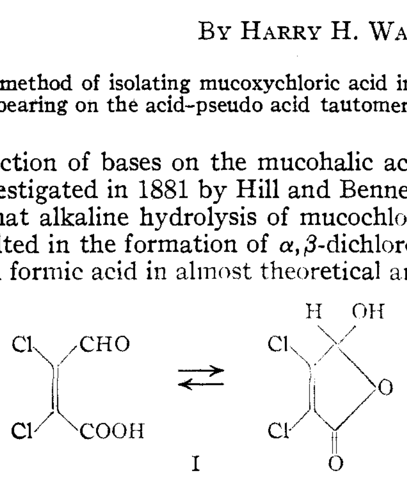
[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

Studies on the Mucohalic Acids. I. The Structure of Mucoxychloric Acid[1]

BY HARRY H. WASSERMAN AND FRANK M. PRECOPIO[2]

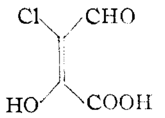
A new method of isolating mucoxychloric acid in good yield is described. Infrared and ultraviolet absorption spectral evidence bearing on the acid-pseudo acid tautomerism of this compound is presented.

The action of bases on the mucohalic acids was first investigated in 1881 by Hill and Bennett[3] who found that alkaline hydrolysis of mucochloric acid (I) resulted in the formation of α,β-dichloroacrylic acid and formic acid in almost theoretical amounts.


I

Some years later, Hill and Palmer[4] reported that the careful addition of barium hydroxide to mucochloric acid in the cold resulted in the formation of the barium salt of a dibasic acid, which they named mucoxychloric acid. In order to isolate the free acid, the barium salt was decomposed with the calculated amount of dilute sulfuric acid and the aqueous solution evaporated in a vacuum desiccator over sulfuric acid. The crude acid thus obtained was recrystallized from warm water with considerable accompanying decomposition.

The main structural features of mucoxychloric acid were established by Hill and Palmer[4] who showed that its composition, $C_4H_3O_4Cl$, and chemical properties corresponded to the aldehyde-acid, structure (II) or (III), formed by the hydrolysis of the halogen alpha to the carboxyl group of mucochloric acid.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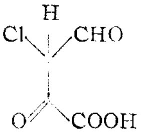
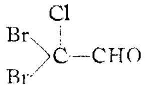

III

The assumption that this particular chlorine atom was replaced by hydroxyl in the above hydrolysis was based on the reaction of mucoxychloric acid with aqueous bromine to form monochlorobromal (IV). Hill[4] offered no conclusive evidence to distinguish between the two possibilities (II) and (III), although, he preferred the enol form (II). The possibility of keto-lactol type tautomerism was not considered.



$$Br_2CCl{-}CHO$$

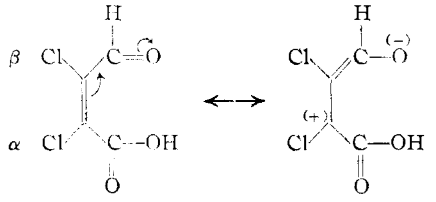
IV

In connection with a synthesis described elsewhere,[5] we had occasion to prepare mucoxychloric acid, and are reporting here an improved isolation procedure and evidence bearing on the acid-pseudo acid tautomerism of this compound.

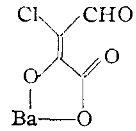
It was found, as previously reported by Hill, that mucoxychloric acid was very unstable and required great care in its preparation. When the crude material was purified by recrystallization from warm water, extensive decomposition took place, and little or no product could be obtained. A much milder method of regenerating the acid from the stable barium salt was therefore employed in this work.

After treatment of the salt with the calculated amount of sulfuric acid at zero degrees, the filtered solution was frozen by cooling in a Dry Ice–acetone mixture and the water removed in a freeze-dryer, the design of which was similar to that recently described by Holzman.[6] This procedure gave excellent yields (90%) of crude acid, m.p. 97–100°, which, after recrystallization from ether, melted at 110–111°. Although the pure dry acid is stable in the cold, it decomposes slowly on standing at room temperature and discolors rapidly when exposed to moisture.

In view of Hill's evidence on the bromination of mucoxychloric acid, it seems clear that the halogen alpha to the carboxyl group in mucochloric acid had been replaced in the hydrolysis reaction. The preferential attack of base at this position is in accord with the enhanced activation, in the open aldehyde-acid tautomer, of the chlorine atom which can take part in vinylogous acid chloride interaction with the aldehyde carbonyl.



There would be less corresponding activation of the halogen atom beta to the carboxyl group. While at the time, Hill could not account for the dibasic nature of mucoxychloric acid, it is clear that the alpha hydroxyl group of mucoxychloric acid is part of a vinylogous acid system, and the structure of the barium salt should be written as (V).


V

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[1] From a dissertation submitted to the Faculty of the Graduate School of Yale University in partial fulfillment of the requirements for the Ph.D. degree by Frank M. Precopio, 1951.

[2] du Pont Fellow in Chemistry, 1950–1951.

[3] H. B. Hill and W. Z. Bennett, *Proc. Am. Acad. Arts Sci.*, **16**, 206 (1881).

[4] H. B. Hill and A. W. Palmer, *Am. Chem. J.*, **9**, 147 (1887); *Proc. Am. Acad. Arts Sci.*, **22**, 327 (1887).

[5] H. H. Wasserman and F. M. Precopio, "Synthesis of γ-Lactam-Thiazolidines Related to Penicillin," in publication.

[6] G. Holzman, *Science*, **3**, 550 (1950).

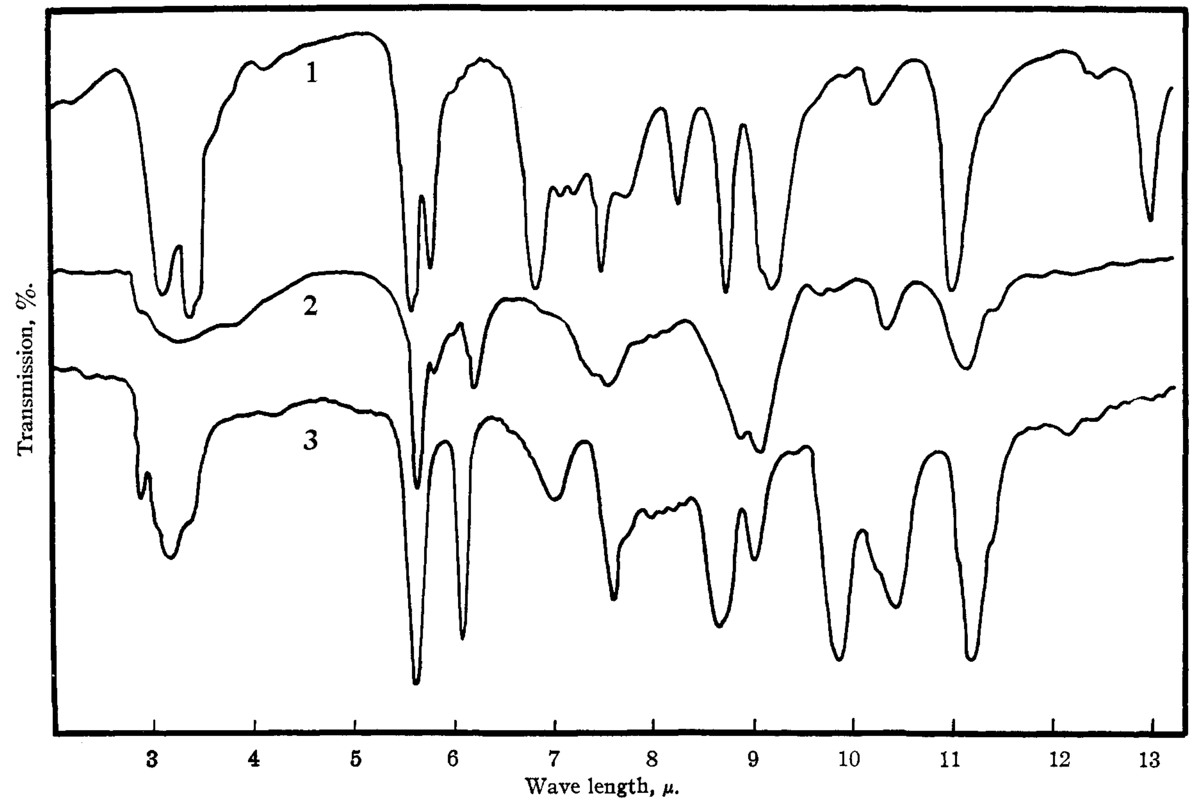
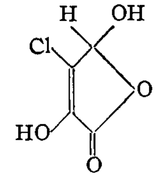
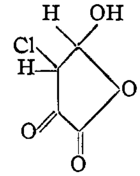


Fig. 1.—Infrared absorption spectra: (1) mucoxychloric acid in a nujol mull; (2) mucoxychloric acid in chloroform; (3) mucochloric acid in chloroform.

As has been shown in the case of other β-formylacrylic acids,[7–10] interaction of aldehyde and carboxyl groups can lead to cyclic hemiacetal-lactone structures existing in equilibrium with the open aldehyde–acids. Such interaction in the case of mucoxychloric acid would lead to cyclic pseudo acid structures (VI) and (VII).



VI



VII

These pseudo acids can be considered to exist in equilibrium with the open aldehyde–acids (II, III) and can react in either form depending on the reaction conditions involved. For example, mucochloric acid reacts with aldehyde reagents,[11–14] but reacts in the pseudo acid form with acetyl chloride,[15] acetic anhydride[7] and in the Friedel–Crafts reaction with aluminum chloride and benzene.[16]

We have, for some time,[17] been investigating the tautomerism between the open and closed forms of aldehyde-acids in the mucochloric and mucobromic acid series, utilizing the characteristic infrared spectra of the carbonyl groups involved as a means of distinguishing between the two possible structural arrangements. This method of determining whether the open or closed form predominates in the solid or in solution has recently been applied in the case of penicillic acid[18,19] and to several aldehydo and keto-acids by Grove and Willis.[10]

Infrared analyses of mucoxychloric acid in the solid state and in chloroform solution indicate that under both conditions the hemiacetal-lactone form predominates (Fig. 1). In each case a sharp band appears in the lactone region at 5.61 to 5.65 μ. The same band appears in mucochloric acid (Fig. 1), indicating a predominance of the lactone structure in chloroform solution, as has been proposed by Mowry[7] who investigated the ultraviolet absorption spectra of mucochloric acid and its esters. There appears to be a difference between the structure of mucoxychloric acid in the solid state and in solution. The solid acid shows a band at 5.82 μ characteristic of the keto group, and there is a notable absence of absorption in the carbon–carbon double bond region at 6.0–6.2 μ. This is in accord with the keto-lactol structure (VII). The solution spectrum, on the other hand, shows only slight absorption in the ketone region at 5.82 μ, but does have a strong band at 6.23 μ characteristic of conjugated carbon–carbon double bonds. The above absorption indicates a

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(7) D. T. Mowry, THIS JOURNAL, **72**, 2535 (1950).

(8) M. M. Shemyakin, *J. Gen. Chem.* (*U. S. S. R.*), **13**, 290 (1943).

(9) E. Z. Vinogradava and M. M. Shemyakin, *ibid.*, **16**, 709 (1946).

(10) J. F. Grove and H. A. Willis, *J. Chem. Soc.*, 877 (1951).

(11) H. Simonis, *Ber.*, **34**, 509 (1901).

(12) H. B. Hill and R. W. Cornelison, *Am. Chem. J.*, **16**, 277 (1895).

(13) A. Bistrzycki and C. Herbst, *Ber.*, **34**, 1010 (1901).

(14) A. Stadler, Inaug. Diss. Berlin, 1903.

(15) O. R. Jackson and H. B. Hill, *Ber.*, **11**, 289, 1671 (1878).

(16) H. B. Hill and F. L. Dunlap, *Am. Chem. J.*, **19**, 642 (1898).

(17) H. H. Wasserman, Doctoral Dissertation, Harvard Univ., 1948; H. H. Wasserman and F. M. Precopio, unpublished work.

(18) C. W. Munday, *Nature*, **163**, 443 (1949).

(19) J. H. Ford, A. R. Johnson and J. W. Hinman, THIS JOURNAL, **72**, 4529 (1950).

predominance of the enolized lactone form (VI) in chloroform solution with but a small contribution from the ketonic tautomer (VII).

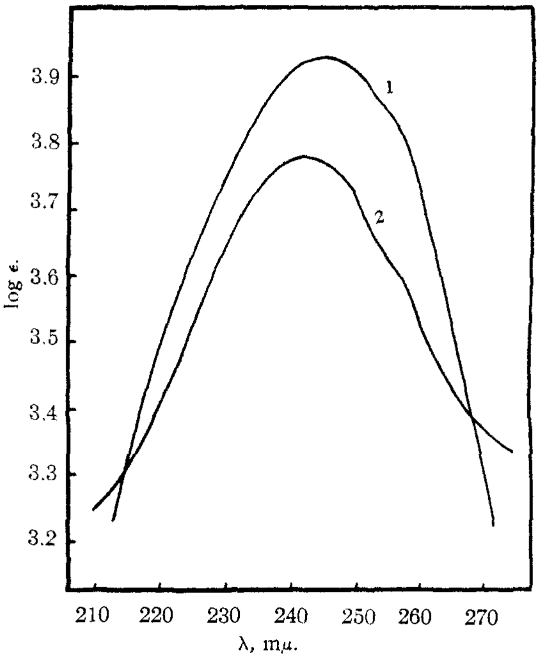
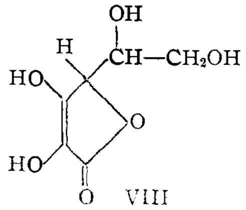


Fig. 2.—Ultraviolet absorption spectra in absolute ethanol: 1. ascorbic acid; 2. mucoxychloric acid.

Further evidence substantiating the assignment of an enolic hemiacetal-lactone structure to mucoxychloric acid in solution is found in ultraviolet absorption studies. The observed absorption at $\lambda_{\max.}$ 243 mμ, log ϵ = 3.75 is indicative of the presence of an α,β-unsaturated carbonyl and is therefore consistent with structure (VI). It is interesting to compare the absorption of this acid with that of the similarly constituted ascorbic acid (VIII) (Fig. 2) which absorbs at $\lambda_{\max.}$ 245 mμ, log ϵ = 3.93 in absolute ethanol. (The reported absorption maximum[20–24] for ascorbic acid is $\lambda_{\max.}$ 240–245 mμ, log ϵ = 4.0.)



VIII

Experimental[25]

Barium Mucoxychlorate.—The preparation of the barium salt was carried out according to the general method outlined by Hill and Palmer.[4] The following description represents the conditions which were found to give the best consistent results in the present work.

A suspension of 25 g. (0.148 mole) of mucochloric acid in 1000 ml. of water was cooled to 0°, and 70.1 g. of powdered $Ba(OH)_2 \cdot 8H_2O$ was added over a period of three hours. (Unless the addition was carried out slowly and the temperature maintained between 0–5°, the reaction appeared to take a different course with corresponding decrease in the yield of the desired barium salt.) The white suspension which resulted was filtered rapidly through a fluted filter on which were placed small pieces of ice to keep the solution cold, and an equal volume of 95% ethyl alcohol was added to the clear filtrate. The microcrystalline precipitate of barium mucoxychlorate which formed almost immediately was collected on a filter and dried. The yield was 14.9 g. The white amorphous residue was redissolved in 500 ml. of warm water, and the solution was filtered and cooled. An equal volume of 95% ethyl alcohol was added to the filtrate, and a second crop of white microcrystalline precipitate of barium salt was collected. The total yield of pure barium salt was 23.3 g. (58.4%).

Anal. Calcd. for $BaC_4HO_4Cl \cdot H_2O$: C, 15.79; H, 0.99; Cl, 11.68. Found: C, 15.48; H, 1.22; Cl, 11.51.

Mucoxychloric Acid.—Ten grams of barium mucoxychlorate was suspended in about 100 ml. of water which had been cooled to 0°. Ninety-five per cent. of the calculated amount of 1 *N* sulfuric acid (*ca.* 75 ml.) was added to the well-stirred suspension. The stirring was continued for one hour with periodic addition of ice. The barium sulfate was separated by filtration. The filtrate was frozen solid in a mixture of Dry Ice and acetone, and the water was removed by freeze-drying. The yield of crude mucoxychloric acid, m.p. 97–100°, was 4.71 g. (89.5%). Recrystallization from ether raised the melting point to 110–111°.

Anal. Calcd. for $C_4H_3O_4Cl$: Cl, 23.55. Found: Cl, 23.39.

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(20) D. K. Baird, *et al.*, *J. Chem. Soc.*, 62 (1934).

(21) R. W. Herbert, *et al.*, *ibid.*, 1270 (1933).

(22) H. Moller, *Helv. Chim. Acta*, **21**, 1036 (1938).

(23) G. Carpeni, *ibid.*, **21**, 1031 (1938).

(24) G. Carpeni, *J. chim. phys.*, **35**, 193 (1938).

(25) Melting points are uncorrected. We are indebted to Dr. Edmund C. Kornfeld of the Lilly Research Laboratories for the infrared spectrum of mucoxychloric acid mulled in mineral oil. All infrared spectra were measured with a Baird Infrared Recording Spectrophotometer.