, gelatine or acacia and smoothing agents, such as magnesium stearate, stearic acid or talc.

Compositions for oral administration may contain conventional suspending agents, such as methyl cellulose, tragacanth or sodium alginate. As netting agents are indicated, e.g., lecithin, polyoxyethylene stearate or polyoxyethylene sorbitan monooleate. As conserving agents e.g. ethyl-o-hydroxybenzoate may be used. As diluent for the preparation of capsules e.g. calcium carbonate, calcium phosphate or kaolin may be used as a diluent.

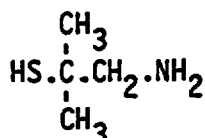
The compounds of formula I may be used in a manner analogous to that for the known standard for these indications, Tiamulin.

The starting materials of formula II are new and may be obtained by reacting a compound of formula IV



IV

wherein R_1 is as defined above and R_5 stands for chlorine, bromine or a $-O.SO_2.R_6$ group, wherein R_6 represents alkyl or aryl, with the compound of formula V



V

This reaction can be carried out for example by dissolving the compound of formula V in a solution of sodium in an anhydrous lower alcohol e.g. in ethanol or methanol. To this solution is then added a solution of a compound of formula IV in a solvent inert under the reaction conditions e.g. in an aliphatic ketone such as ethylmethylketone or acetone. The reaction proceeds preferably at room temperature up to boiling temperature of the reaction mixture, especially 25 to 55°C, and lasts e.g. from 7 to 15 hours.

The starting materials of formula III, IV and V are either known or are preparable analogously to known methods or as described in the Examples, e.g. for compounds V as described in F.J. Carroll, J.D. White and M.E. Wall, J. Org. Chem. 28/1240 (1963).

Alkyl groups appearing as substituents preferably represent lower alkyl groups, especially with 1 to 4 carbon atoms. When R_2 stands for a heterocycle then this may contain one or two heteroatoms, whereby one heteroatom is nitrogen and the optionally present second heteroatom is sulphur.

Protecting groups for the amino function in the starting materials of formula III include those commonly used as amino-protecting groups, for example $-\text{CO.O.CH}_2\text{C}_6\text{H}_5$, $-\text{CO.O.C}(\text{CH}_3)_3$ or $-\text{CO.O.CH}_2\text{CCl}_3$.

Preferred substituent meanings are

R_1 = a) ethyl

b) vinyl

whereby vinyl is especially preferred

R_2 = a) aminoalkyl

b) aminohydroxyalkyl

c) as a) or b) with alkyl having C_{1-6} especially C_{1-4}

d) 5-membered saturated heterocycle

e) 5-membered saturated heterocycle containing one N atom and optionally one S atom.

Combinations of these groups are especially preferred.

A particularly preferred individual compound is 14-O-[1(2-amino-3-methyl-butyrylamino)-2-methyl-propan-2-yl-thioacetyl]-mutilin as free base or hydrochloride, preferably in (D)-Form.

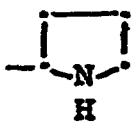
In the following examples which illustrate the invention but in no way limit its scope, references to temperature are in degrees celsius.

EXAMPLE 1 : 14-O-[1-(2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin hydrochloride

A solution of 1.85 g of Z-valin-4-nitrophenylester and 2.35 g of 14-O-[(1-amino-2-methylpropan-2-yl)thioacetyl]-19,20-dihydromutilin in 30 ml of dimethyl formamide is maintained for 7 hours at 25°. The reaction mixture is then poured onto water and repeatedly shaken with ethylacetate. After washing back the organic phase with 0.1 N hydrochloric acid and then with NaCl-saturated water the protected final compound is obtained which can be employed for deprotection without further purification.

A solution of 3.1 g of this Z-protected compound in 150 ml of ethanol is mixed with 60 mg of Pd/active charcoal (palladium on active charcoal, 10%) and stirred under an hydrogen atmosphere for 1 hour. The title compound is obtained in practically quantative yield. The process can also be carried out with BOC-Valin-4-nitro phenylester whereby deprotection is carried out in the following manner: 3mmol of the BOC-protected compound are dissolved at -10° in 25 ml of trifluoroacetic acid and kept at this temperature for 10 minutes. The reaction mixture is then brought to 25°, allowed to react for a further 2 hours and then poured onto 100 ml of 10% NaHCO₃ solution. After repeated extraction with ethylacetate and washing back of the organic phase the crude product is obtained which is chromatographed over silica gel (eluant CHCl₃/CH₃OH=7/1).

The following compounds of formula I may be obtained analogously to Example 1.

Example	R ₁	R ₂
2	-CH=CH ₂	-CH ₂ -NH ₂
3	- " -	-CH-CH ₃ (D) NH ₂
4	- " -	-CH-CH ₂ -CH-CH ₃ NH ₂ CH ₃
5	-C ₂ H ₅	-CH-CH ₃ (D) NH ₂
6	-CH=CH ₂	-CH-CH ₃ (L) NH ₂
7	- " -	 (L)
8	- " -	 (L)
9	-C ₂ H ₅	-CH ₂ CH ₂ -NH ₂
10	-CH=CH ₂	-CH - CH-CH ₃ NH ₂ CH ₃ (L)
11	- " -	 (D)
12	- " -	- CH - CH - CH ₃ NH ₂ CH ₃ (D)
13	- " -	- CH - CH ₂ OH NH ₂ (L)

NMR-Spectra (CDCl₃)

<u>Example</u>	<u>Spectrum</u>
1	5.62 (d, 1H, H ₁₄ , J _{H14H13} = 7,5 Hz); 7.72 (t, 1H, NHCO); 3.42 (d, 1H, N-CH-CO, J = 6,25 Hz); 3.32 (d, 1H, H ₁₁ , J _{H11H10} = 6,25 Hz); AB-System: (V _A = 3.17, V _B = 3.27, J _{AB} = 15 Hz, S-CH ₂ -CO).
2	7.68 (t, 1H, NH); 5.73 (d, 1H, H ₁₄ , J _{H14H13} = 8,75 Hz); 3.75 (s, 2H, CO-CH ₂ -NH ₂); 3.38 (d, 1H, H ₁₁ , J _{H11H10} = 6,25 Hz); 3.28 (m, 2H, ≡C-CH ₂ -NH); 1.25, 1.26 (s, s, 6H, gem. CH ₃).
3	7.78 (t, 1H, NH); 5.74 (d, 1H, H ₁₄ , J _{H14H13} = 8,75 Hz); 4.03 (q, 1H, -CH-CH ₃ , J = 7,5 Hz); 3.37 (d, 1H, H ₁₁ , J _{H11H10} = 6,25 Hz); 1.25 (s, 2xCH ₃ , gem. CH ₃); 3.3 (m, 2H, ≡C-CH ₂ -NH).
4	7.76 (t, 1H, NH); 5.76 (d, 1H, H ₁₄ , J _{H14H13} = 8,75 Hz); $\begin{array}{c} \text{CH}_2 \\ \\ 3.43 \end{array}$ (dd, 1H, CO-CH-NH ₂ , J = 3,75 Hz, J' = 8,75 Hz); 3.25 (d, 2H, CH-CH ₂ -NH ₂); AB-System: (V _A = 3.17, V _B = 3.25, J _{AB} = 15 Hz, -S-CH ₂ CO).
5	5.64 (d, 1H, H ₁₄ , J _{H14H13} = 8,1 Hz); 3.56 (q, 1H, CH ₃ -CH, J = 7,5 Hz); 3.44 (d, 1H, H ₁₁ , J _{H11H10} = 6,25 Hz); AB-System: (V _A = 3.17, V _B = 3.25, J _{AB} = 15 Hz, S-CH ₂ -CO); ABX-System: (V _A = 3.33, V _B = 3.25, V _X = 7.75, J _{AB} = 13,4 Hz, J _{AX} = J _{BX} = 7,5 Hz, C-CH ₂ -NH).
6	7.74 (t, 1H, NH); 5.75 (d, 1H, H ₁₄ , J _{H14H13} = 8,75 Hz); $\begin{array}{c} \text{CH}_3 \\ \\ 3.56 \end{array}$ (q, 1H, CO-CH-NH, J = 7,5 Hz); 3.36 (d, 1H, H ₁₁ ,

$J_{H11H10} = 6,25 \text{ Hz}$; AB-System: ($V_A = 3.17$, $V_B = 3.24$,

$J_{AB} = 15 \text{ Hz}$, S-CH₂-CO); 1.4 (d, 3H, CO-CH-NH₂, $J = 7,5 \text{ Hz}$).

7 7.72 (t, 1H, NH); 5.77 (d, 1H, H₁₄, $J_{H14H13} = 8,75 \text{ Hz}$); AB-System: ($V_A = 4.29$, $V_B = 4.13$, $J_{AB} = 10 \text{ Hz}$, S-CH₂-NH); 3.36 (m, 1H, H₁₁).

8 8.07 (m, 1H, NH); 5.76 (d, 1H, H₁₄, $J_{H14H13} = 8,75 \text{ Hz}$); 3.84 (dd, 1H, CO-CH-NH, $J = 5 \text{ Hz}$, $J' = 8,75 \text{ Hz}$); 3.38 (d, 1H, H₁₁, $J_{H11H10} = 6,25 \text{ Hz}$); AB-System: ($V_A = 3.17$, $V_B = 3.25$, $J_{AB} = 15 \text{ Hz}$, S-CH₂-CO); 3.25 (m, 2H, $\equiv\text{C-CH}_2\text{-NH}$).

9 5.62 (d, 1H, H₁₄, $J_{H14H13} = 7,5 \text{ Hz}$); 3.24 (d, 1H, H₁₁, $J_{H11H10} = 6,25 \text{ Hz}$); ABX-System: ($V_A = 3.34$, $V_B = 3.26$, $V_X = 7.38$, $J_{AB} = 13,5 \text{ Hz}$, $J_{AX} = J_{BX} = 7,5 \text{ Hz}$, NH-CH₂-C $\equiv$); 3.83 (t, 2H, NH₂-CH₂, $J = 5 \text{ Hz}$); 2.38 (t, 2H, CH₂CO, $J = 5 \text{ Hz}$).

10 7.68 (m, 1H, NH); 5.74 (d, 1H, H₁₄, $J_{H14H13} = 8,75 \text{ Hz}$); 3.2 (s, 2H, S-CH₂-CO); 3.38 (m, 1H, H₁₁); 3.25 (d, 1H, CH-CH₃, $J = 3,75 \text{ Hz}$).

11 8.05 (t, 1H, NH, NH-CH₂-C $\equiv$); 5.73 (d, 1H, H₁₄, $J_{H14H13} = 8,75 \text{ Hz}$); 4.48 (dd, 1H, NH-CH-CO, $J = 8,75$, $J' = 6,25$); 1.25, 1.22 (s, s, mixed CH₃); AB System: ($V_A = 3.18$, $V_B = 3.24$, $J_{AB} = 15 \text{ Hz}$, S-CH₂-CO).

12 7.8 (m, 1H, NH); 5.75 (d, 1H, H₁₄, $J_{H14H13} = 8,75 \text{ Hz}$); 3.38 (d, 1H, H₁₁, $J_{H11H10} = 6,25 \text{ Hz}$); 3.24 (d, 1H, CH-NH₂); 3.2 (s, 2H, S-CH₂-CO); 3.31 (m, 2H, CH₂-NHCO).

<u>Example</u>	<u>Spectrum</u>
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13	7.9 (m, 1H, NH); 5.75 (d, 1H, H_{14} , $J_{H_{14}H_{13}} = 8.75$ Hz); AB-System: ($V_A = 3.18$, $V_B = 3.28$, $J_{AB} = 15$ Hz, S-CH ₂ -CO); 3.36 (m, 1H, H_{11}); 3.91 (dd, 1H, -CHH'-OH, $J_1 = 10$ Hz, $J_2 = 5$ Hz); 3.71 (dd, 1H, -CHH'-OH, $J_1 = 10$ Hz, $J_2 = 6.25$ Hz); 3.5 (dd, 1H, NH ₂ -CH-CH ₂ , $J_1 = 6.25$ Hz, $J_2 = 5$ Hz).
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The 14-O-[(1-amino-2-methylpropan-2-yl)thioacetyl]-19,20-dihydro-mutilin required as starting material may be obtained as follows.

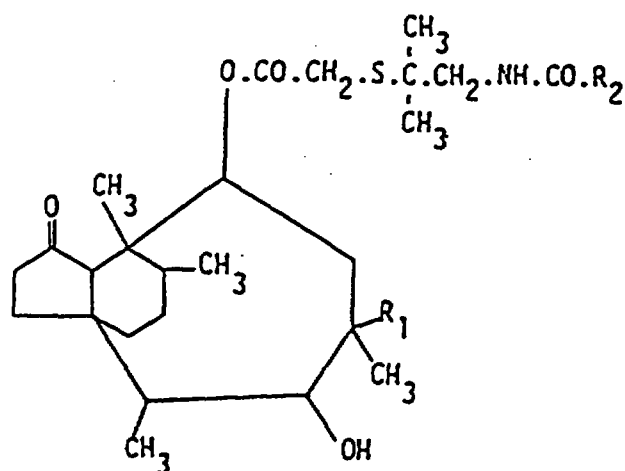
4.6 g of sodium are dissolved in 500 ml of ethanol (absolute), mixed with 14.1 g of 3-amino-2-methyl-2-propyl mercaptane [F.I. Carroll, 5 J.D. White, M.E. Wall, J. Org. Chem. 28, 1240 (1963)] and stirred for one hour at 25°. The reaction mixture is then mixed with a solution of 53.2 g of 19,20-dihydro-pleuromutilin-22-O-tosylate in 300 ml of ethyl-methylketone and maintained at 25° for 15 hours. The result is poured onto ice-water and repeatedly extracted with ethylacetate. After washing 10 back the organic phase with NaCl-saturated water, the crude product is obtained which is chromatographed over silicagel (eluant: CHCl₃/CH₃OH = 7/1).

NMR (CDCl₃): 5.8 (d, 1H, H_{14} , $J_{H_{14}H_{13}} = 9$ Hz); 3.38 (d, 1H, H_{11} , $J_{H_{11}H_{10}} = 6.3$ Hz); 3.17 (s, 2H, S-CH₂-CO); 2.65 (s, 2H, N-CH₂-C≡); 1.7 (b, 2H, NH₂); 1.28 (s, 6H, 2 x CH₃).

Claims for the contracting States BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

1. An N-acyl-14-O-[(1-amino-2-methylpropan-2-yl)thioacetyl]-mutilin or 19,20-dihydromutilin.

2. Pleuromutilin derivatives of formula I



wherein R_1 stands for ethyl or vinyl and
 R_2 stands for an aminoalkyl group the alkyl moiety of
 which can be substituted by hydroxy or for a five-
 membered saturated heterocycle
 and their acid addition or quaternary salts.

3. A compound according to claim 2 wherein

- a) R_1 represents vinyl and R represents a five-membered saturated heterocycle or unsubstituted aminoalkyl and if containing an asymmetric carbon atom is in (D)-Form or
- b) R_1 represents vinyl and R_2 represents aminohydroxyalkyl.



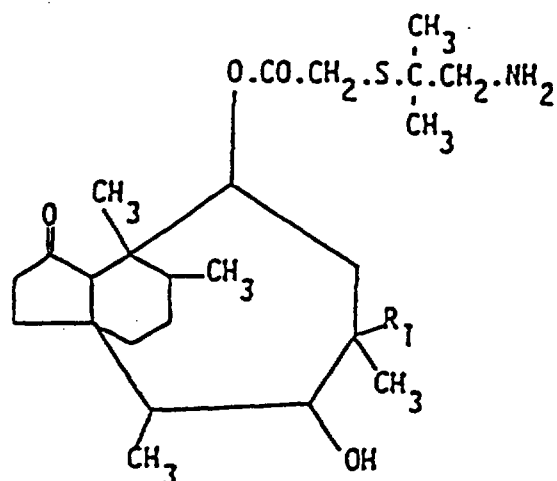
4. A compound selected from 14-0-[1-((D)-2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin, 14-0-[1-(aminoacetyl-amino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((D)-2-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]-mutilin, 14-0-[1-(2-amino-4-methylvaleryl-amino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((D)-2-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin, 14-0-[1-((L)-2-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((L)-thiazolidin-4-yl-carbonylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((L)-pyrrolidin-2-yl-carbonylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-(3-aminopropionyl-amino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin, 14-0-[1-((L)-2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((D)-pyrrolidin-2-yl-carbonylamino)-2-methylpropan-2-yl-thioacetyl]mutilin and 14-0-[1-((L)-2-amino-3-hydroxypropionylamino)-2-methylpropan-2-yl-thioacetyl]mutilin in the form of the free base, the acid addition salts or the quaternary salts.

5. 14-0-[1-((D)-2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]mutilin in the form of the free base, the acid addition salts or the quaternary salts.

6. A chemotherapeutic composition comprising a compound according to one of the claims 1 to 5 in the form of the free base or of a chemotherapeutically acceptable acid addition salt or quaternary salt together with a chemotherapeutically acceptable diluent or carrier or a feed or drinkwater additive composition comprising a compound according to one of the claims 1 to 5 in the form of the free base or of a physiologically acceptable acid addition salt or quaternary salt together with a physiologically acceptable diluent or carrier.

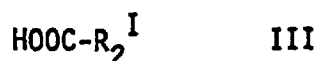


7. A compound according to one of the claims 1 to 5, a) in the form of the free base or of a chemotherapeutically acceptable acid addition salt or quaternary salt, for use as a chemotherapeutic agent or b) in the form of the free base, or of a physiologically acceptable acid addition salt or quaternary salt for use as a veterinary agent.
8. The use of a compound according to one of claims 1 to 5 for preparing agents against bacteria and obligatory anaerobes and for controlling microorganism infections and for promoting growth in domestic animals.
9. A process for preparing N-acyl-14-O[(1-amino-2-methylpropan-2-yl)thioacetyl]mutilin- and -19,20-dihydromutilin derivatives, in particular those of formula I as defined in claim 2, their acid addition salts and quaternary salts, characterised by acylating a compound of formula



II

wherein R_1 stands for ethyl or vinyl in particular with an active ester of the compound of formula

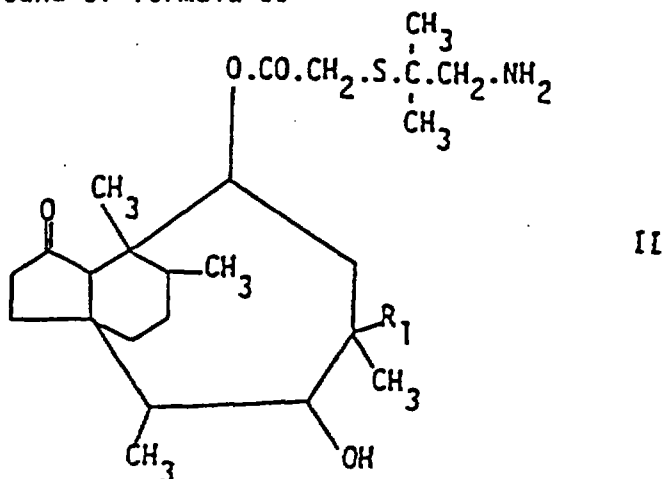


10. A compound of formula II as defined in claim 9.



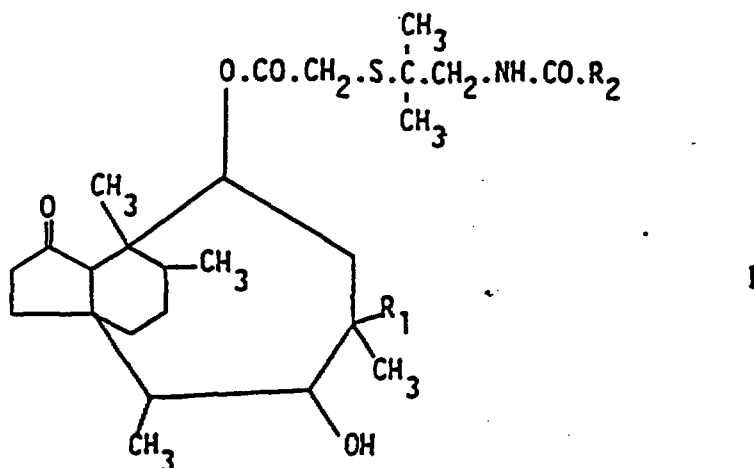
Claims for the contracting State AT

1. Process for preparing N-acyl-14-O-[(1-amino-2-methylpropan-2-yl)thioacetyl]mutilin- and -19,20-dihydromutilin derivatives, their acid addition salts and quaternary salts, characterised by acylating a compound of formula II

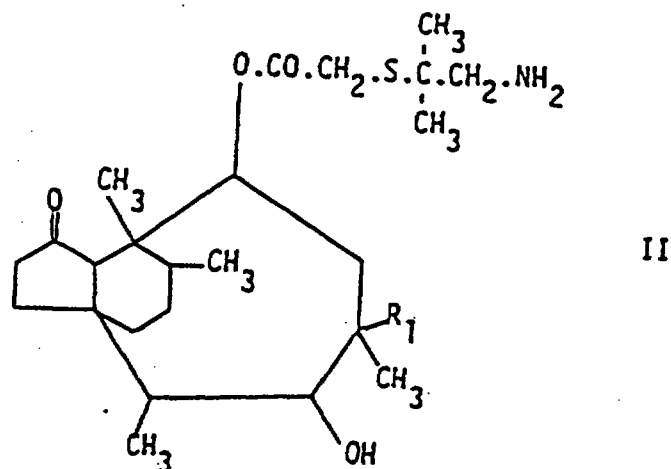


wherein R₁ stands for ethyl or vinyl, and recovering the compounds obtained in free form or in the form of their acid addition or quaternary salts.

2. Process for preparing pleuromutilin derivatives of formula I



wherein R_1 stands for ethyl or vinyl and
 R_2 stands for an aminoalkyl group the alkyl moiety of
 which can be substituted by hydroxy or for a five-
 membered saturated heterocycle
 and their acid addition or quaternary salts characterised by
 acylating a compound of formula II



with an active ester of the compound of formula III



wherein R_2^{I} has the same meaning as R_2 whereby however the amino
 groups contained in R_2 are protected by a protecting group, and
 then splitting off the protecting group and recovering the com-
 pounds obtained in free form or in the form of their acid
 addition salts or quaternary salts.

3. Process according to claim 2 wherein

- a) R_1 represents vinyl and R represents a five-membered saturated
 heterocycle or unsubstituted aminoalkyl and if containing an
 asymmetric carbon atom is in (D)-Form,
- b) R_1 represents vinyl and R_2 represents aminohydroxyalkyl.



4. Process according to claim 2 wherein the compound prepared is selected from 14-0-[1-((D)-2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin, 14-0-[1-(aminoacetyl-amino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((D)-2-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-(2-amino-4-methylvaleryl-amino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((D)-2-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin, 14-0-[1-((L)-2-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((L)-thiazolidin-4-yl-carbonylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((L)-pyrrolidin-2-yl-carbonylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-(3-aminopropionylamino)-2-methylpropan-2-yl-thioacetyl]-19,20-dihydromutilin, 14-0-[1-((L)-2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((D)-pyrrolidin-2-yl-carbonylamino)-2-methylpropan-2-yl-thioacetyl]mutilin, 14-0-[1-((L)-2-amino-3-hydroxypropionylamino)-2-methylpropan-2-yl-thioacetyl]mutilin and 14-0-[1-((D)-2-amino-3-methylbutyrylamino)-2-methylpropan-2-yl-thioacetyl]mutilin in the form of the free base, the acid addition salts or the quaternary salts.

5. A compound selected from

- a) an N-acyl-14-0-[(1-amino-2-methylpropan-2-yl)thioacetyl]-mutilin or -19,20-dihydromutilin.
- b) a compound of formula I whereby the substituents are as defined in claim 2.
- c) a compound of formula I wherein the substituents are as defined in claim 3.
- d) one of the compounds given in claim 4.

6. A compound according to claim 5 in the form of the free base, of an acid addition salt or a quaternary salt.



7. A chemotherapeutic composition comprising a compound according to claim 5 in the form of the free base or of a chemotherapeutically acceptable acid addition salt or quaternary salt together with a chemotherapeutically acceptable diluent or carrier or a feed or drinkwater additive composition comprising a compound according to claim 5, in the form of the free base or of a physiologically acceptable acid addition salt or quaternary salt together with a physiologically acceptable diluent or carrier.

8. A compound according to claim 5, a) in the form of the free base or of a chemotherapeutically acceptable acid addition salt or quaternary salt, for use as a chemotherapeutic agent or b) in the form of the free base or of a physiologically acceptable acid addition salt or quaternary salt for use as a veterinary agent.

9. The use of a compound according to claim 5 for preparing agents against bacteria and obligatory anaerobes and for controlling microorganism infections and for promoting growth in domestic animals.

10. A composition according to claim 7 or the use according to claim 8 or 9 wherein the compounds according to claim 5 are prepared according to claim 1.

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