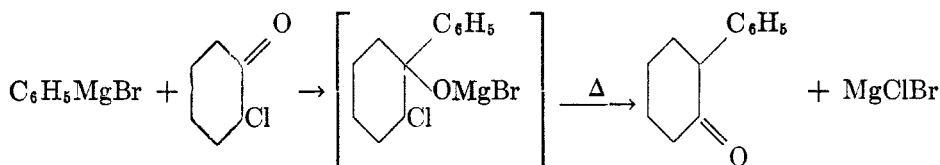


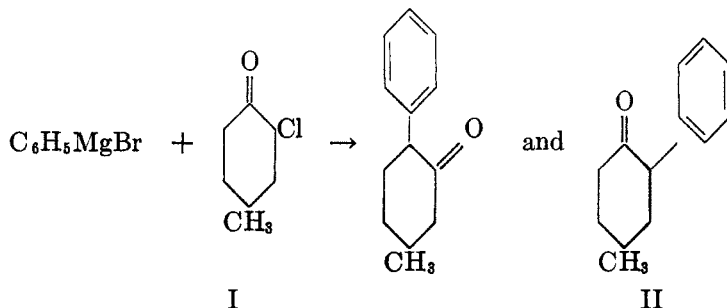
THE REACTION OF PHENYLMAGNESIUM BROMIDE WITH
2-CHLORO-4-METHYLCYCLOHEXANONE¹MELVIN S. NEWMAN AND WILLIAM T. BOOTH, JR.²*Received June 5, 1947*

In previous research on the synthesis of hydroaromatic phenanthrene derivatives, 2-chlorocyclohexanone was reacted with phenylmagnesium bromide to yield 2-phenylcyclohexanone (1). It is well known that this result is not produced by a direct replacement of the chlorine atom by phenyl, but rather by an addition of the Grignard reagent to the carbonyl group followed by loss of magnesium halide, as follows:



It is not known whether the phenyl group in the ketonic product is attached to the carbon which originally formed the carbonyl group or to the carbon which was linked to the chlorine. In this case it is unimportant, as the structure of the final product is the same in either case. However, should there be another substituent in the ketonic ring, different products would result. The object of this investigation was to examine this phase of the reaction.

It has been shown that the reaction of alkylated 2-chlorocyclohexanones with alkyl Grignard reagents results in products in which the entering alkyl group is attached to the carbon which was attached to the chlorine (2). Since we were more interested in aryl Grignard reagents, we have studied the reaction of phenylmagnesium bromide with 2-chloro-4-methylcyclohexanone. The products, I and II, which might be formed are shown below.



¹ The material herein presented was contained in the Ph.D. thesis of W. T. B., Ohio State University, March 1947.

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The product obtained proved to be a mixture of ketones whose composition was exceedingly difficult to determine. After reduction, dehydration, dehydrogenation, and oxidation, a mixture of approximately three parts of *m*-phenylbenzoic acid and one part of *p*-phenylbenzoic acid was obtained. Because of losses along the way, this ratio is only an approximation of the quantities of I and II originally formed. However, the fact that a mixture of isomers was produced proves that the bromomagnesium derivative of the 1-phenyl-2-chloro-4-methylcyclohexanol initially formed in the Grignard reaction rearranges in part to produce a product in which the phenyl group is attached to the carbon which originally held the chlorine. For this reason, the synthetic value of this reaction is considerably decreased.

Our reaction series was carried out with 2-chloro-4-methylcyclohexanone which was probably almost entirely one of the inactive isomers. However, in view of the previous work on isomeric alkylchloro ketones (2), it is likely that a similar result would have been obtained if the other isomer had been used.

EXPERIMENTAL³

2-Chloro-4-methylcyclohexanone. 4-Methylcyclohexanone was chlorinated essentially as described for cyclohexanone (1) to yield 73% of chlorinated ketone together with 25% of recovered ketone. The product was separated into two fractions, b.p. 76–78° and 96–98° at 10 mm., by distillation. The lower-boiling isomer forms about two-thirds of the freshly prepared product but on heating and standing the proportion of the higher-boiling isomer rises to about 75%.⁴

Phenylmethylcyclohexanones. To a solution of 600 cc. of 2 *M* phenylmagnesium bromide was added with cooling 177 g. (1.2 moles) of lower-boiling chloro ketone. After stirring at room temperature for one hour, 600 cc. of xylene was added and the ether was removed by distillation. The xylene solution was refluxed for eight hours during which it changed from a clear orange solution to a semi-solid purple mass. After hydrolysis with ammonium chloride solution there was isolated 150 g. (67%) of phenylmethylcyclohexanones, b.p. 125–135°, at 3 mm. On redistillation, the majority boiled at 116–117° at 1 mm.

Anal.^a Calc'd for C₁₅H₁₈O: C, 82.9; H, 8.6.

Found: C, 83.1; H, 8.9.

The 2,4-dinitrophenylhydrazone of the ketone mixture was prepared in 95% yield. After several recrystallizations, a fraction, m.p. 117–121°, was obtained as bright orange-red plates. The entire remaining derivative was collected, and melted over the range 89–112°.

Anal. Calc'd for C₁₅H₁₆N₄O₄: C, 61.9; H, 5.5; N, 15.2.

Found (for 117–121° crystals):^b C, 62.3, 62.3; H, 5.6, 5.7; N, 15.1, 15.3.

(for 89–112° crystals):^a C, 61.6; H, 5.5.

Phenylmethylcyclohexanols. The ketone mixture was reduced by the Meerwein-Ponndorf method to yield 98% of a mixture of alcohols, b.p. 129–130° at 4 mm. or 277° at 746 mm.

Anal.^a Calc'd for C₁₅H₁₈O: C, 82.0; H, 9.5.

Found: C, 81.6; H, 9.5.

Methylbiphenyls. The above alcohol mixture was treated with thionyl chloride in pyridine-ether, and the whole refluxed for one hour. The phenylmethylcyclohexene mixture, b.p. 105–106° at 2 mm., was obtained in 88% yield. By heating 12.9 g. of this mixture with

³ All melting points corrected, boiling points uncorrected. Analyses marked ^a by the Arlington Laboratories, Fairfax, Virginia; marked ^b by W. J. Polglase, Ohio State University.

⁴ Godchot and Bedos (2b) reported the boiling points of the isomers as 80–82° and 110–112° at 12 mm., but made no mention of their ratio.

4.8 g. of sulfur from 200° to 240° during three hours there was obtained 7.5 g. (60%) of a mixture of methylbiphenyls, b.p. 132-133° at 9 mm., 264-265° at 739 mm. For comparison ortho-, meta-, and para-methylbiphenyl were synthesized in 8, 6, and 6% yields respectively by the Gomberg method (3, 4). The boiling point of the unknown mixture of biphenyls corresponded to that of the meta or para isomer but differed from the ortho (b.p. 125° at 9 mm., 251° at 739 mm.). Attempts to prepare the solid 4-nitro-4'-methylbiphenyl (3) or 4,4'-dinitro-3'-methylbiphenyl (5) from the methylbiphenyl mixture were unsuccessful.

Preparation and separation of phenylbenzoic acids (6). To a solution of 14.2 g. of potassium permanganate in 350 cc. of water was added 5 g. of the methylbiphenyl mixture, and the whole was refluxed until the permanganate was decolorized. The acid fraction thus produced was separated, and the neutral portion refluxed again with a solution of 5.6 g. of potassium permanganate in 125 cc. of water. There was thus obtained 3.6 g. (61%) of acid, m.p. 128-158°. An ether solution of one gram of the acids was shaken with 10% sodium carbonate solution. The insoluble sodium salt was collected, washed with ether, and acidified to yield 0.18 g. of *p*-phenylbenzoic acid, m.p. 222-224°. From the water-soluble sodium salts was obtained 0.70 g. of acid mixture, m.p. 143-158°. Recrystallization yielded mostly *m*-phenylbenzoic acid, m.p. 158-160°.

SUMMARY

It has been shown that when phenylmagnesium bromide reacts with 2-chloro-4-methylcyclohexanone, the final product is a mixture of 2-phenyl-4-methylcyclohexanone and 2-phenyl-5-methylcyclohexanone.

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