

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]
**THE HALOFORM REACTION. VII. THE EFFECT OF ORTHO
 CHLORINE ATOMS**

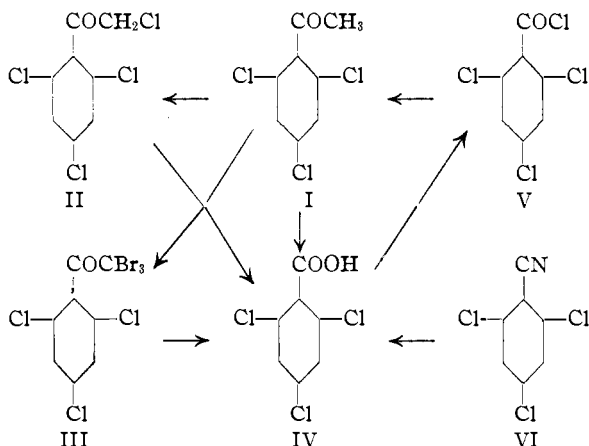
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It has been shown that the cleavage of methyl ketones by the action of hypohalite solutions involves the intermediate formation of corresponding trihalomethyl ketones. These intermediates have been found to be stable to cold solutions of alkali in those cases in which the positions ortho to the carbonyl group are occupied. The stabilizing effect of methyl groups¹ and of bromine atoms² in the ortho positions has been found to be very great. Cleavage of the trihalomethyl ketones in these cases has been effected only by long treatment with hot, concentrated solutions of alkali. The effect of methoxy groups³ has, however, proved to be less pronounced. The di-*o*-methoxy trihalomethyl ketones, while sufficiently stable toward cold solutions of alkali, have been found to be cleaved readily by hot alkaline solutions.

The present paper is a report of a similar study of the effect of ortho chlorine atoms. For this purpose 2,4,6-trichloroacetophenone (I) was used.



In the synthesis of this ketone, 2,4,6-trichloroaniline was used as the starting material. It was converted into 2,4,6-trichlorobenzonitrile (VI) by means of the Sandmeyer reaction.⁴ The hydrolysis of the nitrile to 2,4,6-trichlorobenzoic acid (IV) was effected by heating it with a mixture of

¹ Fuson and Walker, *THIS JOURNAL*, **52**, 3269 (1930); Gray, Walker and Fuson, *ibid.*, **53**, 3494 (1931).

² Fuson, Lewis and DuPuis, *ibid.*, **54**, 1114 (1932).

³ Fuson, Farlow and Stehman, *ibid.*, **53**, 4097 (1931).

⁴ Compare Sudborough, Jackson and Lloyd, *J. Chem. Soc.*, **71**, 231 (1897).

concentrated sulfuric acid and glacial acetic acid. The yield in this step was about 50% of the theoretical. A good yield of 2,4,6-trichlorobenzoyl chloride (V) was obtained from the acid by treatment with phosphorus pentachloride.

The ketone was prepared from the acid chloride by treatment of the latter with a solution of methylmagnesium chloride. The rate of this reaction is remarkably slow. Four hours of heating of the reaction mixture left the acid chloride largely unchanged, and it was necessary to heat for twenty-four hours in order to obtain the ketone. This treatment gave 2,4,6-trichloroacetophenone in yields of about 50% of the theoretical.⁵

By treatment with a solution of sodium hypobromite, the ketone was converted into α,α,α -tribromo-2,4,6-trichloroacetophenone (III). The yield was very good, showing that the tribromomethyl ketone is not affected by protracted treatment with cold solutions of alkali. When heated with a 50% solution of sodium hydroxide, however, the ketone was almost quantitatively converted into the corresponding acid, 2,4,6-trichlorobenzoic acid (IV).

Attempts to prepare the $\alpha,\alpha,\alpha,2,4,6$ -hexachloroacetophenone led to unexpected results. Treatment of 2,4,6-trichloroacetophenone with solutions of hypochlorite failed to yield the hexachloro compound but gave instead $\alpha,2,4,6$ -tetrachloroacetophenone. This result was surprising because it is the first case of the formation of a monochloromethyl ketone by treatment of a methyl ketone with a hypochlorite solution. Moreover, attempts to convert the tetrachloro compound into the hexachloro derivative by further treatment with hypochlorite solutions were likewise unavailing. In these attempts the tetrachloro compound was either recovered unchanged or was converted into the corresponding acid, 2,4,6-trichlorobenzoic acid. It was found possible also to obtain this acid by prolonged treatment of the methyl ketone with hypochlorite solutions. Although in both of these cases the hexachloro compound must have been formed as an intermediate, direct evidence of its existence was not obtained.

Experimental

2,4,6-Trichlorobenzonitrile.—The method of Sudborough, Jackson and Lloyd⁴ was used. The average yield of nitrile obtained was about 35% of the theoretical.

2,4,6-Trichlorobenzoic Acid.—Forty-five grams of 2,4,6-trichlorobenzonitrile was placed in a 2-liter flask fitted with a reflux condenser and containing 500 cc. of a mixture of two parts concentrated sulfuric acid, one part water, and one part glacial acetic acid—all by volume. The mixture was refluxed for three hours. It was cooled to

⁵ This reaction between 2,4,6-trichlorobenzoyl chloride and methylmagnesium chloride is interesting because it shows the effect of steric hindrance on a reaction which may be either additive or metathetical. In view of the fact that reactions of the former type are generally much more greatly affected by steric factors than are those known to be of the latter type, the results here reported suggest that the primary reaction between RMgX and an acid chloride is one of addition.

10° and the calculated amount of sodium nitrite, dissolved in as little water as possible, was run in slowly, vigorous stirring being maintained all the while and the sodium nitrite solution being run beneath the surface of the liquid. The mixture was then heated on the steam cone until all of the gas was expelled. The acid was filtered, dissolved in sodium hydroxide solution and reprecipitated with hydrochloric acid. An average yield of 34% of the theoretical was obtained from three runs. The acid precipitated as nearly colorless platelets which melted at 162°.

2,4,6-Trichlorobenzoyl Chloride.—Sixteen grams of 2,4,6-trichlorobenzoic acid was mixed with 15 g. of phosphorus pentachloride in a small beaker. The mixture liquefied at once. After the mixture was allowed to stand for half an hour, the phosphorus oxychloride was distilled under slightly diminished pressure and the acid chloride was collected from 107–107.5° under 6 mm. pressure. An average yield of 73% of the theoretical was obtained.

2,4,6-Trichloroacetophenone.—Twenty-five cubic centimeters of two-molar methylmagnesium chloride was placed in a 200-cc. flask fitted with a condenser. Twelve and three-tenths grams of the acid chloride was dissolved in 50 cc. of dry ether and added at one time to the Grignard reagent. The mixture was refluxed for twenty-four hours. At the end of this time the reaction mixture was decomposed with dilute hydrochloric acid and the ketone extracted with ether. It was recrystallized from alcohol, from which it precipitated in the form of fine, almost colorless needles. The product melted from 156–157°. A yield of 50% of the theoretical was obtained.

Anal. Calcd. for $C_8H_5OCl_3$: Cl, 47.6. Found: Cl, 47.8.

α,α -Tribromo-2,4,6-trichloroacetophenone.—Five grams of 2,4,6-trichloroacetophenone was placed in a 500-cc. three-necked flask, fitted with a mercury-sealed stirrer and a thermometer and containing 500 cc. of sodium hypobromite solution. The sodium hypobromite solution was prepared by dissolving 50 g. of bromine in 500 cc. of 10% sodium hydroxide solution at 0°. The mixture was stirred for eighty hours. The temperature was kept around 50° for the first thirty hours and then raised to 70°. The product was filtered, washed several times with water and recrystallized from alcohol. Eight grams of the tribromo compound, melting at 126–127°, was obtained. The compound crystallizes in fine, almost colorless granules. A yield of 80% of the theoretical was obtained.

Anal. Equivalents of halogen per gram of substance: Calcd. for $C_8H_2OCl_3Br_3$: X, 0.0130. Found: X, 0.01284.

Action of Alkali on α,α -Tribromo-2,4,6-trichloroacetophenone.—Three grams of α,α -tribromo-2,4,6-trichloroacetophenone was heated for four hours on a steam cone at 90° with 200 cc. of 50% sodium hydroxide solution. Nothing appeared to happen to the ketone, but on diluting the solution, all of the suspended material went into solution. The solution was made acid with hydrochloric acid and the 2,4,6-trichlorobenzoic acid precipitated. One and three-tenths grams of the acid was obtained, which corresponds to a nearly quantitative cleavage of the halogenated ketone. The acid melted at 161–162° after one precipitation.

$\alpha,2,4,6$ -Tetrachloroacetophenone.—Two grams of 2,4,6-trichloroacetophenone was shaken with 200 cc. of sodium hypochlorite solution for fifty hours at room temperature. The sodium hypochlorite solution was prepared by bubbling chlorine into 200 cc. of 10% sodium hydroxide solution, cooled to 0°, until the solution was acidic. Another 200 cc. of 10% sodium hydroxide solution was then added to this. Two and one-half grams of material was obtained. After three recrystallizations from alcohol, the compound melted at 106.5–107.5°.

The tetrachloro compound was also obtained by heating 2,4,6-trichloroacetophenone with sodium hypochlorite solution for eight hours at 90°.

Anal. Calcd. for $C_8H_4OCl_4$: Cl, 55.0. Found: Cl, 55.1.

2,4,6-Trichlorobenzoic Acid from 2,4,6-Trichloroacetophenone.—Five-tenths gram of 2,4,6-trichloroacetophenone was shaken with a mixture of 100 cc. of 10% sodium hypochlorite solution and 20 cc. of pyridine for seventy-two hours at room temperature. The solution was acidified with hydrochloric acid and extracted with ether. The material obtained on evaporation of the ether was dissolved in dilute sodium hydroxide solution and reprecipitated with hydrochloric acid. It melted from 159–162°. The conversion of the ketone to the acid was practically quantitative.

2,4,6-Trichlorobenzoic Acid from $\alpha,2,4,6$ -Tetrachloroacetophenone.—Five-tenths gram of $\alpha,2,4,6$ -tetrachloroacetophenone was stirred with 100 cc. of 10% sodium hypochlorite solution and 10 cc. of pyridine at 90° for twenty-four hours. The solution obtained on evaporation of the ether was dissolved in dilute sodium hydroxide solution and reprecipitated with hydrochloric acid. It melted at 160°. The yield of the acid was 97% of the theoretical.

Summary

2,4,6-Trichloroacetophenone has been prepared and its reaction with solutions of sodium hypochlorites has been studied. When hypobromite solutions were used, α,α,α -tribromo-2,4,6-trichloroacetophenone was obtained. Treatment with hot, concentrated solutions of sodium hydroxide converted this ketone into 2,4,6-trichlorobenzoic acid.

With sodium hypochlorite solutions 2,4,6-trichloroacetophenone gave $\alpha,2,4,6$ -tetrachloroacetophenone. Prolonged treatment with the hypochlorite solutions converted both the trichloro and the tetrachloro compounds into 2,4,6-trichlorobenzoic acid.

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PHENACYL AND *p*-BROMOPHENACYL ESTERS OF MONOSUBSTITUTED BENZOIC ACIDS¹

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The use of phenacyl and *p*-bromophenacyl esters was introduced by Reid and co-workers² as a means of identifying acids. Since easily prepared and easily purified esters of organic acids are highly desirable the present investigation was undertaken.

Experimental

The procedure for the preparation of the esters was essentially the same as that of Reid. In the case of the amino acids, however, a modified procedure was used. By using the method of Reid on the amino acids very low yields were obtained. It was then considered possible that one mole

¹ This paper is constructed from a thesis submitted by Hartley W. Howard to the Faculty of Holy Cross College in partial fulfillment of the requirements for the degree of Master of Science.

² Reid and co-workers, *THIS JOURNAL*, **41**, 75 (1919); *ibid.*, **42**, 1043 (1920).