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STRUCTURE ELUCIDATION AND SYNTHESIS OF A NEW ANTICOCCIDIAL SUBSTANCE ISOLATED FROM STREPTOMYCES AURANTICOLOR

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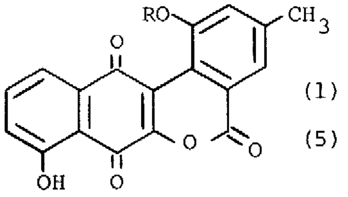
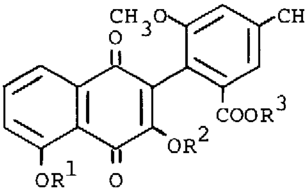
Summary: The structure elucidation and synthesis of WS 5995, produced by Streptomyces auranticolor, were described.

As reported in a previous paper,[1] a new strain of Streptomyces designated Streptomyces auranticolor produced several pigments efficient to coccidial disease (Eimeria tenella) of chickens. In this report, we deal with the structure elucidation and synthesis of one of the pigments, the trivial name of which was WS 5995.

The i.r. spectrum (ν_{max} 1750, 1670 and 1640 cm^{-1}) and u.v. spectrum(λ_{max} 242, 303 and 426 nm) of WS 5995 ($C_{19}H_{12}O_6$, M^+=336) (1) suggested the presence of peri-hydroxy-1,4-naphthoquinone moiety [2] in addition to a lactone group in this molecular. Its n.m.r. spectrum ($NaOD-D_2O$) exhibited the signals at δ 2.38 (3H, s, Me), 3.72 (3H,s, OMe) and 6.80-7.45 (5H,m, aromatic protons).

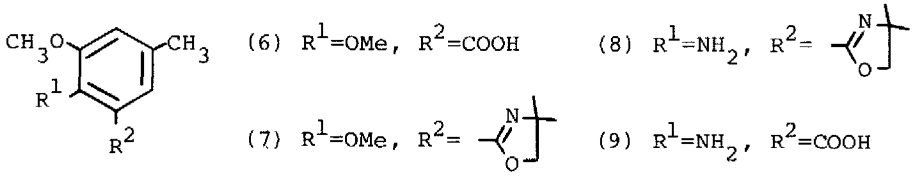


(1) R=Me
(5) R=H



(2) $R^1=R^2=R^3=H$
(3) $R^1=H$, $R^2=R^3=Me$
(4) $R^1=Ac$, $R^2=R^3=Me$

Hydrolysis of 1 with 5% aqueous sodium hydroxide gave a hydroxy-acid (2) which regenerated the parent compound (1) by treatment with trifluoroacetic anhydride. Methylation of 2 with diazomethane gave an ester (3), acetylation of which afforded an acetate (4) in the usual manner. Its n.m.r. spectrum ($CDCl_3$) showed the signals corresponding to five aromatic protons, three of which exhibited an ABC type pattern (δ7.36, 7.72 and 8.08) and signals (δ7.00 and 7.52 each 1H, d, J=1.8 Hz) due to two other protons indicated that the protons were arranged in meta-position each other. Treatment of 1 with boron tribromide resulted in cleavage of a methoxyl group to give a di-phenol (5), which showed no carbonyl band at 1670 cm^{-1} observed in 1. Based on the above results, the structure (1) is most plausible to WS 5995. Confirmation of the structure (1) was provided by the synthesis of 1 indicated as follow.

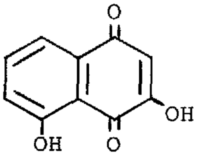


(6) R^1=OMe, R^2=COOH

(7) R^1=OMe, R^2=

(8) $R^1=NH_2$, R^2=

(9) $R^1=NH_2$, R^2=COOH



(10)

The carboxylic acid group of 6[3] was protected as an oxazoline ring in the usual manner.[4] Treatment of the oxazoline (7)[5] with lithium amide in tetrahydrofuran[6] gave an amine (8)[5] in 45% yield. Hydrolysis of 8 with 10% hydrochloric acid furnished the anthranilic acid (9).[5] Coupling of 9 and 3-hydroxy-juglone (10)[7] was accomplished using the corresponding diazonium salt of 9 in aqueous potassium hydroxide solution[8] and led to the hydroxy-acid (2) which was converted to 1 as mentioned above. All the spectral data of the synthetic WS 5995 were also identical with those of WS 5995 from natural sources, confirming the structure of 1.

To our knowledge, WS 5995 (1) is the first naturally occurring compound possessing 5H-benzo[d]naphtho[2,3-b]pyran as mother skeleton.

References and Notes

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