

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]
**THE MECHANISM OF CARBOHYDRATE OXIDATION. V. THE
 OXIDATION OF DIHYDROXY-ACETONE TO
 HYDROXYPYRUVIC ALDEHYDE**

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RECEIVED JULY 8, 1926

PUBLISHED OCTOBER 6, 1926

Since it is known that acetol¹ and benzoyl carbinol² can be oxidized in aqueous solutions of copper acetate to pyruvic aldehyde and benzoyl-formaldehyde, respectively, we thought that this reaction might also be used to prepare the unknown hydroxypyruvic aldehyde from dihydroxy-acetone. It is evident that mesoxalic-dialdehyde might also be a possible product of the proposed reaction. The hydroxypyruvic aldehyde was needed in connection with some carbohydrate studies in progress in this Laboratory. That copper sulfate is also an effective oxidizing agent in reactions of this general character has been established through the conversion of benzoyl carbinol to mandelic acid² by means of this salt. These two compounds of copper have very definite advantages for our purposes: (1) they act so slowly that the reaction may easily be stopped at a desired point; (2) the cuprous oxide and copper formed by the use of copper acetate, and the copper obtained through the use of copper sulfate are accurate indices of the oxygen consumed in the reaction; (3) the excess of copper ion is most easily removed from the reaction mixture.

Experimental Part

Dihydroxy-acetone and Copper Acetate.—To a solution of 4.64 g. of dihydroxy-acetone in 100 cc. of water was added 30 g. of copper acetate, an amount that preliminary experiments had shown to be sufficient to maintain the solution saturated with copper salt throughout the experiment. The reaction mixture was allowed to stand at room temperature for one week. When the solution was prepared, a precipitate of red cuprous oxide began to form almost immediately. After a week it was found that metallic copper was also present in the cuprous oxide. The reaction residue containing the unused copper acetate was transferred to a Gooch crucible and washed with sufficient water to dissolve the soluble salts, then washed with alcohol and dried in a vacuum. After the mixture of cuprous oxide and copper had been weighed, the cuprous oxide was dissolved in concd. hydrochloric acid, the residual copper then being washed with water and alcohol, dried and weighed. The data in Table I were obtained in two separate experiments.

TABLE I
 OXYGEN CONSUMED BY DIHYDROXY-ACETONE

Expt.	(CH ₂ OH) ₂ - CO, used, g.	Cu(C ₂ H ₃ O ₂) ₂ - H ₂ O used, g.	Time, days	Water used, cc.	Cu + Cu ₂ O g.	Cu, g.	Cu ₂ O equiv. to Cu ₂ O + Cu	Cu ₂ O equiv. to one atom of oxygen	Oxygen consumed, %
1	4.64	30	7	100	6.67	0.32	7.15	7.37	97
2	15.00	80	10	200	18.63	3.03	22.3	23.80	94

¹ Denis, *Am. Chem. J.*, **33**, 568 (1907).

² Evans, *ibid.*, **35**, 115 (1906).

These data show that only one gram atom equivalent of oxygen was used in these experiments; hence, our product could be only hydroxypyruvic aldehyde. The excess of copper ion in the filtrate from the cuprous oxide and copper was removed with hydrogen sulfide. The golden-yellow solution thus obtained gave a pronounced purple reaction with Schiff's reagent while our dihydroxy-acetone gave the expected negative test with the same procedure. On adding 10 cc. of the solution to 10 cc. of a 50% acetic acid solution of phenylhydrazine, the yellow osazone was obtained which, on crystallizing from 95% ethyl alcohol, melted at 131°. This osazone was found to be identical with that of glyceric aldehyde and dihydroxy-acetone. The soluble reaction product was further identified by its conversion into the *p*-nitrophenylosazone, m. p. 228–230°, while that obtained from dihydroxy-acetone melted at 230–232°. These tests were accepted as conclusive evidence for the presence of hydroxypyruvic aldehyde.

The golden-yellow solution obtained in Expt. 2 was divided into two equal portions, one of which was evaporated under diminished pressure at 31°, at which temperature most of the water and acetic acid was removed. On lowering the pressure to 9 mm. the remaining portions of the acid and water were removed, leaving a golden-yellow oil which began to solidify into white crystals (m. p., 99°, uncorr.) after ten minutes; yield, 5.95 g., or 80%. The aqueous solution of the solid reduced Fehling's solution and ammoniacal silver nitrate in the cold.³ The solid is easily soluble in water and alcohol, but almost insoluble in ether and acetone.

An aqueous solution of the solid prepared in cold water gave no color reaction with Schiff's reagent. However, a characteristic reaction was obtained after the aqueous solution had been previously boiled for five minutes, evidence that seemed to indicate that the solid was a polymolecular form. Accordingly a series of molecular-weight determinations of the solid was made by the cryoscopic method. Our data are summarized in Table II.

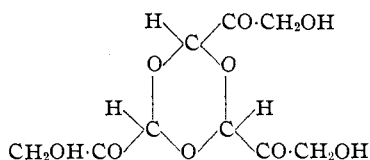
TABLE II
MOLECULAR WEIGHT OF HYDROXYPYRUVIC ALDEHYDE
25 g. of water was used in each experiment

Aldehyde used, g.	Lowering, °C.	Mol. wt.	Time
0.3	0.08	279	Freshly prepared
.3	.128	175	Standing for 18 hrs.
.6	.162	272	Freshly prepared
.6	.334	134	Standing for 24 hrs.
.6	.500	89.3	After boiling for 10 min.

Since the calculated value of the molecular weight for the monomolecular form is 88, it is obvious that white, crystalline hydroxypyruvic aldehyde is a trimer (mol. wt., 264) which is slowly converted in cold water, yet very rapidly in hot water, into the monomolecular form. This be-

³ Evans and Hoover, THIS JOURNAL, 44, 1735 (1922).

havior is very suggestive of the discovery made by Wohl,⁴ that glyceric aldehyde in the solid condition is a dimolecular compound since this form



gives the molecular weight of a hexose. Since the cold aqueous solution of the solid hydroxypyruvic aldehyde shows no positive reaction with Schiff's reagent, and in view of the above evidence with reference to its molecular weight, the illustrated molecular structure may be tentatively assigned until further data are obtained.

When an aqueous solution of dihydroxy-acetone and copper acetate, prepared as above indicated, was heated to 65° for 72 hours, mesoxalic acid was obtained as the chief reaction product.⁵ The weight of copper obtained from solution was 13.76 g. while the weight equivalent to four gram atoms of oxygen is 14.10 g.

The identity of this substance was established through the analysis of its well-known barium salt, $Ba(C_3O_5) \cdot H_2O$.

Dihydroxy-acetone and Copper Sulfate.—To a solution of 4.27 g. in 100 cc. of water was added 35 g. of copper sulfate, an amount sufficient to maintain the reacting system at saturation with respect to the salt throughout the course of the experiment. Preliminary experiments had shown that the rate of this reaction was very slow at room temperature, a conclusion which was based upon the very small yields of metallic copper obtained after the reaction mixture had stood for several days. This marked difference between copper sulfate and the acetate in the action on dihydroxy-acetone is probably intimately associated with the hydrogen-ion⁶ concentration of the reaction mixtures. After attaching our flask to a reflux condenser, the reaction mixture was heated to 80° for three days, when it was found that 5.44 g. of copper had been precipitated. This corresponds to 87.3% of two gram atom equivalents of oxygen ($3.129 = 1$ gram atom equivalent). After removing the excess of copper ion, it was found that Schiff's reagent gave a negative test in the reaction solution, which indicated the probable absence of mesoxalic-dialdehyde. The osazone prepared from this solution was identical with that obtained by Fenton and Ryffel⁷ for hydroxypyruvic acid.

Further work on dihydroxy-acetone and glyceric aldehyde is now in progress in this Laboratory.

We wish to thank Mr. G. C. Strouse of this Laboratory for valuable assistance which he gave us during a part of this work.

Summary

1. Dihydroxy-acetone is oxidized by saturated aqueous solutions of copper acetate at room temperature to hydroxypyruvic aldehyde. This aldehyde exists in the solid form as a trimer; m. p., 99°. In cold, aqueous solution it depolymerizes very slowly, but in hot solutions very rapidly.

2. At 65° dihydroxy-acetone is oxidized by saturated aqueous solutions of copper acetate to mesoxalic acid.

⁴ Wohl, *Ber.*, **31**, 2395 (1898).

⁵ Ref. 3, p. 1740.

⁶ Wind, *Biochem. Z.*, **159**, 61 (1925).

⁷ Fenton and Ryffel, *J. Chem. Soc.*, **81**, 426 (1902).

3. A tentative molecular structure for the trimeric form has been suggested.

4. Dihydroxy-acetone is oxidized by saturated aqueous solutions of copper sulfate at 80° to hydroxypyruvic acid.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE COUPLING ACTION OF THE GRIGNARD REAGENT. II METHYLMAGNESIUM IODIDE AND THE BENZYL HALIDES

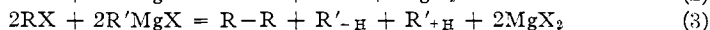
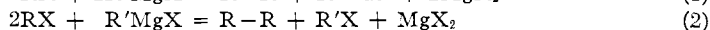
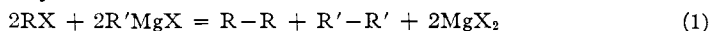
BY REYNOLD C. FUSON¹

RECEIVED JULY 16, 1926

PUBLISHED OCTOBER 6, 1926

Introduction

It was pointed out in the first paper of this series² that the Grignard reagent reacts with a number of alkyl halides as a coupling agent removing the halogen atoms and uniting the resulting residues. The reaction is analogous to the Wurtz reaction, the Grignard reagent here playing the role of the metal in the Wurtz synthesis. No agreement, however, has been reached as to what becomes of the Grignard reagent itself in the reaction. Various equations have been written for the reaction; one of these (1) supposes the generation of a hydrocarbon by a coupling together of the radicals attached to magnesium, and another (2) assumes the formation of an alkyl halide. Späth³ has shown that where R' is an alkyl group other than methyl, the reaction probably takes place according to Equation 3, the two radicals reacting to form equal quantities of a saturated and an ethylenic hydrocarbon.



Equation 1 was proposed by Schmidlin.⁴ By treating triphenylmethyl chloride with phenylmagnesium iodide he obtained a 27% yield of triphenylmethyl along with some tetraphenylmethane and a small amount of diphenyl. He formulated his results by the following equation: $2(C_6H_5)_3CCl + 2C_6H_5MgI = 2(C_6H_5)_3C + C_6H_5-C_6H_5 + 2MgICl$.

By treating iodoform and carbon tetrachloride with phenylmagnesium bromide, Binaghi and Oddo⁵ and Binaghi⁶ obtained *sym.*-tetraphenylethane and hexaphenylethane, respectively. They assume the intermediate formation of diphenylchloromethane in the one case and of triphenyl-

¹ National Research Fellow in Chemistry.

² Fuson, *THIS JOURNAL*, **48**, 830 (1926).

³ Späth, *Monatsh.*, **34**, 1965 (1913).

⁴ Schmidlin, *Ber.*, **43**, 1141 (1910).

⁵ Binaghi and Oddo, *Gazz. chim. ital.*, [II] **51**, 330 (1921).

⁶ Binaghi, *ibid.*, **53**, 879 (1923).