

solutions was studied, being calculated from a knowledge of the "direct" and "indirect" figures.

5. Maximum absorption of water is shown to occur at a concentration of alkali of about 14% by weight at 25°, which corresponds with that concentration at which maximum swelling has been observed by other workers.

6. Direct quantitative analysis of a soda cellulose which has been washed once with alcohol leads to the assumption that the product formed may be the result of an equilibrium reaction of the nature of  $(C_6H_{10}O_5 \cdot NaOH)_x \rightleftharpoons (C_6H_9O_5Na)_x + xH_2O$ . The nature of the structure of each of these compounds is uncertain but possibly in each case inter-micellary and residual-valence forces are involved.

MONTREAL, CANADA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

## THE CLEAVAGE OF CARBONYL COMPOUNDS BY ALKALIES.

### I. TRIHALOMETHYL KETONES OF THE MESITYLENE SERIES

BY REYNOLD C. FUSON AND JOSEPH T. WALKER

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The large number of carbonyl compounds which undergo cleavage of the carbon chain when treated with alkalies suggests a cleavage mechanism arising from some property inherent in the carbonyl group. If we consider the cleavage of  $\beta$ -diketones,  $\beta$ -keto acids, nitromethyl, cyanomethyl and trihalomethyl ketones, for example, it is apparent that the carbonyl group is the structural element characteristic of the type. It is true also that the carbon atom which separates from the carbonyl carbon atom in the cleavage bears in each case one or more so-called negative groups, but the wide variety of these which are effective shows that this influence is of a very general nature. It seemed probable, therefore, that the explanation of this type of chain cleavage would be found in the properties of the carbonyl group. The purpose of the present paper is\* to present a theory developed on this basis.

It is assumed, in the first place, that in the *active form* of the carbonyl group the oxygen atom is singly bound to the carbon atom. The latter has, therefore, only six electrons in its valence shell (A). This

idea has been used by Carothers<sup>1</sup> and by Latimer and Porter.<sup>2</sup> Latimer and Rodebush<sup>3</sup> have called attention to the fact that the carbon atom in solid carbonates probably has only six

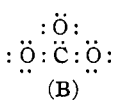
electrons in its shell (B). As Carothers has pointed out, this picture of the carbonyl group furnishes a satisfactory basis for the interpretation of addition reactions. The carbonyl carbon

has a tendency to complete its octet of electrons by coördinating with an

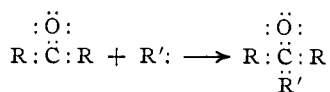
<sup>1</sup> Carothers, *THIS JOURNAL*, **46**, 2226 (1924).

<sup>2</sup> Latimer and Porter, *ibid.*, **52**, 206 (1930).

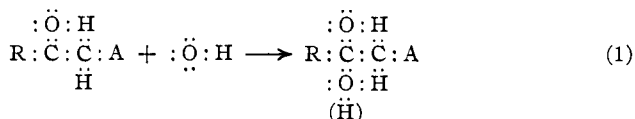
<sup>3</sup> Latimer and Rodebush, *ibid.*, **42**, 1419 (1920).



atom which has an unshared pair of electrons. Thus the reaction with the Grignard reagent would consist in the coordination of the carbonyl carbon atom with the alkide ion of the Grignard reagent



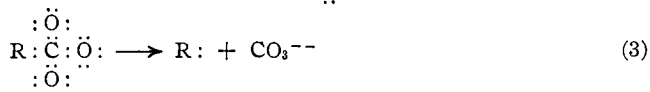
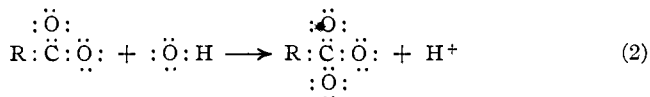
If it is now assumed that the carbonyl carbon will tend to coordinate in a similar way with hydroxyl ion, we arrive at the following results



This tendency of ketones to take up hydroxyl is, moreover, well known. It is also known that the tendency is enhanced by the presence of a "negative" group, A, on the adjacent carbon atom. An example of this is the hydration of chloral. It will be noted that the deficiency of the carbonyl carbon atom will increase with increase in the residual atomic charge on the  $\alpha$ -carbon atom. In other words, the tendency of the carbonyl carbon atom to complete its octet by coordination will increase as the negative nature of A is increased.

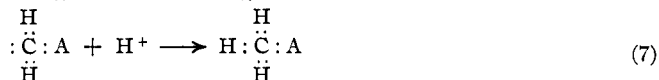
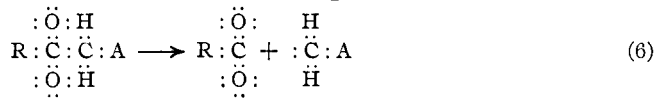
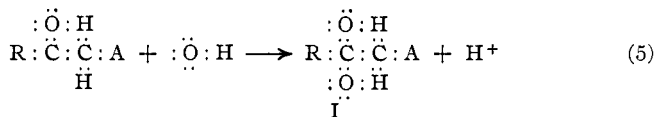
It is postulated that when the carbonyl carbon atom has united with an oxygen atom its hold on the pair of electrons joining it to the  $\alpha$ -carbon atom will be decreased, enabling the latter in certain cases to separate as an ion. The tendency for this carbon atom to separate in this manner will be favored by negative groups which it may hold.

The argument may be illustrated by the case of the decarboxylation of acids by heating with alkalies. The foregoing theory leads to the following steps



Equation 2 shows the coordination of the carbonyl atom in the acylate ion with hydroxyl (the latter would probably lose its proton in the process). When it is remembered that the carbonate ion is very stable, the ionization shown in Equation 3 seems to follow as a consequence of Equation 2.

Returning now to the case of ketones, it is apparent that, formally at least, the possibilities are the same as those presented by the case of the carboxyl group.

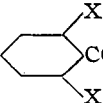


In the case of ketones, the tendency to coördinate with hydroxyl and the tendency of the resulting complex (I) to break down into an acylate ion and an alkide ion will depend on the nature of A. The greater the residual atomic charge on A, the greater will be the tendency for coördination and likewise for subsequent cleavage by ionization. This, of course, is in agreement with the facts.

It should be pointed out that the process represented in Equation 5 is simply an electronic formulation of the commonest type of reaction of a carbonyl group, an addition. It is well known that certain ketones will not undergo these typical addition reactions. It seemed reasonable to suppose, accordingly, that these same ketones would not suffer cleavage by alkalis. This, indeed, provides a means of testing the validity of the mechanism here proposed.

The iodoform type of reaction involving methyl ketones seemed most suitable for this study. The test of the addition theory for the cleavage may be stated as follows.

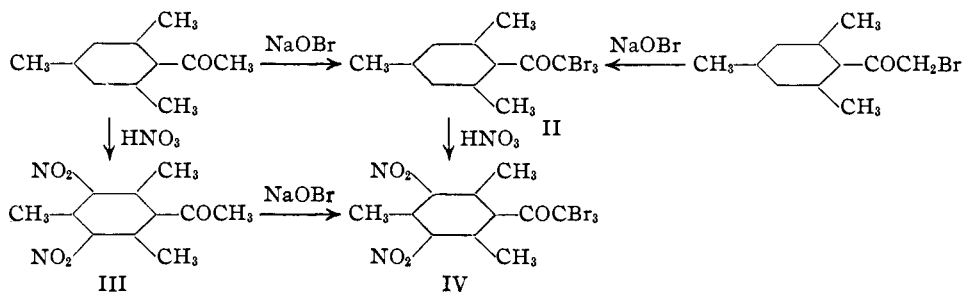
The cleavage of trihalomethyl ketones in the presence of alkalis proceeds with extreme ease. If, now, the cleavage is dependent, as postulated, on an addition reaction of the carbonyl group, it should be slowed down or

inhibited in the case of ketones of the type , in which the

carbonyl group is known to be practically inert as far as addition reactions are concerned. Experiment has supported the theory. Trihalomethyl acetophenones in which both ortho positions are filled have been prepared and have been found to be stable to alkali.

**Trihalomethyl Mesityl Ketones.**—The preparation of  $\alpha,\alpha,\alpha$ -tribromo-2,4,6-trimethylacetophenone (II) was accomplished by the bromination of acetomesitylene by treatment with a solution of sodium hypobromite. The resulting compound melts at 68.5–69° and contains three atoms of bromine. Although the method of synthesis left little doubt as to the position of the three atoms of bromine in the molecule, it was necessary, of course, to prove beyond any doubt that none of these was in the mesityl group.

That the two nuclear positions were unsubstituted was demonstrated by preparing the dinitro derivative,  $\alpha,\alpha,\alpha$ -tribromo-2,4,6-trimethyl-3,5-dinitroacetophenone (IV).

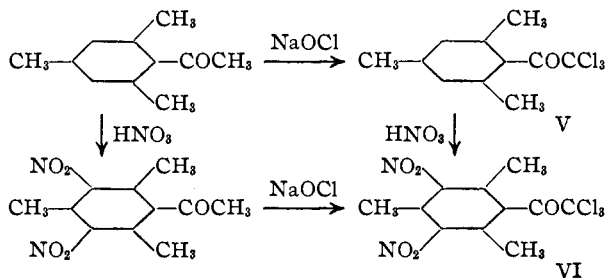


It was obtained by nitration of II. It was found possible to prepare IV in another way which, it is felt, adds to the evidence in favor of the structure written for this compound. By nitration of acetomesitylene, 3,5-dinitroacetomesitylene (III) was obtained, and this compound when treated with a solution of sodium hypobromite gave a tribromo derivative which was shown by the method of mixed melting points to be identical with IV.

That the bromine atoms occupy the *alpha* positions is further supported by the fact that  $\alpha$ -bromo-2,4,6-trimethylacetophenone when treated with a sodium hypobromite solution gave the tribromo derivative, II.

It was later found possible to demonstrate the position of the bromine atoms by a decomposition method. Although attempts at hydrolysis of the tribromo compound gave only oils which could not be identified, treatment with silver nitrate yielded  $\beta$ -isodurylic acid. Although the mechanism involved in this decomposition is not clear, the result shows beyond question that the three bromine atoms of the tribromo compound are in the acetyl side chain.

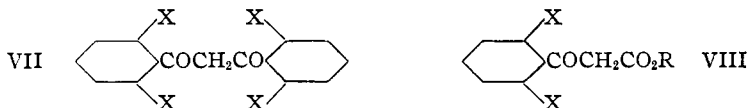
By use of the methods just described for the tribromo ketones, the corresponding trichloro ketones have been prepared. The series offers a close parallel to that of the bromine derivatives.  $\alpha,\alpha,\alpha$ -Trichloro-2,4,6-trimethylacetophenone (V) was obtained by treating acetomesitylene with a solution of sodium hypochlorite. This compound was an oil which gave



a dinitro derivative,  $\alpha, \alpha, \alpha$ -trichloro-2,4,6-trimethyl-3,5-dinitro-acetophenone (VI), melting at 100.1–100.6°. Compound VI was obtained also by treating 2,4,6-methyl-3,5-dinitro-acetophenone with a solution of sodium hypochlorite. The two samples prepared in the two ways indicated were shown to be identical by the method of mixed melting points.

Returning to the point in question, the stability of trihalomethylmesityl ketones toward alkalis, it is believed that the above methods of synthesis of II, IV, V and VI not only show these compounds to be of the desired type but also that they are, indeed, stable to alkali. Experiments showed, in fact, that these compounds could be prepared in 40% solutions of sodium hydroxide. There can, therefore, be no question as to their stability toward this reagent.

The cleavage theory here presented carries with it certain implications which must be recognized. It follows, for example, that compounds of the types VII and VIII



will not readily undergo the "acid" cleavage on treatment with alkali. This prediction is borne out by the work of Behal and Anger,<sup>4</sup> who found that di-isoduryloymethane, a compound of type VII, could be cleaved only by heating with concentrated alkali in a sealed tube at 300°.

### Experimental Part

**$\alpha, \alpha, \alpha$ -Tribromo-2,4,6-trimethylacetophenone (II).**—A dilute solution of sodium hypobromite was prepared by slowly adding 150 g. of bromine to an ice-cold solution of 150 g. of sodium hydroxide in 1500 cc. of water. To this solution in a 3-liter flask equipped with a stirrer was added 16 g. (0.1 mole) of acetomesitylene. The reaction mixture was stirred at room temperature for a period of two days, at the end of which time a colorless crystalline substance was obtained. This, when filtered and recrystallized from alcohol, separated as thick colorless needles melting at 68.5–69°. The yield was 35.5 g. or 89% of the theoretical.

*Anal.* Calcd. for  $C_{11}H_{11}OBr_3$ : Br, 60.1. Found: Br, 59.9.

**$\alpha, \alpha, \alpha$ -Tribromo-2,4,6-trimethyl-3,5-dinitro-acetophenone (IV).**—Five grams of the tribromo-acetomesitylene was dissolved in 25 cc. of ice-cold fuming nitric acid (sp. gr. 1.60). The solution was then poured slowly with stirring into 200 cc. of ice water, and the precipitate allowed to crystallize. This material was filtered and recrystallized from alcohol. It separated in the form of long, slender needles melting at 114.6–115.1° (corr.); yield, 4.9 g. or 80% of the theoretical.

*Anal.* Calcd. for  $C_{11}H_9O_5N_2Br_3$ : Br, 49.0. Found: Br, 48.8.

**3,5-Dinitro-acetomesitylene (III).**—Five grams of acetomesitylene was poured slowly with stirring into 50 cc. of ice-cold fuming nitric acid. The solution was then poured slowly into 200 cc. of ice water. The colorless precipitate was filtered and the dinitro-acetomesitylene extracted from a small amount of insoluble material with al-

<sup>4</sup> Behal and Anger, *Bull. soc. chim.*, [3] 9, 702 (1893).

cohol. The solution upon cooling deposited colorless crystals melting at 139.6–140.6° (corr.); yield, 4.5 g. or 58% of the theoretical.

*Anal.* Calcd. for  $C_{11}H_{12}N_2O_8$ : C, 52.3; H, 4.8. Found: C, 52.3; H, 4.8.

**$\alpha,\alpha,\alpha$ -Tribromo-2,4,6-trimethyl-3,5-dinitro-acetophenone (IV).** (Second Method.)—Two grams of dinitro-acetomesitylene was placed in a 150-cc. flask with 150 cc. of dilute sodium hypobromite solution prepared as described above. The reaction mixture was shaken occasionally during a period of two weeks, and was finally heated for about an hour on a steam-bath. After cooling, the precipitate was filtered and extracted twice with small portions of hot alcohol. Upon cooling the alcohol solution deposited colorless crystals melting at 114°; yield, 1.8 g. or 64% of the theoretical. A mixture of these crystals with a sample of  $\alpha,\alpha,\alpha$ -tribromo-2,4,6-trimethyl-3,5-dinitro-acetophenone (prepared by the first method) showed no lowering of the melting point.

**$\alpha,\alpha,\alpha$ -Tribromo-2,4,6-trimethylacetophenone (II).** (Second Method.)—Two grams of finely powdered  $\alpha$ -bromo-2,4,6-trimethylacetophenone was added to 150 cc. of sodium hypobromite solution, prepared in the manner previously described. The mixture was allowed to stand with occasional shaking for about a week, after which time it was heated on a steam-bath, cooled and the precipitate filtered. The solid material after recrystallization from alcohol melted at 68.5–69°; yield, 1.5 g. A mixture of the crystals with a sample of  $\alpha,\alpha,\alpha$ -tribromo-2,4,6-trimethylacetophenone (prepared by the first method) showed no depression of the melting point.

**$\beta$ -Isodurylic Acid from the Decomposition of  $\alpha,\alpha,\alpha$ -Tribromo-acetomesitylene.**—Five g. of  $\alpha,\alpha,\alpha$ -tribromo-acetomesitylene and 7 g. of silver nitrate were placed in a 400-cc. flask equipped with a reflux condenser. To this mixture was added 150 cc. of alcohol. The resulting mixture was heated under reflux for two days. Seventy-five cc. of 10% aqueous sodium hydroxide solution was then added and the heating was continued for two hours. The silver chloride and silver oxide were removed by filtration and the alcohol by distillation. The resulting aqueous solution when acidified with dilute sulfuric acid gave an oil which soon crystallized. The compound after two recrystallizations from benzene melted at 147–149.5°. A mixture of this compound with a known specimen of  $\beta$ -isodurylic acid (m. p. 149–151.5°) melted at 149–151°. The yield of  $\beta$ -isodurylic acid obtained was very small.

**$\alpha,\alpha,\alpha$ -Trichloro-2,4,6-trimethylacetophenone (V).**—A dilute solution of sodium hypochlorite was prepared by passing chlorine slowly into an ice-cold solution of 150 g. of sodium hydroxide in 1500 cc. of water. To this solution in a 2-liter flask was added 16.1 g. (0.1 mole) of acetomesitylene; the resulting mixture was stirred continuously for three days at room temperature. The heavy oil which was formed was extracted with ether, dried and distilled under reduced pressure. A yield of 22.5 g., or 88% of the theoretical, was obtained. The trichloro ketone boiled at 130–140° at 5 mm.

*Anal.* Calcd. for  $C_{11}H_{11}OCl_3$ : Cl, 40.1. Found: Cl, 39.8.

**$\alpha,\alpha,\alpha$ -Trichloro-2,4,6-trimethyl-3,5-dinitro-acetophenone (VI).**—One gram of  $\alpha,\alpha,\alpha$ -trichloro-2,4,6-trimethylacetophenone (V), prepared in the manner just described, was dropped slowly into 15 cc. of ice-cold fuming nitric acid (sp. gr. 1.60), the mixture being stirred continuously. After being allowed to stand for a short time in the cold, the solution was poured into a large amount of ice water and the precipitate was allowed to crystallize. The solid was filtered and recrystallized from alcohol. It separated in long, colorless needles melting at 100.1–100.6° (corr.); yield, 1.2 g. or 89% of the theoretical.

*Anal.* Calcd. for  $C_{11}H_9O_8N_2Cl_3$ : Cl, 29.9. Found: Cl, 29.9.

**$\alpha,\alpha,\alpha$ -Trichloro-2,4,6-trimethyl-3,5-dinitro-acetophenone (VI).** (Second Method.)—Two g. of dinitro-acetomesitylene was placed in a 300-cc. flask with 150 cc.

of sodium hypochlorite, prepared as described above. The reaction mixture was shaken occasionally during a period of two weeks, and was finally heated for about an hour on a steam-bath. After cooling, the precipitate was filtered and recrystallized from alcohol. It separated in long needles which proved to be identical with those prepared by the other method. The yield was 2 g. or 70% of the theoretical. A mixture of these crystals with a sample of  $\alpha,\alpha,\alpha$ -trichloro-2,4,6-trimethyl-3,5-dinitro-acetophenone (prepared by the first method) showed no lowering of the melting point.

### Summary

1. The cleavage of the carbon chain of carbonyl compounds under the influence of alkali is ascribed to the coördination of the carbonyl carbon atom with hydroxyl. It is assumed that the polarity of the bond between the carbonyl carbon atom and the  $\alpha$ -carbon atom is thus enhanced. In case the substituents on the  $\alpha$ -carbon atom are sufficiently "negative" dissociation occurs.

2. It is pointed out that, according to this theory, certain trihalomethyl ketones whose carbonyl groups do not undergo addition reactions should be stable to alkali.

3. Several such trihalomethyl ketones have been prepared and found to be unaffected by alkali.

4. These results strongly support the assumption that chain cleavage of this type is dependent on an *addition* reaction of the carbonyl group. That this is the addition of hydroxyl, as postulated by the theory here developed, seems probable.

URBANA, ILLINOIS

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[FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY]

## THE ESTIMATION OF SULFUR IN ORGANIC COMPOUNDS<sup>1</sup>

BY H. ZAHND AND H. T. CLARKE

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In 1923 Hoffman and Gortner<sup>2</sup> drew attention to the applicability to organic compounds of the method for estimating sulfur in biological material devised by Benedict<sup>3</sup> and modified by Denis.<sup>4</sup> This procedure which, in the hands of the biological chemist, has practically superseded the methods of Carius and of alkaline fusion, tends to give rise to mild explosions under conditions which cannot always be controlled. In the method described below this disadvantage is almost entirely eliminated by observing suitable precautions.

The process consists in the oxidation of organic matter by means of

<sup>1</sup> This work was aided by the Research Grant from the Chemical Foundation to the Department of Biological Chemistry.

<sup>2</sup> Hoffman and Gortner, *THIS JOURNAL*, **45**, 1033 (1923).

<sup>3</sup> Benedict, *J. Biol. Chem.*, **6**, 363 (1909).

<sup>4</sup> Denis, *ibid.*, **8**, 401 (1910).