An ionic atmosphere of tetramethylammonium bromide decreases the rate of hydrolysis in both acidic and basic solutions. Thus, at 90° the tripoly-to-pyro rate constant in hr.$^{-1}$ decreases from 0.46 to 0.37 at *p*H 4 and from 0.0172 to 0.0158 at *p*H 10 on adding ten per cent. of tetramethylammonium bromide to the tetramethylammonium tripolyphosphate solution. This is added proof that the hydrolyses of pyro- and tripolyphosphates are not catalyzed by hydroxyl ions.

As would be expected from complex formation, it was found that substitution of tetramethylammonium ion by sodium ion increases the rate of hydrolysis, and this increase is intensified by the presence of excess sodium. For example, at 90° and *p*H 7 the tripoly-to-pyro constants in hr.$^{-1}$ are, for sodium ion, 0.192 and 0.152, and, for tetramethylammonium ion, 0.108 and 0.147, with the first number in each group corresponding to the presence of 0.6 *N* bromide of the respective cation and the second to a pure solution without swamping electrolyte.

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RECEIVED JULY 31, 1952

DEGRADATION OF AUREOMYCIN. III. 3,4-DIHYDROXY-2,5-DIOXOCYCLOPENTANE-1-CARBOXAMIDE

Sir:

The isolation and identification of dimethylamine and β-(4-chloro-7-hydroxy-3-methylphthalide-3)-glutaric acid as degradation products of aureomycin have been outlined.[1] Reported herein is the isolation and characterization of a $C_6H_7NO_5$ compound, I.

These degradation products thus account for the carbon, chlorine and nitrogen of the original molecule.

When aureomycin is treated with 5 *N* sodium hydroxide, desdimethylaminoaureomycinic acid, m.p. 210–212°, *anal.* Calcd. for $C_{20}H_{18}NClO_9$: C, 53.26; H, 4.04; N, 3.15; Cl, 7.86. Found: C, 52.83; H, 4.32; N, 2.99; Cl, 7.59, and dimethylamine are formed. The former compound is an optically active ($[\alpha]^{25}D$ + 100° (in methanol)), tribasic, monocarboxylic acid with *pKa*'s of 6.4, 7.8 and 10.2.

On air (or oxygen) oxidation in *N* sodium hydroxide desdimethylaminoaureomycinic acid cleaves to yield β-(4-chloro-7-hydroxy-3-methylphthalide-3)-glutaric acid and a $C_6H_7NO_5$ monobasic acid, I, (*pKa* 2.65) m.p. 198–200° (dec.), *anal.* Calcd. for $C_6H_7NO_5$: C, 41.63; H, 4.05; N, 8.09. Found: C, 41.78; H, 4.19; N, 8.26. The bulk of the C_6 acid is isolated as a *dl* compound but the residual crops have a specific rotation of −65°. The product forms ketonic derivatives, crystalline basic salts, a triacetate (isolated as a pyridine or sodium salt), but no carboxylic acid derivatives. The compound exhibits an ultraviolet absorption spectra characteristic of a cyclic β-diketone with maxima at 252 mμ (*E* 22,500) in 0.1 *N* sodium hydroxide and at 247 mμ (*E* 17,200) in 0.1 *N* hydrochloric acid.

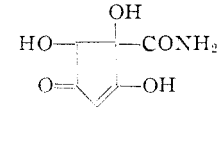
On refluxing I with hydriodic acid and red phosphorus a mole of ammonia and carbon dioxide is evolved, and a $C_5H_6O_2$ monobasic acid, II (*pKa* 4.5), m.p. 151–152° is isolated, *anal.* Calcd. for $C_5H_6O_2$: C, 61.22; H, 6.12. Found: C, 61.33; H, 6.56. This latter product was identified as 1,3-cyclopentanedione by oxidation to succinic acid and by a positive iodoform reaction. The compound has a characteristic ultraviolet absorption spectrum with maxima at 257 mμ (*E* 29,400) in 0.1 *N* sodium hydroxide and 242 mμ (*E* 20,700) in 0.1 *N* hydrochloric acid.

When I is heated in 48% hydrobromic acid, a mole of ammonia and carbon dioxide is evolved and a $C_5H_4O_3$ monobasic acid, III (*pKa* 3.0), m.p. 172.5–173° (dec.) is formed, *anal.* Calcd. for $C_5H_4O_3$: C, 53.6; H, 3.57. Found: C, 53.56, H, 3.90. The ultraviolet absorption spectra are characterized by maxima at 310 mμ (*E* 13,450) in 0.1 *N* sodium hydroxide and at 267 mμ (*E* 10,850) in 0.1 *N* hydrochloric acid. The compound was identified as 1,2,4-cyclopentanetrione by a positive iodoform reaction and by formation of an *o*-phenylenediamine derivative. Reduction of III with zinc and hydrochloric acid gives 4-hydroxy-1,3-cyclopentanedione, IV. This product and III can be converted to 1,3-cyclopentanedione by treatment with hydriodic acid and phosphorus. The synthesis[2] of II and III unequivocally proved their assigned structures.

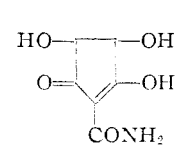
When the pyridine salt of the triacetate of I is refluxed with acetic anhydride, a descarboxamido triacetate, $C_5H_3O(OCOCH_3)_3$, V, is formed. The acetyl groups are removed by dilute acid hydrolysis to yield a monobasic acid, $C_5H_6O_4$, VI, m.p. 153–154°, *anal.* Calcd. for $C_5H_6O_4$: C, 46.2; H, 4.62. Found: C, 46.77; H, 4.84, positive iodoform reaction. This acid is also obtained from barium hydroxide hydrolysates of I. On refluxing V or VI with hydrobromic acid or hydriodic acid and phosphorus III and II are formed, respectively.

The ultraviolet and infrared spectra and the chemical characteristics of the $C_5H_6O_4$ compound (VI) are consistent with its formulation as 4,5-dihydroxy-1,3-cyclopentanedione.

Structures VII or VIII are therefore possible for the $C_6H_7NO_5$ compound.



VII



VIII

The inability to condense I with aldehydes and the marked stability of I to alkaline hydrolysis[3] es-

(1) B. L. Hutchings, C. W. Waller, S. Gordon, R. W. Broschard, C. F. Wolf, A. A. Goldman, and J. H. Williams, THIS JOURNAL, **74**, 3710 (1952).

(2) J. H. Boothe, R. G. Wilkinson, S. Kushner and J. H. Williams, to be published.

(3) The stability of I is analogous to the stability of C-acetyl dimedone to alkaline cleavage, A. J. Birch, *J. Chem. Soc.* 3026 (1951).

tablishes the structure of I as 3,4-dihydroxy-2,5-dioxocyclopentane-1-carboxamide (VIII).

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RECEIVED SEPTEMBER 15, 1952

DEGRADATION OF AUREOMYCIN. IV. DESDIMETHYLAMINOAUREOMYCINIC ACID

Sir:

The formation of β-(4-chloro-7-hydroxy-3-methylphthalide-3)-glutaric acid, I, and 3,4-dihydroxy-2,5-dioxocyclopentane-1-carboxamide, II, from desdimethylaminoaureomycinic acid, III, has been described.[1] In this "Communication" sufficient additional chemical data are presented for the structural formulation of III.

Desdimethylaminoaureomycinic acid, III, contains a phthalide nucleus as shown by the lactone band in the infrared spectra at 5.7 μ and by its ultraviolet absorption spectra before and after methylation. The presence of a free carboxyl group is apparent from the formation of the half ester of I on methylation and oxidation of III. A carboxamide grouping is shown by the formation of ammonia and carbon dioxide on hydrolysis of III with 1 *N* sodium hydroxide in ethylene glycol.[2] Furthermore, the ready elimination of carbon dioxide indicates this position to be activated.

The *pKa*'s of 6.4, 7.8 and 10.2 of III allows for the assignment of the carboxylic acid and the 7-hydroxyl of the phthalide to the *pKa*'s of 6.4 and 7.8, respectively, while the 10.2 value might be a polyhydroxylated benzene ring. The acidity of II (*pKa* 2.65) definitely excludes this structure in III.

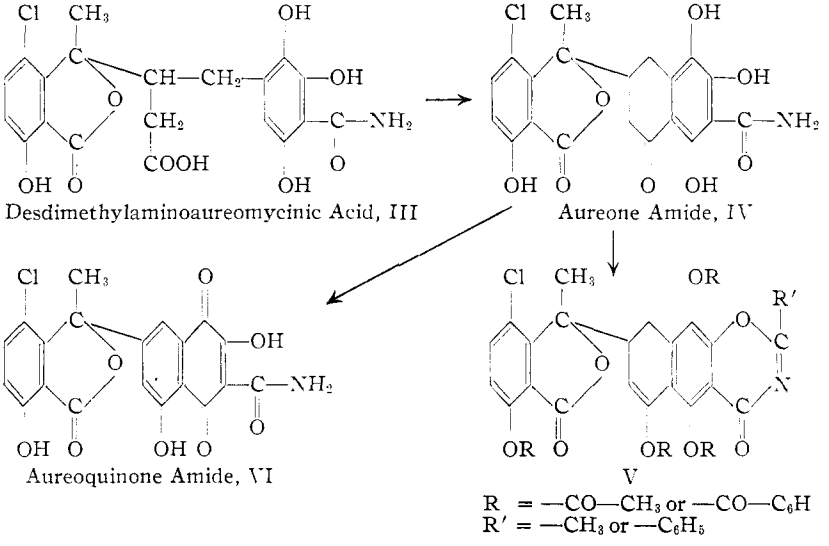
The subtraction of the ultraviolet absorption spectra of I from the spectra of III gives a remaining chromophore comparable to that of a 2,6-dihydroxybenzoic acid (dihydrocitrinin). Thus, the structure of I must contain a 2,6-dihydroxybenzamide further substituted with a hydroxyl group and with the γ-(β-[4-chloro-7-hydroxy-3-methylphthalide-3])-butyric acid radical.

When III is dehydrated with heat or sulfuric acid, aureone amide, IV, m.p. 295–305° (dec.), $[\alpha]^{25}D$ +24.6° (methyl cellosolve), *anal.* Calcd. for $C_{20}H_{16}NClO_8$: C, 55.35; H, 3.71; N, 3.25; Cl, 8.17; C—CH_3, 3.43. Found: C, 55.31; H, 4.11; N, 3.18; Cl, 7.97; C—CH_3, 3.41, is obtained. Acetylation or benzoylation of IV results in penta acylation with the loss of the elements of water. This acylation allows for the presence of three hydroxyl groups, an enolizable ketone and oxazine formation between one hydroxyl and the carboxamide group (Structure V). The presence of the ketonic group is also established by the formation of a 2,4-dinitrophenylhydrazone. Furthermore, the spectra of IV show this ketone to be conjugated with an existing chromophore.

Methylation of IV yields a methyl ether in the 7 position of the phthalide. This methylated compound (and IV) forms a stable crystalline diborate complex indicating the presence of two pairs of adjacent hydroxyl groups (or *peri* positions of a naphthalene type) in the non-phthalide portion of the molecule.

On air oxidation in 5*N* sodium hydroxide aureone amide is aromatized to aureoquinone amide, VI, m.p. 142–148°, *anal.* Calcd. for $C_{20}H_{12}NClO_8$: C, 55.81; H, 2.79; N, 3.26; Cl, 8.25. Found: C, 55.31; H, 3.15; N, 3.02; Cl, 8.15. The ultraviolet absorption spectra and *pKa* values of VI identify the compound as a 2-hydroxy-1,4-naphthoquinone.

Aureone amide on hydrolysis[2] yields aureone, VII, m.p. 296–300 (dec.), $[\alpha]^{25}D$ +19° (in ethanol), *anal.* Calcd. for $C_{19}H_{15}ClO_7$: C, 58.39; H 3.84; Cl, 9.09. Found: C, 58.16; H, 4.08; Cl, 9.04. Spectra studies and the formation of a mono 2,4-dinitrophenylhydrazone of aureone establish the presence of a ketonic group. Reduction of this ketone gives a product which has the same ultraviolet absorption spectra as a composite sample of I and 1,2,4-trihydroxybenzene.



The data allow the exact assignment of structure to III, IV and VI. The arrangement of the hydroxyl groups in the terminal benzene ring are in the 1,2,4-positions as shown by the spectra of reduced aureone and by the formation of a 2-hydroxy-1,4-naphthoquinone. The identification of II and the spectral characteristics of III and VI places the carboxamide at the 3 position. The cyclization of III to IV and the formation of a diborate complex of the ether of IV requires the arrangement in the dihydronaphthalene system of IV to be a 1,2,4,5-tetrahydroxy-7,8-dihydronaphthalene-3-carboxamide.

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