[Contribution from the Research Laboratories, Chemical Department of the City of Chicago, Municipal Tuberculosis Sanitarium]

THE IODINATION OF ACETYLENE DERIVATIVES. I. THE PREPARATION OF DI-IODOFUMARIC ACID

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Di-iodofumaric acid can be prepared more efficiently by the method presented here than by the other ways described in the literature.

Bruck[1] was the first to prove that the acetylene-dicarboxylic acid combined with iodine when an alcohol solution of the two was heated in a sealed tube for ten hours at 100°. Later, Peter[2] substituted chloroform for the alcohol. The last effort was that of James and Sudborough[3] who tried two methods; first, the potassium salt of the acetylene dicarboxylic acid was dissolved in water and "nascent" iodine liberated in the solution by the action of copper sulfate on potassium iodide; second, the potassium salt of the acetylene-dicarboxylic acid dissolved in water was treated with an excess of iodine in a potassium iodide solution for three to five days at 15°. No addition compound could be isolated by them with either method. The failure of these last investigators to obtain the di-iodofumaric acid is strange since their method is approximately the same as that found to be successful, differing only in the proportion of potassium iodide used and in the working temperature.

Since a previous study of the chlorination and bromination of the ethylene-dicarboxylic acids, fumaric and maleic acid,[4] indicated that the iodination of acetylene-dicarboxylic acid must occur on treatment of the neutral salt with iodine, if an excess of potassium iodide were used to suppress any activity of the hydrolyzed iodine and if proper conditions of time and temperature are allowed, the preparation of di-iodofumaric acid, by an analogous method, was attempted.

Rate of the Reaction.—Measurement of the rate of reaction of iodine and acetylene-dicarboxylic acid in equimolar proportions at concentrations of 0.0419 M and 0.0838 M each, fits the equation for a bimolecular change. The specific reaction rate in both instances is 0.0095 at 25°, when concentrations are expressed in moles per liter and time in minutes. This indicates that the salt ion and molecule react at equal rates[5] with either iodine, KI_3 or K_2I_{14}. However, it seems more probable that this agreement is merely apparent and that conflicting influences are balanced over the interval of concentration represented. The principal interest at present is

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[1] Bruck, *Ber.*, **24**, 4118 (1891); **26**, 843 (1893).

[2] Peter, *Ann.*, **369**, 129 (1909).

[3] James and Sudborough, *J. Chem. Soc. Trans.*, **91**, 1037 (1907).

[4] Terry and Eichelberger, This Journal, **47**, 1067 (1925).

[5] Linhart, *ibid.*, **40**, 158 (1918).

the coefficient of the reaction since this reveals the necessary conditions for control.

Experimental Part

All materials used were purified and standardized by conventional methods.

Preparations

Dibromosuccinic Acid.[4,6]—Fifty g. of pure fumaric acid was placed in a 2-liter flask, 700 cc. of water was added and the acid neutralized to the pink point of phenolphthalein with approximately 150 cc. of 20% sodium hydroxide solution. Two hundred g. of finely powdered sodium bromide was then added slowly during constant shaking to prevent the salting out of the sodium fumarate by a local excess of the sodium bromide. Thirty cc. of bromine dissolved in 500 cc. of a 20% solution of sodium bromide was added slowly to the sodium fumarate mixture while the flask was rotated. The addition of the bromine water required about ten minutes, after which an excess of bromine must be present; this was determined by the color of the solution. The reaction mixture was allowed to stand for 30 minutes to complete the bromination, and the excess of bromine removed by the addition of sodium bisulfite. Concd. hydrochloric acid was added and the dibromosuccinic acid was precipitated at once. The flask with its contents was placed in a refrigerator overnight, after which the crystals were collected upon a filter, washed with water and dried in a vacuum over sulfuric acid. This method of brominating fumaric acid gives an 80% yield of dibromosuccinic acid and a 10% yield of *iso*-dibromosuccinic acid. Since the latter is very soluble in water, only the pure dibromosuccinic acid is obtained in the acid precipitate. All of the brominated acids may be recovered by extracting the water filtrate with ether thrice.

Anal. Subs., 0.2122: 12.54 cc. of 0.1227 *N* barium hydroxide soln. Calcd. from equiv. wt., 12.55 cc.

Acetylene-dicarboxylic Acid.—The method of Baeyer[7] was followed for this preparation.

For purification of the compound the crystals were dissolved in ether and reprecipitated with 40° to 60° petroleum ether; m. p., 178°, with decomposition. A titration of a weighed sample of this compound showed that it was the pure acetylene-dicarboxylic acid.

Anal. Subs., 0.1510: 21.58 cc. of 0.1227 *N* barium hydroxide soln. Calcd. from equiv. wt., 21.59 cc.

Di-iodofumaric Acid.—A solution of 8 g. of acetylene-dicarboxylic acid in 50 cc. of distilled water was neutralized to the pink point of phenolphthalein with potassium hydroxide. A solution of 100 g. of potassium iodide and 24 g. of iodine in 250 cc. of water was added and the total volume made up to 400 cc. The flask was then stoppered and placed in a 37° incubator for five to seven days.

After the reaction was complete the excess of iodine was removed by the addition of a solution of sodium bisulfite. To obtain the free acid, the reaction mixture was treated with concd. hydrochloric acid and extracted four times with ether. The ether was then dried over anhydrous sodium sulfate and, after evaporation of the ether, light yellow crystals were obtained. For purification, the slightly impure crystals were dissolved in a small amount of ether and precipitated by adding an equal volume of petroleum ether, b. p. 40° to 60°. In this way colorless crystals were obtained. The yield

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[6] The complete statement of the preparation is given here for the first time.

[7] Baeyer, *Ber.*, **677**, 2269 (1885).

depends upon the length of time and the temperature at which the reaction mixture is allowed to stand. The approximate rate of the reaction at 37° follows: after one day a 53% iodination occurs; after three days, 75%; after four days, 79%; and after five days, 81% iodination. Diffused daylight does not have an effect upon the speed of this reaction.

Anal. Subs., 0.2438: AgI, 0.3121. Calcd. for $C_4O_4H_2I_2$: I, 69.01. Found: 69.20.

Subs., 0.4489: 19.90 cc. of 0.1227 *N* barium hydroxide soln. Calcd. for $C_4O_4H_2I_2$: 19.89 cc.

The di-iodofumaric acid does not give a sharp melting point. It begins to give off a small amount of iodine vapor at 220° and as the temperature is raised more vapor is given off until at 250° the white crystals become light brown and at 275° finally melt. The acid is soluble in ether, alcohol and water and insoluble in benzene, ligroin and chloroform. Crystals are slightly decomposed by direct light. The two most important experimental factors in this preparation are: first, the five-to-seven days of heating at 37°—which is probably equal to 20–28 days at 15°, or the temperature that James and Sudborough used—and second, the excess of potassium iodide which prevents the volatilization and the hydrolysis of the iodine.

Rate of the Reaction.—The measurement of the rate of the reaction was carried out as follows. Samples of a given solution of the potassium salt of the acetylene-dicarboxylic acid, potassium iodide and iodine were sealed in Pyrex tubes and immersed for selected intervals of time in a 25° bath, the temperature of which was constant to 0.05°. At the proper time the tubes were removed from the bath, opened and the concentration of the unused iodine was titrated with 0.05 *N* sodium thiosulfate solution. The function that was found to describe the rate of change was $dx/dt = k(a-x)^2$, where x represents the concentration of the acetylene dicarboxylic acid iodinated at any interval of time t, and a represents the initial concentration of the acetylene-dicarboxylic acid. The concentration of iodine was always equivalent to that of the carboxylic acid.

A summary of the experiments is given in Table I.

TABLE I

SUMMARY OF EXPERIMENTS AT 25°

M concn. of reactants	0.1546	0.0838	0.0419	
Mean *K*	.0097	.0096	.0094	Av., 0.0096

Summary

1. A simple and convenient method for the addition of iodine to the triple bond has been suggested.

2. A method for the preparation of di-iodofumaric acid in water solution has been described.

3. The rate of the iodination of acetylene-dicarboxylic acid in water solution at 25° in the presence of potassium iodide has been measured and the reaction has been shown to be bimolecular.

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