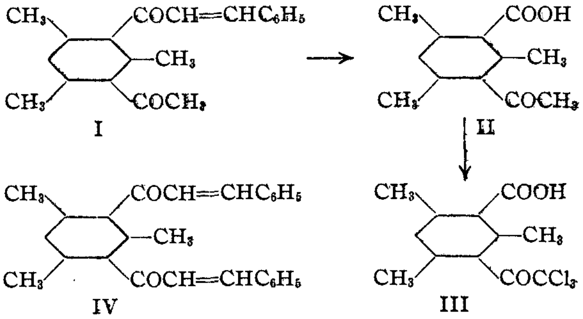
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Haloform Reaction. XIII. Trihalomethylketonic Acids of the Mesitylene Series

BY ROBERT JOHNSON AND REYNOLD C. FUSON

The retardation of the cleavage phase of the haloform reaction is most striking in the case of the hindered methylketonic acids.[1] Of these the most interesting one which has been studied so far is 3-acetyl-2,4,6-trimethylbenzoic acid (II). This acid has been synthesized from diacetomesitylene by conversion of one of the acetyl groups into a carboxyl group. Attempts to accomplish this by direct oxidation were unavailing.

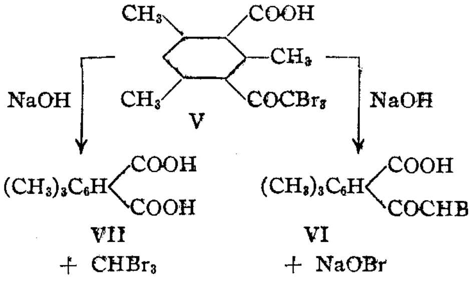


It was finally found that a monobenzal derivative (I) could be made in good yield and that by means of ozone this could be oxidized to the desired keto acid.

By the action of sodium hypochlorite and of sodium hypobromite on the keto acid the corresponding trichloromethyl (III) and tribromomethyl (V) ketonic acids were prepared *in alkaline media*. When an alkaline solution of II was mixed with a solution of the hypohalite the halogenation took place rapidly. In the case of V the sodium salt crystallized from the solution, in which it was only slightly soluble.

The free trihalomethylketonic acids, after being carefully purified, were redissolved in 5% sodium hydroxide solution at low temperatures. After five minutes the acids were recovered by acidification of the solutions and were found to be essentially unchanged. Moreover, these acids were sufficiently stable toward alkali to give satisfactory neutral equivalents when titrated with a standard solution of sodium hydroxide. However, in these titrations the end-point was not permanent. These results show that the trihalomethylketonic acids are gradually decomposed by alkali even in the cold. At higher temperatures cleavage to the corresponding dicarboxylic acid (VII) was rapid.

Yet, even under these conditions, the cleavage of the tribromo compound was very incomplete. It was discovered, however, that the cleavage could be effected much more readily and completely by the use of solutions of alkali *containing sodium hypobromite*. Still more striking was the fact that carbon tetrabromide was formed *even when no hypobromite was used*. These results demonstrate that the tribromomethylketonic acid undergoes two different types of reaction with alkali—one yielding VII and bromoform, and the other VI and sodium hypobromite. Carbon tetrabromide is then produced by the action of the hypobromite on the bromoform



This explanation has been verified by the isolation of the dibromo compound (VI) from the reaction mixture. The structure of this acid has been confirmed by the fact that with hypobromite it is converted into VII.

Experimental

Benzaldiacetomesitylene (I).—To a mixture of 100 g. of diacetomesitylene, 31 g. of sodium hydroxide, 145 g. of alcohol and 270 cc. of water was added gradually, with stirring, 33 g. of benzaldehyde. The addition was completed in the course of one hour and the stirring was continued for an additional six hours. A yellow insoluble mass separated. The mixture was diluted with an equal volume of water and the product was taken up in ether. Vacuum distillation of the residue obtained by evaporation of the ether gave 47 g. boiling at 155–190° (6 mm.), 63 g. boiling at 220–235° (6 mm.) and 14 g. of residue. From the second fraction by repeated recrystallization from methyl alcohol was obtained 30 g. of benzaldiacetomesitylene melting at 93–95°. After further recrystallization from petroleum ether the product melted at 95–96°.

---

[1] Bull and Fuson, THIS JOURNAL, 55, 3424 (1933); 56, 736 (1934).

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.1; H, 6.9. Found: C, 82.0; H, 7.1.

3-Acetyl-2,4,6-trimethylbenzoic Acid (II).—The benzaldiacetomesitylene was ozonized in 5-g. lots using carbon tetrachloride as solvent. The ozonide was decomposed by the addition of water and hydrogen peroxide. The solution was made alkaline and heated for several hours on a steam cone with excess hydrogen peroxide, cooled, and acidified. The crude acid obtained in this way was recrystallized from toluene. Fourteen grams of the benzal compound yielded 3.1 g. of the acid melting at 141–143°. After further recrystallization from water the product melted at 144–145°.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8; neut. equiv., 206.1. Found: C, 69.9; H, 6.9; neut. equiv., 207.7.

3-Tribromoacetyl-2,4,6-trimethylbenzoic Acid (V).—The methyl ketonic acid (II) was dissolved in 10% sodium hydroxide solution and this was added to a 10% solution of sodium hypobromite at 0°. After four minutes crystals began to form and at the end of ten minutes these were removed by filtration on a sintered glass funnel and washed with cold 20% sodium hydroxide solution. The sodium salt was decomposed with dilute sulfuric acid and the free acid separated on a filter. After repeated crystallization from aqueous methanol it melted at 189°, with decomposition.

Anal. Calcd. for $C_{12}H_{11}O_3Br_3$: C, 32.5; H, 2.5; Br, 54.1. Found: C, 32.5; H, 2.4; Br, 54.3.

3-Trichloroacetyl-2,4,6-trimethylbenzoic Acid (III).—Seven-tenths of a gram of the keto acid (II) was dissolved in 10% sodium hydroxide solution and this was added to 5% sodium hypochlorite solution at 0°. After fifteen minutes the solution was acidified with dilute sulfuric acid and the insoluble material was removed by filtration. After repeated recrystallization from aqueous methanol 0.53 g. of product was obtained, melting at 147–149°. Further recrystallization from a petroleum ether–ether mixture gave a product melting at 148–149°.

Anal. Calcd. for $C_{12}H_{11}O_3Cl_3$: C, 46.5; H, 3.6; Cl, 34.4. Found: C, 46.2; H, 4.3; Cl, 34.1.

Dibenzaldiacetomesitylene (IV).—To a mixture of 20 g. of diacetomesitylene, 10 g. of sodium hydroxide, 30 g. of alcohol and 90 cc. of water was added gradually, with stirring, 30 g. of benzaldehyde. The addition was completed in the course of one hour and the stirring was continued for several hours. A yellow insoluble mass separated. An additional 30 g. of alcohol was added and stirring was continued overnight. A solid separated. The solution was diluted with an equal volume of water and the product was taken up with ether. The residue obtained by evaporation of the ether was crystallized from methyl alcohol and from petroleum ether. A yield of 41% of the theoretical amount of dibenzaldiacetomesitylene was obtained; m. p. 133–135°. Further recrystallization gave a product melting at 134–135°.

Anal. Calcd. for $C_{27}H_{24}O_2$: C, 85.3; H, 6.3. Found: C, 85.0; H, 6.5.

2,4,6-Trimethylisophthalic Acid (VII).—Dibenzaldiacetomesitylene was ozonized in a manner similar to that described for benzaldiacetomesitylene. The crude acids, benzoic and 2,4,6-trimethylisophthalic acids, were recrystallized from water. Six grams of dibenzaldiacetomesitylene yielded 0.9 g. of VII, melting at 280°, with decomposition. After recrystallization from ethyl acetate the product melted at 289° (corr.), with decomposition. The melting point reported by Breed[2] for this acid is 283°, with decomposition.

Anal. Neut. equiv. calcd., 104.0; found, 105.0.

The Action of Alkali on 3-Trichloroacetyl-2,4,6-trimethylbenzoic Acid (III).—A small amount of the trichloro compound was dissolved in 10% sodium hydroxide solution and allowed to stand for fifteen minutes. Acidification gave a product melting at 289° (corr.), with decomposition. A mixed melting point with VII showed no depression.

A small amount of the trichloro keto acid was dissolved in 5% sodium hydroxide solution at 0° and was allowed to stand for five minutes before acidification. The recovered product showed no depression of the melting point when mixed with the trichloro keto acid.

The end-point in a titration with tenth-normal alkali shows a slight tendency to fade. The neutral equivalent found was 315.8 and that calculated 309.4.

The Action of Alkali and of Alkaline Hypobromite on 3-Tribromoacetyl-2,4,6-trimethylbenzoic Acid (V).—The tribromo keto acid was dissolved in 5% sodium hydroxide at 0° and stirred for five minutes. At the end of this time the solution was filtered and acidified. The crystals formed in the filtrate when mixed with the pure tribromo keto acid caused no depression of the melting point.

Two grams of V were placed in 75 cc. of 10% sodium hydroxide solution and agitated overnight. Agitation was necessary because the tribromo compound was only slightly soluble in strong alkaline solution. At the end of this time the carbon tetrabromide was removed by filtration. Carbon tetrabromide was identified by melting point and by a mixed melting point with an authentic specimen. The solution was diluted to 300 cc. and acidified and the solid material thus formed was collected on a filter. The solid was recrystallized twice from aqueous methanol to yield 0.5 g. of a product melting at 173.5–174.5°. This proved to be **2-dibromoacetyl-2,4,6-trimethylbenzoic acid** (VI).

Anal. Calcd. for $C_{12}H_{12}O_3Br_2$: C, 39.6; H, 3.3; Br, 43.9; neut. equiv., 363.9. Found: C, 39.3; H, 3.6; Br, 44.1; neut. equiv., 361.9.

A small amount of the dibromo compound was dissolved in a 10% sodium hydroxide solution and sodium hypobromite solution was added. A crystalline solid, presumably the tribromo compound, separated after several minutes. The mixture was agitated for several hours and carbon tetrabromide was removed by filtration. The filtrate was acidified and excess bromine was removed with bisulfite. The crystals thus formed were collected on a filter; m. p. 289° (corr.) with decomposition. A mixed melting point with 2,4,6-trimethylisophthalic acid showed no depression.

The filtrate obtained by filtration of the acidified alkaline solution was concentrated to a small volume and cooled. The solid which separated was dried and ex-

---

(2) Breed, "Bryn Mawr College Monographs," **1**, 1 (1901).

tracted with acetone. The residue obtained by evaporation of the acetone was crystallized twice from ethyl acetate to yield 0.1 g. of VII, melting at 289° (corr.), with decomposition. A mixed melting point with a sample of this acid obtained from the dibenzal compound showed no depression.

The end-point in a direct titration of V with 0.1 normal alkali is not permanent. The neutral equivalent found was 436.0 and that calculated was 442.8. The titration was also performed by adding a large excess of 0.1 normal alkali, allowing the solution to stand overnight and then back-titrating with 0.1 normal acid. In this manner one mole of V neutralized four moles of alkali.

Summary

3-Acetyl-2,4,6-trimethylbenzoic acid (II) has been prepared by ozonization of benzaldiacetomesitylene (I).

Hypohalites convert the acid into the corresponding trihaloacetyl compounds (III and V). These are sufficiently stable toward alkali to be titrated in cold solutions. Warm solutions of alkali cleave them to the corresponding dicarboxylic acid (VII).

The tribromo acid is partially hydrolyzed by alkali to give the corresponding dibromo compound (VI) and hypobromite. The latter acts upon the bromoform present to give carbon tetrabromide.

URBANA, ILLINOIS RECEIVED APRIL 13, 1934

NOTE

The Isomerization of *n*-Butyl Phenyl Ether

BY RICHARD A. SMITH

Straight chain alkyl phenyl ethers have not as yet been rearranged to substituted phenols with the aid of rearranging agents. Previous attempts in this direction have been unsuccessful. There is one reference to the action of very high temperatures on phenetole to yield ethylphenol.[1]

The author has described a satisfactory method of rearranging alkylphenyl ethers with anhydrous aluminum chloride.[2] By utilizing this method, it has been found possible to convert *n*-butyl phenyl ether to *o*- and *p*-butyl phenols. Interestingly enough, the yield of phenols is comparable to that in cases of branched chain isomerizations.

A more complete study of this phase of alkyl phenyl ether rearrangement is being conducted.

Experimental

***n*-Butyl phenyl ether** was prepared by the conventional method of the action of *n*-butyl bromide on the sodium salt of phenol in absolute alcohol: b. p. 206°, n_D^{26} 1.5019, d^{26} 0.9547. The agreement with data reported by other workers is satisfactory.[3]

***o*- and *p*-Butylphenols.**—One molar equivalent of anhydrous aluminum chloride was added in small portions to the phenyl ether. The heat generated was absorbed with an external cooling bath. The reaction mixture was allowed to stand for thirty-six hours at room temperature. The resultant products were hydrolyzed with ice and hydrochloric acid. The organic layer was separated and water washed. It was 95% soluble in 10% sodium hydroxide, from which it was precipitated with hydrochloric acid. The product was then water washed, dried with anhydrous sodium sulfate and separated into the two butyl isomers by distillation. There was a small quantity (approximately 5–10%) of higher boiling material—probably polyalkylated butylphenols: *o*-butylphenol, b. p. 238°, n_D^{22} 1.5205, d^{22} 0.973; *p*-butylphenol, b. p. 248°, n_D^{22} 1.5165, d^{22} 0.976.

The agreement with data reported by other workers is satisfactory.[4]

THE CHEMICAL LABORATORY
WASHINGTON SQUARE COLLEGE
OF NEW YORK UNIVERSITY
NEW YORK, N. Y.

RECEIVED APRIL 17, 1934

---

[1] Schering-Kahlbaum A. G., Austrian Patent 125,216.

[2] R. A. Smith, THIS JOURNAL, **55**, 849, 3718 (1933).

[3] Sekera and Marvel, *ibid.*, **55**, 375 (1933).

[4] Sandulesco and Girard, *Bull. soc. chim.*, [4] **47**, 1300 (1932).