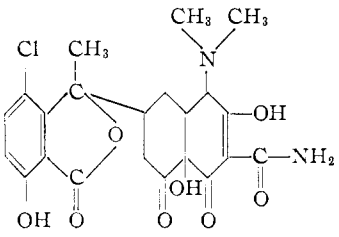
DEGRADATION OF AUREOMYCIN. VI. ISOAUREOMYCIN AND AUREOMYCIN

Sir:

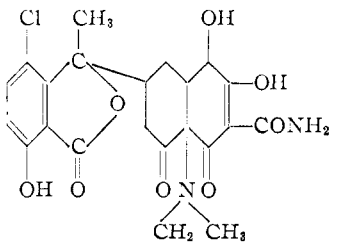
When aureomycin is dissolved in dilute alkali and allowed to stand for twenty-four hours at room temperature, isoaureomycin, I, m.p. 195–197°, and 248–250° as the hydrochloride,[1] $[\alpha]^{25}D$ −94° (dilute hydrochloric acid), *anal.* Calcd. for $C_{22}H_{23}NClO_8 \cdot HCl$: C, 51.26; H, 4.66; N, 5.44; Cl, 13.79. Found: C, 51.29; H, 4.91; N, 5.29; Cl, 13.88, is formed.

The infrared and ultraviolet absorption spectra of I establishes the presence of the phthalide nucleus. Alkaline hydrolysis[2] indicates the presence of the carboxamide grouping. The two acid functions of I have *pKa* values of 6.8 and 8.1, respectively. The latter value is due to the 7-hydroxyphthalide. When the ultraviolet absorption spectra of the phthalide nucleus are subtracted from the spectra of I, a chromophore similar to that in aureomycinic acid[3] is found to be present. The diketone bands in the 6–7 μ region of the infrared spectra again substantiates the conclusions from the *pKa* and ultraviolet data that a cyclic β-diketone structure exists in I. In addition, an absorption band at 5.80–5.85 μ is present. The absorption in this region is typical of a non-conjugated ketone of a cyclohexanone.[4]

When isoaureomycin subsequently reacts with 5 *N* sodium hydroxide in the presence of sodium hydrosulfite, α-aureomycinic acid is formed. This reaction involves a ketonic hydrolysis and causes the formation of a carboxyl group from the non-conjugated β-diketone of I. Since the central carbon atom of the hydrolyzed β-diketone is completely substituted, isoaureomycin has structures II or III.



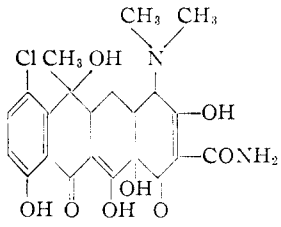
II



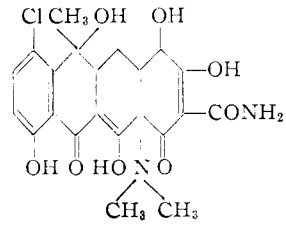
III

The infrared absorption spectrum of aureomycin[5,6] showed no absorption bands between 5 and 6 μ which not only eliminates the presence of a phthalide structure but also excludes the presence of a non-conjugated ketonic group. The formation of isoaureomycin involves the alkaline cleavage of a carbon to carbon bond of an enolizable β-diketone to form a carboxyl group which subsequently lactonizes to give a phthalide. The remaining ketonic group of the original β-diketone is now not capable of forming a conjugated system.

Since there are only two possible structures for isoaureomycin, aureomycin must have structure IV or V.



IV



V

(1) The compound reported by A. C. Dornbush, J. J. Oleson, A. L. Whitehill and B. L. Hutchings, *Proc. Soc. Exptl. Biol. Med.*, **76**, 676 (1951), when dried over boiling toluene lost water of hydration.

(2) S. Olesen, *Die Chemie*, **56**, 202 (1943).

(3) B. L. Hutchings, C. W. Waller, R. W. Broschard, C. F. Wolf, P. W. Fryth and J. H. Williams, THIS JOURNAL, **74**, 4980 (1952).

(4) Cyclopentanones absorb from 5.70–5.75 μ.

(5) B. M. Duggar, U. S. Patent 2,482,055 (1949).

(6) Analytical data obtained subsequent to the preliminary values reported by R. W. Broschard, *et al.*, *Science*, **109**, 2826 (1949), are: *Anal.* Calcd. for $C_{22}H_{23}N_2ClO_8 \cdot HCl$: C, 51.26; H, 4.66; N, 5.44; Cl, 13.79. Found: C, 51.12; H, 4.75; N, 5.39; Cl, 13.75.

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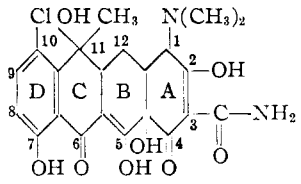
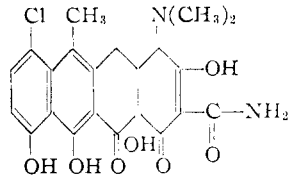
DEGRADATION OF AUREOMYCIN. VII.[1] AUREOMYCIN AND ANHYDROAUREOMYCIN

Sir:

The existence of a naphthacene nucleus in Aureomycin I has been postulated.[2]



Aureomycin I



Anhydroaureomycin II

Substituents and the nature of rings D and A have been rigorously established with the one exception the 1-dimethylamino and the 4a-hydroxyl groups may be reversed (the acidity of I would not allow the dimethylamino group to be on carbon 2 or 4).

Ring C of aureomycin is further established by dehydration and aromatization. In concentrated hydrochloric acid at 60° for thirty minutes I is converted in excellent yields to anhydroaureo-

(1) The data in this series of papers was presented at the Medicinal Section of the Gordon Research Conferences, New London, N. H., on August 20, 1952.

(2) (VI) C. W. Waller, B. L. Hutchings, C. F. Wolf, A. A. Goldman, R. W. Broschard, and J. H. Williams, THIS JOURNAL, **74**, 4981 (1952).