

[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

A Novel Type of Cannizzaro Reaction

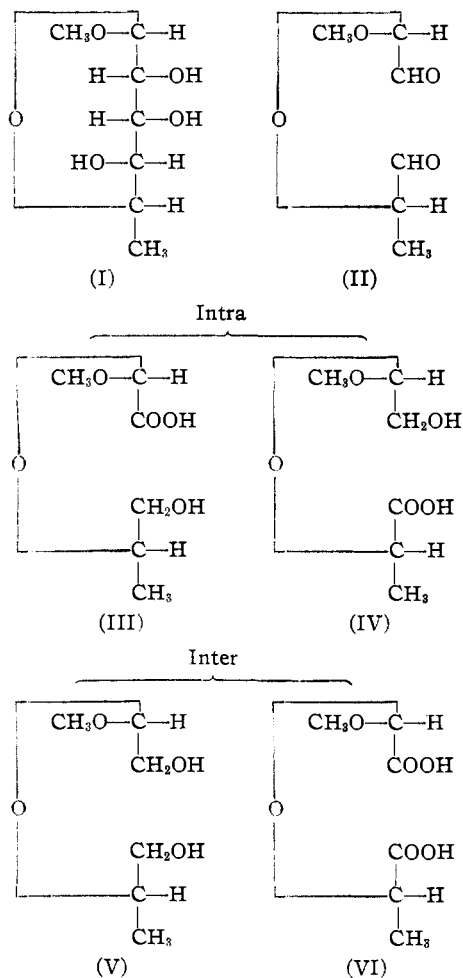
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The structure and properties of the dialdehyde derived from starch through the action of periodate¹ have been under our recent investigation. During the course of the work it was observed that solutions of "starch dialdehyde" in aqueous sodium hydroxide showed gradual loss of alkalinity corresponding to approximately 70% of the amount of dialdehyde in solution, the reaction being accompanied by considerable decomposition to colored products. In order to account for this effect and to develop a possible method of treatment of the starch dialdehyde, it was decided to study the action of alkali on the simpler analogous substance, crystalline L'-methoxy-L-methylidiglycolic aldehyde (II), obtained by oxidation of α -methyl-L-rhamnopyranoside (I) with periodic acid.² The present article describes the results obtained in this latter study.

In this case no color developed in 1 *N* alkaline solution, and the quantitative reaction was completed rapidly (less than five minutes at 100°), exactly one mole of sodium hydroxide having been removed from the excess added. The Cannizzaro type of oxidation-reduction with acid formation would account for this change, and the experimental evidence indicated such to be the case. It should be mentioned that examples of Cannizzaro dismutation with aldehydes having a hydrogen atom on the carbon atom adjacent to the aldehyde group are few,³ since such substances usually undergo the aldol condensation; no example of dismutation of the type to be described appears to have been reported.

Four products are possible, the amounts of each depending on whether the reaction takes place *inter*- or *intramolecularly*, or in both ways. However, the sodium salt of the total reaction mixture was found to be completely insoluble in ether, whereas the free acid mixture was completely soluble; hence the presence of the diglycol (V) (which would be expected to be soluble in ether), and thus of the diacid (VI), is excluded, and we conclude that the reaction proceeds en-

tirely according to an *intramolecular* mechanism



Unsuccessful attempts were made to crystallize fractionally the brucine salt of the product, in the hope of separating (III) and (IV). After hydrolysis, however, the glyoxylic acid and propylene glycol from (III) (identified as semicarbazone and di-phenylurethan, respectively), and the glycolic aldehyde and L-lactic acid from (IV) (identified as glyoxal phenylosazone and zinc salt, respectively) were isolated. The propylene glycol was optically inactive, and the lactic acid derivatives appeared to be largely racemized. Based on the yield of glyoxylic acid semicarbazone obtained, the dismutation yielded approximately 60% of (III) and 40% of (IV).

The applicability of this procedure to the study

(1) Jackson and Hudson, *THIS JOURNAL*, **59**, 2049 (1937); **60**, 989 (1938).

(2) Jackson and Hudson, *ibid.*, **59**, 994 (1937); Maclay, Hann and Hudson, *ibid.*, **61**, 1660 (1939).

(3) Elderfield, *J. Chem. Ed.*, **7**, 594 (1930); Mastagli, *Ann. Chim.*, **10**, 285 (1938).

of starch dialdehyde is now under examination in this Laboratory.

Experimental

Identification of Glycolic Aldehyde.—A 2.0727-g. sample of *L*'-methoxy-*L*-methyl-diglycolic aldehyde in 15 cc. of 1 *N* sodium hydroxide was held on the steam-bath for five minutes, cooled, and the excess alkali neutralized to phenolphthalein with 2.40 cc. of 1 *N* hydrochloric acid. The amount of alkali consumed was thus 0.01260 mole as compared with 0.01264 mole of dialdehyde taken. The addition of acid was continued to a total of 15 cc. and the mixture returned to the steam-bath for forty minutes. It was then cooled to 15° and 1 cc. of phenylhydrazine added. A red gummy precipitate of glyoxylic acid phenylhydrazone formed and was removed by filtration. The filtrate was kept at 40° for twenty-four hours with 1.5 cc. of phenylhydrazine and 1.5 cc. of glacial acetic acid after the manner of Fischer⁴ and the orange crystalline product (0.35 g. or 12%⁵ of the theoretical) was purified from alcohol. It melted at 172–173° (cor.) in agreement with reported values¹ for glyoxal phenylosazone and gave no depression when mixed with an authentic sample.

Anal. Calcd. for $C_{14}H_{14}N_4$: N, 23.51. Found: N (Dumas), 23.80, 23.55.

Identification of Glyoxylic Acid.—A 2.0030-g. (0.01223 mole) sample of *L*'-methoxy-*L*-methyl-diglycolic aldehyde was treated with alkali as above. It was found to have consumed 0.01236 mole of sodium hydroxide on titration with hydrochloric acid, addition of which was then continued equivalent to the amount of alkali originally added. After warming on the steam-bath for forty minutes, the solution was cooled and treated with 1.36 g. (theoretical quantity) of semicarbazide hydrochloride. Rapid precipitation of glyoxylic acid semicarbazone gave a yield of 0.916 g. (57.2%). Solution in alkali, followed by acidification, gave the pure substance melting at 211° (cor., dec.), in agreement with reported values of 202° to 207° (uncor.).⁸

Anal. A sample of 0.4162 g. of semicarbazone was neutralized with 3.24 cc. of 0.963 *N* sodium hydroxide (phenolphthalein). Calcd. for $C_3H_5N_3O_3$: mol. wt., 131.09. Found: mol. wt., 133.1.

Identification of Propylene Glycol and *L*-Lactic Acid.—The filtrate from the above semicarbazone precipitation was neutralized (phenolphthalein) with 17 cc. of 1 *N* sodium hydroxide. After removal of the water *in vacuo*, the organic material was taken up in ethanol and the sodium chloride filtered off. The alcohol was next concentrated to dryness, the resulting oil being exhaustively extracted with warm acetone in order to remove propylene glycol. After filtration from a small amount of unidentified crystalline material, the acetone solution was evaporated and the oil taken up in ether, the major portion being soluble. The crude propylene glycol from the ether

weighed 0.40 g. (43% yield); it was optically inactive. To it was added 1.6 cc. of phenyl isocyanate and the mixture heated on the steam-bath for three minutes. Upon removal of excess phenyl isocyanate with an ether and petroleum ether mixture, the crude propylene glycol di-phenylurethan weighed 1.47 g. (38% yield). After recrystallization from aqueous ethanol it melted at 142–144° and showed no optical activity, being thus the *D,L*-form. It gave no depression when mixed with a recrystallized authentic sample prepared from optically inactive commercial propylene glycol and melting at 144–145.5°.⁷

Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.95; H, 5.77; N, 8.91. Found: C, 65.52; H, 5.65; N, 8.88.

The sodium lactate gum remaining behind after the above acetone extraction was dissolved in 4.97 cc. of 1 *N* hydrochloric acid and the solution concentrated to dryness *in vacuo*. The free lactic acid was taken up in acetone, filtered from sodium chloride and semicarbazide hydrochloride, and evaporated. Solution in a little water followed by the addition of 0.20 g. of zinc hydroxide gave 0.233 g. of zinc lactate (12% yield) showing $[\alpha]^{20}_D -2.5^\circ$ in water (*c*, 2.8). Repetition of the above procedure with the addition of brucine instead of zinc hydroxide gave a 25.4% yield of the brucine salt. After one recrystallization from absolute alcohol-ether it melted 211–212° (cor. dec.) and showed $[\alpha]^{20}_D -27.2^\circ$ in water (*c*, 0.8).

Anal. Calcd. for $C_{28}H_{32}N_2O_7$: OCH_3 , 12.81. Found: OCH_3 , 13.19.

The acid recovered from this salt was converted into the zinc salt, which after crystallization from water showed $[\alpha]^{20}_D -5.7^\circ$ (*c*, 1.0). Since $[\alpha]^{20}_D -8.7^\circ$ (*c*, 1.5) is accepted for pure zinc *L*-lactate,⁸ it is apparent from the above data that the lactic acid in the reaction mixture is a largely racemized product, undergoing partial resolution through the brucine salt. The zinc salt was dried at 78° *in vacuo*.

Anal. Calcd. for $(C_3H_5O_3)_2Zn$: C, 29.59; H, 4.14. Found: C, 29.38; H, 4.16.

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Summary

The action of alkali upon *L*'-methoxy-*L*-methyl-diglycolic aldehyde has been studied. The substance has been shown to undergo an intramolecular Cannizzaro dismutation of a hitherto unreported type, the reaction being nearly quantitative and rapid at 100°. Application of the procedure to the dialdehyde obtained from the periodate oxidation of starch is under examination.

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(4) Fischer and Landsteiner, *Ber.*, **25**, 2553 (1892).

(5) All yields in this article are based on the amount of the original dialdehyde taken.

(6) Beilstein, "Handbuch der organischen Chemie," IV Auflage, **3**, 800 (209).

(7) A recorded melting point of 152.5–153.5° [Walpole, *Proc. Royal Soc. (London)*, **B33**, 272–286 (1911)] for inactive propylene glycol di-phenylurethan could not be confirmed.

(8) Maclay, Hann and Hudson, *This Journal*, **61**, 3234 (1939).