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THE IDENTIFICATION OF CICLACIDINE

AN ANTIBIOTIC FROM STREPTOMYCES CAPOAMUS SP. NOV.

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In a previous communication (1), the isolation of a red pigment from Streptomyces capoamus sp. nov. which formed on a solid culture and consisted of ciclacidine m.p. 240°, and ciclamicine m.p. 157° was described. Both ciclamicine and ciclacidine show antibiotic activity and anti-tumoral activity on Sarcoma 180 S.

Ciclacidine was purified by crystallization from benzene or chloroform as red crystals m.p. 242°.

The molecular formula, $C_{22}H_{16}O_7$ was based on analytical results. (Found: C,67.35, H, 3,83; calc : C, 67.34, H, 4,11%).

The presence of a quinone group was established by reduction with zinc dust-AcOH and reoxidation by air and supported by UV and IR spectra.

Distillation with zinc dust yields tetracene. therefore an antracycline quinone structure can be attributed to ciclacidine.

The 60 Mc NMR spectrum in trifluoroacetic acid shows a $COO-CH_3$ group (singlet, 3H, δ = 4,35), a CH_2-CH_3 (quartet, J = 7,5 cps, 2H, δ = 2,88; and triplet, J = 7,5 cps, 3H, δ = 1,4). Furthermore five aromatic protons are present: singlet, 1H, δ = 8; quartet, J = 9 cps, 2H, δ = 7,6-8,4; singlet, 2H, δ = 7,24).

The UV spectrum of (I) in cyclohexane shows λ_{max} 252, 275, 482, 492, 503, 516, 526 ($\varepsilon 10^4$ = 6,5; 3,8; 2,3; 2,4; 2,1; 2,4; 2 respectively).

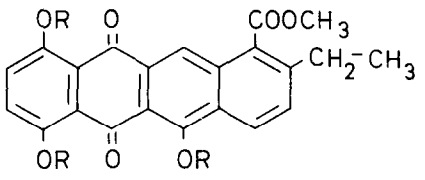
IR spectrum of (I) indicates the presence of chelate OH and CO groups.

The quinone (I) gives with acetic anhydride and anhydrous pyridine (overnight) a triacetyl derivative (II) as yellow crystals from methanol m.p. 212-213°. A $C_{28}H_{22}O_{10}$ formula was calculated from analytical data. (Found: C, 64.80, H, 3.84; calc : C, 64.86, H, 4.28%).

The 60 Mc NMR spectrum of (II) in $CDCl_3$ shows three acetyl groups

(δ = 2,48; δ = 2,53; δ = 2,6); a $COO-CH_3$ group, singlet, 3H, δ = 4,17; a CH_2-CH_3 (quartet, J = 8 cps, 2H, δ = 2,82; triplet, J = 8 cps, 3H, δ =1,3). The UV spectrum of (II) in methanol shows λ_{max} 248, 299, 391, 396, ($\varepsilon 10^4$ = 4,9; 2,8; 6,7; 6,8 respectively).

On the basis of these findings formula (I) is proposed for ciclacidine and formula (II) for the acetyl derivative



(I) R = H

(II) R = $COCH_3$

This structure is identical with that proposed by Ollis et al. (2) for the bisanhydro-rutilantinone, a transformation product obtained by heating rutilantinone (an antracycline quinone from an Actinomyces, strain A 220).

Elementary analysis m.p. IR, UV spectra of (I) and (II) are identical with those of bisanhydro-rutilantinone (3).

From the metabolites of Streptomyces purpurascens studied by Brockmann and Lenk, several antibiotics were isolated. One of these, called η-pyrromicinone (4) was found to be identical with bisanhydro-rutilantinone (5).

Consequently, ciclacidine must be identical with bisanhydro-rutilantinone and η-pyrromicinone, and provide another example of this antibiotic occurring in the metabolites of micro-organisms.

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