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

THE REPLACEMENT OF HALOGEN BY HYDROGEN IN ALPHA HALO-KETONES UNDER THE INFLUENCE OF THE GRIGNARD REAGENT

BY C. HAROLD FISHER, THOMAS S. OAKWOOD AND REYNOLD C. FUSON

RECEIVED SEPTEMBER 18, 1930 PUBLISHED DECEMBER 18, 1930

The action of the Grignard reagent on certain alpha halo-ketones has been under investigation in this Laboratory in connection with the study of the coupling action of the Grignard reagent on certain types of halogen compounds.[1] The results obtained so far have been to some extent anticipated by Löwenbein and Schuster[2] in an article which has just appeared. For this reason our work, although not fully completed, is being reported in its present form.

In our work the original object in view was to extend if possible the coupling reaction to other types of active halogen compounds. Only the benzyl halides and their derivatives had been used in previous studies. Inasmuch as α-halo-ketones have a very reactive halogen atom, it seemed likely that the coupling reaction might take place when compounds of this type were treated with the Grignard reagent. Experiments with ω-bromo-acetophenone showed that the great rapidity with which the carbonyl group was attacked by the Grignard reagent precluded the possibility of testing the behavior of the α-halogen atom toward this reagent. It was found possible, however, to get around this difficulty by introducing substituents into the two ortho positions, thus effectively inhibiting the tendency of the carbonyl group to undergo addition reactions. Further, in order to avoid the possibility of enolization, the α-hydrogen atoms were replaced by methyl groups. The compound eventually obtained which fulfilled all of these requirements was α-3,5-tribromo-2,4,6-trimethylisobutyrophenone (III).

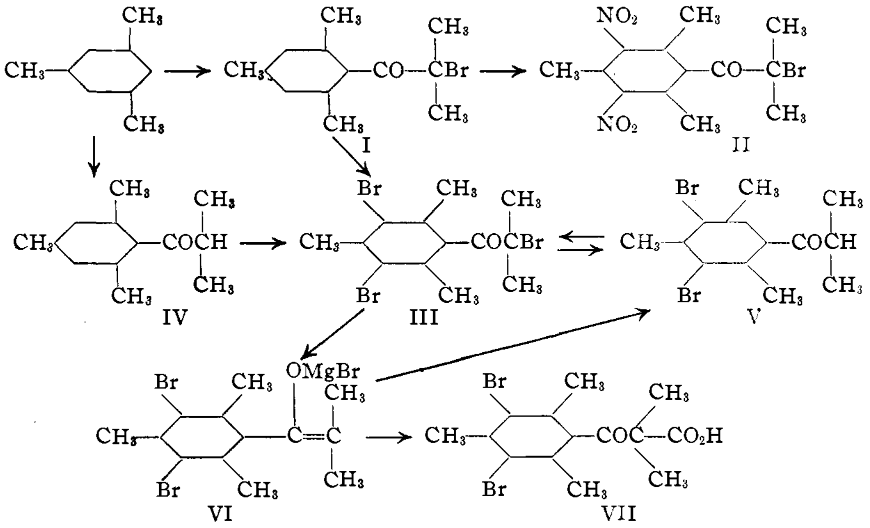
This compound was prepared in two ways. The method first used involved the synthesis of α-bromo-2,4,6-trimethylisobutyrophenone (I) from mesitylene and α-bromoisobutyryl chloride by use of the method of Friedel and Crafts. The monobromo compound was low-melting and for this reason difficult to study. Its dinitro derivative (II) was prepared as a check on the structure. By direct bromination of I was obtained the tribromo compound (III) which was used in the Grignard study. This compound was prepared more advantageously from isobutyrylmesitylene (IV) by direct bromination.

When this α-bromo ketone was treated with methylmagnesium chloride or ethylmagnesium bromide neither coupling nor alkylation was observed.

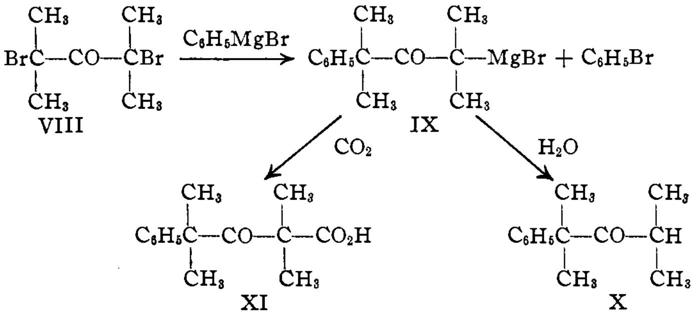
---

[1] For earlier papers in this field see Fuson, THIS JOURNAL, **48**, 830, 2681, 2937 (1926).

[2] Löwenbein and Schuster, *Ann.*, **481**, 106 (1930).



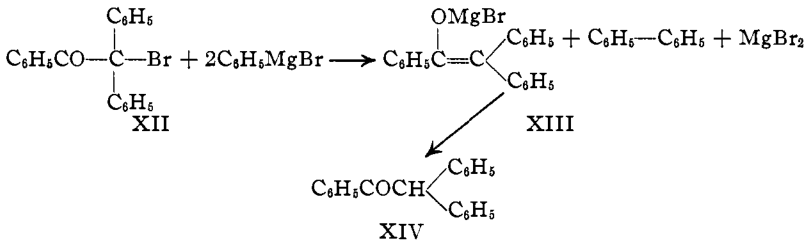
Instead the bromine was smoothly replaced by hydrogen. This result resembles that obtained by Umnova[3] who showed that when α,α'-dibromoisobutyrone (VIII) was treated with phenylmagnesium bromide there resulted a Grignard reagent having the formula IX. The simultaneous production of bromobenzene seems to establish this reaction as one of alkylation and radical interchange. The structure of IX was assigned on the basis of its reaction with water and with carbon dioxide followed by water. In the first case the product was α-phenylisobutyrone (X) and in the second, α,α,γ-trimethyl-γ-phenyl-β-keto-valeric acid (XI).



Löwenbein and Schuster, in the investigation mentioned above, worked with benzoyldiphenylmethyl bromide (XII). With phenylmagnesium bromide this compound reacted to give diphenyl and the bromomagnesium enolate of triphenylethanone (XIII). The last-named compound when treated with water gave triphenylethanone (XIV).

---

[3] Umnova, *J. Russ. Phys.-Chem. Soc.*, **45**, 881 (1913).



It will be noted that these authors write their intermediate compound (XIII) as an enolate instead of as a true Grignard reagent such as Umnova used to explain the reaction with carbon dioxide (IX). Our results in the present work with α,3,5-tribromo-2,4,6-trimethylisobutyrophenone seem to parallel those of Löwenbein and Schuster rather than those of Umnova. When treated with methylmagnesium chloride or with ethylmagnesium bromide, the tribromo compound (III) gave the enolate, VI. This when treated with water gave 3,5-dibromo-2,4,6-trimethylisobutyrophenone (V). The structure of V follows from the fact that bromination converted it into α,3,5-tribromo-2,4,6-trimethylisobutyrophenone, from which it could be regained by reduction with zinc dust. Treatment with carbon dioxide, however, failed to convert VI into α,α-dimethyl-β-keto-β-(2,4,6-trimethyl-3,5-dibromophenyl)-propionic acid (VII). The reaction of our intermediate compound (VI) with benzoyl chloride, carbon dioxide and other typical reagents for the detection of the Grignard reagent is being further investigated.

Experimental Part

α-Bromoisobutyrylmesitylene (I).—A mixture of 50 g. (0.22 mole) of α-bromoisobutyryl bromide, 26 g. (0.22 mole) of mesitylene and 170 g. of carbon disulfide was placed in a 500-cc. three-necked flask equipped with a mercury-sealed stirrer and a reflux condenser with a tube to carry off the evolved hydrogen chloride. Through the remaining side neck of the flask was added in small portions over a period of one and one-half hours 40 g. of anhydrous aluminum chloride. The reaction flask was kept in an ice-water bath and the stirring was continuous throughout the period of addition of the aluminum chloride and for an hour afterward. A dark red color developed during the addition; this color gradually faded to a light red toward the end of the reaction.

The product was poured on cracked ice and a vigorous reaction took place. The crude product when distilled came over at 145–175° at 24 mm. Redistillation gave 41 g. of a golden-brown oil boiling at 160–170° at 24 mm. The yield was 69.5% of the theoretical. On long standing the oil deposited crystals of the α-bromoisobutyryl mesitylene, melting at 27°.

Anal. Calcd. for $C_{13}H_{17}OBr$: Br, 29.79. Found: Br, 29.22.

α,3,5-Tribromo-2,4,6-trimethylisobutyrophenone (III).—The α-bromoisobutyrylmesitylene described above was brominated by treatment with bromine in ice water. The oil boiling at 160–170° at 24 mm. was covered by a layer of water and cracked ice and an excess of bromine was added. During the addition of the bromine the mixture was shaken vigorously. The oil became very viscous and finally set to a solid. This was treated with a solution of sodium bisulfite to remove excess bromine. The product crystallized from 95% alcohol in colorless needles melting at 106–107° (corr.). The yield was nearly quantitative.

Anal. Calcd. for $C_{13}H_{15}OBr_3$: Br, 56.2. Found: Br, 56.1.

α-Bromo-3,5-dinitro-2,4,6-trimethylisobutyrophenone (II).—Four and one-half grams of α-bromoisobutyryl mesitylene was added slowly with agitation to a mixture of 10 cc. of concentrated nitric acid and 15 cc. of concentrated sulfuric acid. The temperature rose but was kept below 60° by immersion of the container in cold water. On standing for fifteen minutes the emulsion which had formed separated into two layers; the upper layer was orange in color and contained a finely divided solid. The reaction mixture was poured into cold water; a white solid came out. Thick needles melting at 117.8–118.5° were obtained after several recrystallizations from alcohol.

Anal. Calcd. for $C_{13}H_{15}O_5BrN_2$: Br, 22.3. Found: Br, 22.4.

α,3,5-Tribromo-2,4,6-trimethylisobutyrophenone (III) (Second Method).—It was found that this preparation could be carried out more conveniently by direct bromination of isobutyrylmesitylene. The procedure used was essentially that described in the preparation by the first method. A mixture of the products from the two sources showed no depression of the melting point.

The Action of Methylmagnesium Chloride on α,3,5-Tribromo-2,4,6-trimethylisobutyrophenone.—A solution of 9.5 g. (0.022 mole) of the tribromo ketone in 125 cc. of ether was added dropwise and with stirring (mercury-sealed stirrer) to a three-fold excess of the Grignard reagent contained in a three-necked flask. During the addition, which required about thirty minutes, the reaction mixture boiled gently without external heating. When the addition was complete the stirring and refluxing (from external heat) were continued for two and one-half hours. Cold dilute hydrochloric acid was added; this caused violent refluxing if added rapidly. The clear, colorless ether layer was washed twice with water and the ether carried off by a stream of air, leaving a white solid. All of the solid dissolved in hot 70% alcohol. On cooling the solution deposited a crystalline solid which melted at 62–64°. Further recrystallization from methyl alcohol changed the melting point to 70–71° (corr.). This product was found to be 3,5-dibromo-2,4,6-trimethylisobutyrophenone (IV) by the reaction described below. The yield was 5.5 g. or 71% of the theoretical.

3,5-Dibromo-2,4,6-trimethylisobutyrophenone.—Five-tenths gram of the pulverized product and an excess of bromine were intimately mixed in a test-tube cooled by an ice–salt mixture. After ten minutes a solution of sodium bisulfite was added to remove excess bromine. After one recrystallization from alcohol 0.6 g. of a solid melting at 102–104.5° was obtained. This was shown to be α,3,5-tribromo-2,4,6-trimethylisobutyrophenone by the method of mixed melting points.

Anal. Calcd. for $C_{12}H_{16}OBr_2$: Br, 46.0. Found: Br, 45.7

Reduction of α,3,5-Tribromo-2,4,6-trimethylisobutyrophenone with Zinc and Acetic Acid.—The method used was similar to that which Stephen and Weizmann[4] used to reduce ω-chloro-2,4-dihydroxy-acetophenone. One and one-half grams of the tribromo ketone, 4 cc. of glacial acetic acid, 16 cc. of water, and 100 cc. of 95% ethyl alcohol were placed in a 200-cc. flask fitted with a reflux condenser, and the temperature of the water-bath surrounding the flask was brought to 60°. Five grams of zinc dust was added and the temperature of the water-bath maintained at 60° for one hour, when 16 cc. of water and 4 cc. of acetic acid were again added. The temperature was kept at 60° for five additional hours.

The zinc dust was filtered, part of the solvent evaporated and water added, which

---

[4] Stephen and Weizmann, *J. Chem. Soc.*, **105**, 1050 (1914).

caused the precipitation of a fine white solid. Two extractions with ether were made and the ether was allowed to evaporate. The residue after several recrystallizations from methyl alcohol melted at 69–70°. This was shown to be 3,5-dibromo-2,4,6-trimethylisobutyrophenone by the method of mixed melting points.

The Action of Ethylmagnesium Bromide on α,3,5-Tribromo-2,4,6-trimethylisobutyrophenone.—Several experiments similar to that described for methylmagnesium chloride were run with ethylmagnesium bromide. The tribromo compound was in all cases smoothly converted into the dibromo compound. In two runs the reaction mixture was treated for long intervals with carbon dioxide before being decomposed with water. The product was the same as in those runs in which no carbon dioxide was used. No acid could be isolated in any case.

Summary

α,3,5-Tribromo-2,4,6-trimethylisobutyrophenone (III) has been prepared by the bromination of isobutyrylmesitylene (IV) and of α-bromoisobutyrylmesitylene (I).

Treatment with methylmagnesium chloride or ethylmagnesium bromide transformed the tribromo compound (III) into an enolate (VI) which reacted with water to give 3,5-dibromo-2,4,6-trimethylisobutyrophenone (V).

The structure of the dibromo compound (V) was proved by its synthesis from III by zinc reduction and by the fact that bromination reconverted it into the tribromo compound.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORIES, PICATINNY ARSENAL]

THE NITRATION OF SYM.-DIPHENYLETHANE[1,2]

BY WM. H. RINKENBACH[3] AND H. A. AARONSON[4]

RECEIVED SEPTEMBER 19, 1930 PUBLISHED DECEMBER 18, 1930

Although various workers have reported the preparation and properties of a number of nitro derivatives of symmetrical diphenylethane (dibenzyl), it was considered advisable to carry out a more thorough investigation of the nitration of this compound. The object of this study was to determine the practicability of preparing the symmetrical hexanitro derivative by direct nitration, although it was considered probable that steric hindrance would prevent the formation of a high yield of hexanitrodiphenylethane.

Several dinitrodiphenylethanes are recorded in the literature, the 4,4′-dinitro compound being the most important. Stelling and Fittig[5] prepared this compound by the direct nitration of diphenylethane with nitric acid (sp. gr. 1.52) and reported the simultaneous formation of the 2,4′-

---

[1] Published by permission of the Chief of Ordnance, U. S. War Department.

[2] Work undertaken at the suggestion of Mr. Lambert Thorpe.

[3] Chief Chemist, Picatinny Arsenal, U. S. War Department.

[4] Assoc. Organic Chemist, Picatinny Arsenal, U. S. War Department.

[5] Stelling and Fittig, *Ann.*, **137**, 260 (1866).