

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Addition of Methylmagnesium Iodide to Benzalpropiofenone¹

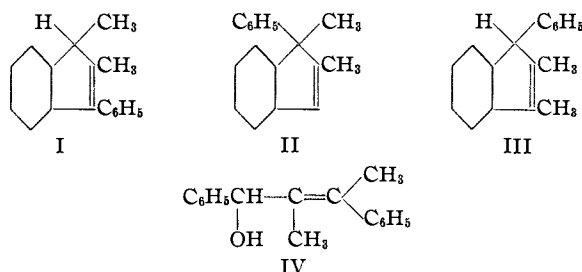
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The original purpose of this research was the synthesis of α,β -dimethylbenzalacetophenone by the method of Kohler,² the first step of which was to consist of a 1,4 addition of methylmagnesium iodide to benzalpropiofenone. As ethyl- and phenylmagnesium bromides were reported to give 100% 1,4-addition with this ketone,³ no difficulty was anticipated in adding methylmagnesium iodide in the same way, but the reaction took an entirely different course and no 1,4 addition product was obtained.

When an ethereal solution of benzalpropiofenone was added to methylmagnesium iodide, followed by decomposition of the metallic derivative in the usual way with iced hydrochloric acid, the sole product isolated (75% yield) was a white, crystalline hydrocarbon, $C_{17}H_{16}$. The formation of this product involved the addition of one molecule of the reagent, followed by the loss of water after hydrolysis

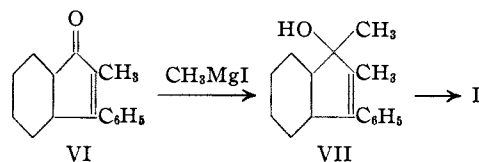
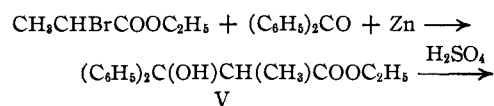


When oxidized with aqueous permanganate, this hydrocarbon gave *o*-benzoylbenzoic acid, which showed that ring closure had occurred when the molecule of water was eliminated and that the hydrocarbon was an indene derivative. Depending upon the mode of addition of methylmagnesium iodide to the unsaturated ketone, and whether or not the resulting hydroxy compounds were rearranged by acids, three structures for the indene were considered as possible. Indene I was derived from a primary 1,4 addition by elimination of water from the enol first formed; indene II was similarly derived from a primary 1,2 addition product, while indene III was derived from a primary 1,2 addition product after it had undergone an α - γ transposition (either as the hydroxy compound or as the chloride) to IV. Rearrangements of the indenenes themselves (such as I \rightarrow III) were not considered likely, for such rearrangements require basic media, and the reaction mixtures in these experiments were always neutral or acid. All of these indenenes



would give *o*-benzoylbenzoic acid on oxidation, and, since, in spite of many attempts, it was not possible to isolate any definite oxidation products intermediate between the hydrocarbon and *o*-benzoylbenzoic acid, oxidation alone was not sufficient to determine the structure.

Structure I was considered most likely, as a 1,4 addition of the Grignard reagent was believed to have occurred. Consequently, the synthesis of I was undertaken, as follows



The synthesis was successful as far as VII, but it was not possible to convert VII to I by any of the methods tried. Reduction, catalytically or with hydriodic acid, gave an uncrystallizable oil; and cleavage of the methyl ether of VII with sodium amalgam could not be tried because the action of methyl alcohol and sulfuric acid upon VII gave only resins. After the failure of this first synthesis it was decided to synthesize III, hoping that this compound could be rearranged into I by the action of bases.⁴ This synthesis was successful, and was carried out as shown.

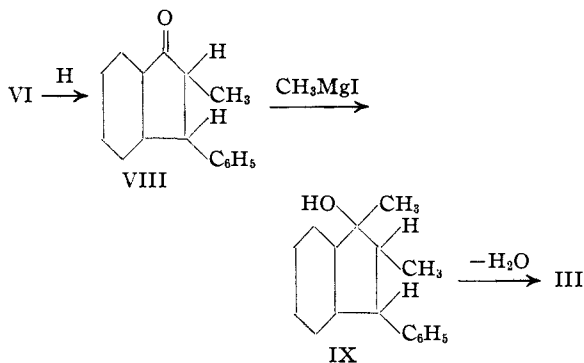
The final product (III) proved, however, to be *identical* with the hydrocarbon $C_{17}H_{16}$ obtained from the reaction between methylmagnesium iodide and benzalpropiofenone. This result can only be explained by an initial 1,2 addition of the Grignard reagent to the unsaturated ketone.

(1) Based on the thesis of L. I. Hanson, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the M.S. degree, June, 1935.

(2) Kohler, *Am. Chem. J.*, **31**, 652 (1904).

(3) Kohler, *ibid.*, **38**, 511-561 (1907).

(4) Koelsch, *THIS JOURNAL*, **56**, 1337 (1934).



After the structure of the hydrocarbon became known, the addition of methylmagnesium iodide to benzalpropiophenone was repeated, but the addition product^{4a} was decomposed with iced ammonium chloride in place of hydrochloric acid. The product was a colorless oil which showed no carbonyl reactions, nor could it be converted into a carbonyl compound with acids or bases. With methyl alcohol containing a few drops of hydrochloric acid, the oil gave the indene quantitatively, while sodium acetate, acetic anhydride or bases produced an apparently different (less soluble) oil. When the oil was treated with methylmagnesium iodide, one equivalent of methane was evolved, indicating one hydroxyl group, but no benzoate could be obtained. On oxidation the oil gave benzoic acid and acetophenone, but no *o*-benzoylbenzoic acid. The oil was not stable, gradually changing on standing to yellow, then red, and becoming insoluble in hot alcohol. No (enolic) peroxides of any sort were formed,⁵ although several attempts were made to obtain them. A great deal of decomposition resulted when the oil was distilled, even when an inert atmosphere and low pressures were used, and the distillates consisted entirely of thick, green, insoluble oils.

All these facts lead to the conclusion that the primary product of the Grignard reaction is the unsaturated tertiary alcohol $\text{C}_6\text{H}_5\text{CH}=\text{C}(\text{CH}_3)\text{CC}_6\text{H}_5(\text{CH}_3)\text{OH}$ (X) formed by 1,2 addition. If the metallic derivative is decomposed in the absence of acids, this alcohol can be obtained as a yellow oil; but if hydrochloric acid is present, this substance (or more likely the chloride) undergoes an α - γ transposition to give IV (or the corresponding chloride) and this then loses water (or the chloride loses hydrogen chloride) to give the

(4a) The addition product was inert toward an ethereal solution of bromine.

(5) Kohler, *Am. Chem. J.*, **36**, 189, 192 (1906).

indene III. The changes in X on standing or on distillation are probably due to elimination of water from X to give a butadiene derivative which polymerizes to the thick oils.

These results show that there may be considerable differences between methylmagnesium iodide and other Grignard reagents in their modes of addition to certain conjugated systems, for while ethyl- and phenylmagnesium bromides both give 100% 1,4 addition with benzalpropiophenone, methylmagnesium iodide gives, in 75% yield, a product derived from a primary 1,2 addition, and no detectable amount of any product formed by 1,4 addition.⁶

Experimental Part

Benzalpropiophenone was prepared by the method described by Abell⁷ and by Kohler.² In half molar runs the yield was 96%. The product was a light yellow oil, b. p. 212–214° at 25 mm., which gave a phenylhydrazone of m. p. 127–128°.

1,2-Dimethyl-3-phenylindene (III).—Benzalpropiophenone was added to methylmagnesium iodide essentially in the manner described by Kohler.⁸ The addition product was decomposed with iced hydrochloric acid, the solution extracted several times with ether, the ethereal layers dried over calcium chloride and the solvent evaporated. The product was obtained as a red oil, which solidified on standing. Recrystallized from alcohol, the solid melted at 68–69° and boiled at 145–153° under 4 mm. The yields varied from 68 to 75%, depending upon the size of the runs (0.023 to 0.21 molar).

Anal. Calcd. for $\text{C}_{17}\text{H}_{16}$: C, 92.72; H, 7.27; mol. wt., 220. Found: C, 92.31; H, 7.23; mol. wt. (Rast), 224, 217.

Oxidation.—The indene (2 g.) was refluxed for three hours with 100 cc. of 2% aqueous potassium permanganate. The hot solution was filtered, cooled, acidified and extracted with ether and the ether allowed to evaporate spontaneously. There remained 1.5 g. of a red sirup, from which 1 g. of *o*-benzoylbenzoic acid was obtained. This was identified by the m. p. (126–127°); the m. p. of the methyl ester (79–80°); and the formation of anthraquinone (m. p. 281–282°) on treatment with 80% sulfuric acid. Various other oxidizing agents were tried, as were varying concentrations of the same oxidizing agent. All procedures gave the same red sirup, from which nothing but *o*-benzoylbenzoic acid could be obtained.

1,3-Diphenyl-2-methylbutene-1-ol-3 (X).—The Grignard reaction was carried out as before, using 0.045 mole

(6) Kyriakides, *THIS JOURNAL*, **36**, 661 (1914) [see also Gry, *Bull. soc. chim.*, [4] **3**, 377 (1908)] reported that ethylidene acetone, with methylmagnesium iodide, reacted in an analogous manner. The product was largely (80% yield) the unsaturated tertiary alcohol formed by 1,2 addition, and very little of the saturated ketone (1,4 addition) was obtained. Ethylidene acetone was reported by Kohler to give 75% 1,4 addition with ethylmagnesium bromide, 40% 1,4 addition with phenylmagnesium bromide, and 75% 1,4 addition with methylmagnesium bromide [*Am. Chem. J.*, **38**, 511 (1907)].

(7) Abell, *J. Chem. Soc.*, **79**, 934 (1901).

(8) Kohler, *Am. Chem. J.*, **31**, 652, 657 (1904).

(10 g.) of benzalpropiophenone, and the addition product^{4a} was decomposed with iced ammonium chloride. The mixture was extracted with ether, the ether extract washed thoroughly with ice water and dried over calcium chloride. The ether was then removed by applying suction. The residue was a pale yellow (almost colorless) oil which weighed 9.5 g. (91%). The color deepened somewhat within a few hours, and after several days it became red. When colorless to yellow, 1 g. of the oil was soluble in 5 cc. of hot alcohol; after changing to red, 100 cc. of hot alcohol was required to dissolve 1 g.

Anal. (Benzene solution dried over "drierite" and the solvent removed *in vacuo*.) Calcd. for $C_{17}H_{18}O$: C, 85.7; H, 7.57. Found: C, 85.01; H, 7.13.

No peroxide was formed when the procedure was carried out as directed by Kohler,⁵ nor could the oil be benzoylated by the Schotten-Baumann method, the method of Einhorn,⁹ or by the action of benzoyl chloride upon the intermediate magnesium derivative.^{2,5}

The substance liberated one equivalent of methane when treated with methylmagnesium iodide, but it gave no precipitate with copper acetate, nor any coloration with ferric chloride. It also failed to react with phenyl isocyanate, and was completely inert toward hydroxylamine and semicarbazide.

When 1 g. of the oil was refluxed for an hour in 15 cc. of methanol containing a few drops of concentrated hydrochloric acid, the indene III was formed quantitatively; when treated with alkali, the product was a red, insoluble oil.

When oxidized by permanganate in water or in acetone, or when ozonized, the products were benzoic acid and acetophenone (semicarbazone, m. p. 197–199°).

The substance decomposed on distillation, over half of it forming a non-volatile red resin. The distillate was a green oil which came over at 135–138° under 12 mm. This green oil did not react with hydroxylamine. On oxidation with aqueous permanganate, the green oil gave oily products from which a little *o*-benzoylbenzoic acid was isolated.

Ethyl β -Hydroxy- β,β -diphenyl- α -methylpropionate (V).—This substance was prepared by the method of Rupe, Steiger and Fiedler.¹⁰ From 20 g. of benzophenone, and 24 g. of ethyl α -bromopropionate, the yield of pure V was 18 g. (60%). Crystallized from alcohol, the product melted at 101–102°, as reported by Rupe, Steiger and Fiedler.

2-Methyl-3-phenylindone (VI).—This substance was prepared from V by the action of sulfuric acid according to the procedure of Rupe, Steiger and Fiedler,¹⁰ as modified by Bergmann and Weiss.¹¹ The yield from 20 g. of V was 16 g. (96%). The indone crystallized from alcohol in orange leaflets, m. p. 83–84°, and gave an orange semicarbazone, m. p. 198–200°. These melting points are in agreement with those reported in the literature.

(9) Einhorn and Hollandt, *Ann.*, **301**, 95 (1898).

(10) Rupe, Steiger and Fiedler, *Ber.*, **47**, 63–75 (1914).

(11) Bergmann and Weiss, *Ann.*, **480**, 64–75 (1930).

1,2-Dimethyl-3-phenylindene-1 (VII).—The indone VI was added to two moles of methylmagnesium iodide¹² at room temperature. The product was isolated in the usual way. Crystallized from alcohol containing a little water, it was white and melted at 107–109°. The yield was 14 g. from 15.3 g. of the indone (87%).

Anal. Calcd. for $C_{17}H_{18}O$: C, 86.43; H, 6.77. Found: C, 86.24; H, 6.89.

The indeneol was converted to an amorphous material by boiling it with hydriodic acid in acetic acid and no reduction product was obtained. Catalytic hydrogenation (low pressure) with the platinum oxide catalyst of Adams and Shriner was tried, but the indeneol was recovered unchanged. When the indeneol (2 g.) was boiled for half an hour with methyl alcohol (65 cc.) and sulfuric acid (2 cc.), the product was an insoluble resin, and the same result was obtained when an attempt was made to prepare the ether using dimethyl sulfate and alkali.

2-Methyl-3-phenylindane (VIII).—The indone VI (5 g.) was reduced¹³ by refluxing it for three hours with acetic acid (125 cc.), constant boiling hydriodic acid (25 cc.), and red phosphorus (10 g.). The mixture was filtered while hot, the filtrate cooled and extracted with ether, the ether layer washed with bicarbonate, dried over calcium chloride and evaporated. The residue, crystallized from petroleum ether or methanol, melted at 64–65°, as reported in the literature; yield 3 g. (60%).

1,2-Dimethyl-3-phenylindanol-1 (IX).—The indanone VIII (6.5 g., 0.023 mole) in ether (35 cc.) was added slowly to the Grignard reagent prepared from 1.14 g. (0.046 mole) of magnesium, 6.6 g. (0.046 mole) of methyl iodide and 40 cc. of ether. After the addition, the mixture was refluxed for half an hour and the product was then worked up in the usual way. The substance crystallized from alcohol containing a little water in white, cubic crystals, m. p. 101–102°; yield 5 g. (62%).

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.75; H, 7.56. Found: C, 85.57; H, 7.46.

1-Phenyl-2,3-dimethylindene (III).—The indanol IX was dehydrated by refluxing 2 g. of it for ten minutes with acetic acid (50 cc.) and sulfuric acid (2 cc.). The yield was quantitative. Crystallized from alcohol, it melted at 68–69°, and mixtures of varying proportions of the synthetic indene and the product obtained from methylmagnesium iodide and benzalpropiophenone all melted at 68–69°.

Anal. Calcd. for $C_{17}H_{16}$: C, 92.72; H, 7.27. Found: C, 92.86; H, 7.26.

Summary

Methylmagnesium iodide has been added to benzalpropiophenone. The reaction gave, in 75% yield, an indene derived from a primary 1,2 addition product. No detectable amount of any product formed by 1,4 addition was found.

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(12) Stoermer and Laage, *Ber.*, **50**, 982 (1917).

(13) Bergmann and Taubadel, *ibid.*, **65**, 467 (1932).