The data further require that the benzamide nucleus of III have the three hydroxyl groups at the 2, 3 and 6 positions with the γ-(β-[4-chloro-7-hydroxy-3-methylphthalide-3])-butyric acid radical at position 4. Position 5 is free for ring closure in the formation of IV.

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RECEIVED SEPTEMBER 15, 1952

DEGRADATION OF AUREOMYCIN. V. AUREOMYCINIC ACID

Sir:

When aureomycin is treated with 5 *N* sodium hydroxide containing a reducing agent, α- or β-aureomycinic acid, I, is formed. With sodium hydrosulfite and a reaction time of 2.5 hours at room temperature α-aureomycinic acid, m.p. 225–230° for the hydrochloride, $[\alpha]^{25}D$ +54° (dilute hydrochloric acid), *anal.* Calcd. for $C_{22}H_{25}N_2ClO_9 \cdot HCl$: C, 49.53; H, 4.88; N, 5.25; Cl, 13.32; C-CH_3, 2.82. Found: C, 49.38; H, 5.20; N, 5.34; Cl, 13.58; C-CH_3, 2.54, is obtained. If the reaction time is increased to four days, β-aureomycinic acid, m.p. 174–185° (dec.) for the hydrochloride, $[\alpha]^{25}D$ −10.2° (dilute hydrochloric acid), *anal.* Calcd. as for the α-isomer. Found: C, 49.60; H, 5.62; N, 5.23; Cl, 13.35, is isolated. The β-isomer also results if zinc dust is used in lieu of hydrosulfite and the reaction mixture is heated for two hours on the steam-bath.

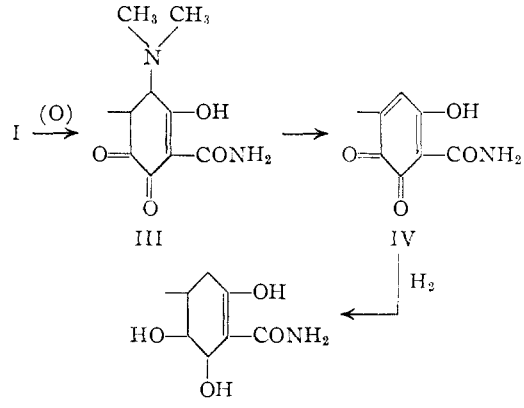
A free carboxyl group in I is indicated by the facile formation of a monoester, *anal.* Calcd. for $C_{21}H_{24}N_2ClO_7COOCH_3 \cdot HCl$: OCH_3, 5.66. Found: OCH_3, 5.11, with methanolic hydrogen chloride. The preparation of the monomethyl ester monomethyl ether, II, of I with diazomethane or methsulfate and sodium carbonate and the subsequent oxidation of II to the half ester of β-(4-chloro-7-methoxy-3-methylphthalide-3)-glutaric acid confirms the presence of a carboxyl group in I.

The lactone band at 5.7 μ in the infrared spectra of I establishes the presence of the phthalide nucleus. Similarly, the ultraviolet absorption spectra of I and II clearly show the presence of a phthalide moiety.

The titration curve of I, in addition to showing the acid functions due to the carboxyl and 7-hydroxyphthalide, demonstrates the presence of an acid function of *pKa* 7.2.

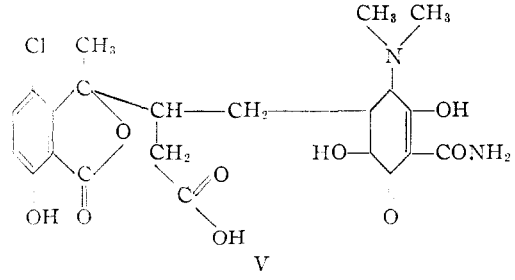
Subtraction of the ultraviolet absorption spectra of β-(4-chloro-7-methoxy-3-methylphthalide-3)-glutaric acid from those of I, gives spectra with absorption maxima at 282 mμ (E 15,500) in 0.1 *N* sodium hydroxide and at 267 mμ (E 15,400) in 0.1 *N* hydrochloric acid. The spectra of this added chromophore compares favorably with those of dimedone which has maxima at 282 mμ (E 23,700) in 0.1 *N* sodium hydroxide and at 260 mμ (E 14,000) in 0.1 *N* hydrochloric acid, except the extinction coefficient of dimedone in alkali is greater. The molecular extinction coefficient in alkaline solution is decreased when a carboxamide group is located on the central carbon of a β-diketone system.[1] The presence of this added chromophore and the acidic function at *pKa* 7.2 suggests that an isolated cyclic β-diketone is present in I. The infrared bands in the 6 to 7 μ region substantiate this conclusion.

When aureomycinic acid, I, is further treated with 5 *N* sodium hydroxide (in the absence of reducing agents), dimethylamine and desdimethylaureomycinic acid is formed. This elimination of dimethylamine with the introduction of a double bond readily explains the formation of the aromatic group, 2,3,6-trihydroxybenzamide, of desdimethylaminoaureomycinic acid.[2] The placing of dimethylamine in the 5 position of the cyclohexanedione ring makes possible the β-elimination of this group when a trace of oxygen forms the α-diketone, III, from I.



The final step in the reaction shows the *o*-quinone, IV, acting as a hydrogen acceptor for the oxidation of another molecule of I. If more than a trace of oxygen is present, further changes are initiated.

The formulation of the structure of aureomycinic acid as V is consistent with the chemical and physical data.



V

Aureomycinic Acid

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RECEIVED SEPTEMBER 5, 1952

(1) For comparison of 1,3-cyclopentanedione with that of 3,4-dihydroxy-2,5-dioxocyclopentane-1-carboxamide see C. W. Waller, B. L. Hutchings, C. F. Wolf, R. W. Broschard, A. A. Goldman and J. H. Williams, THIS JOURNAL, **74**, 4978 (1952).

(2) C. W. Waller, B. L. Hutchings, A. A. Goldman, C. F. Wolf, R. W. Broschard and J. H. Williams, *ibid.*, **74**, 4979 (1952).