

160°. ^{3,4} The dihydroxyamine hydrochlorides are more hygroscopic and difficult to crystallize than the methoxy amines. The crystalline condition of the hydrochloride has much to do with its deliquescence. When alcohol-ether cannot be used for crystallization, alcohol-benzene, alcohol-toluene, or ethyl-acetate-alcohol may be used. The usefulness of the solvent varies with the amine hydrochloride even in such a closely related group of isomers as reported here.

The author wishes to thank Dr. Earl Pierson, Dr. John P. Lambooy and Dr. William E. Burt for their assistance while holders of Kalamazoo College Fellowships and Mr. Harold Emerson and Mr. William A. Struck for the micro analyses.

Summary

All of the nuclear dimethoxy- and dihydroxy- β -phenyl-*n*-propylamines and their hydrochlorides have been prepared. The properties are reported for the cinnamic acids, hydrocinnamic acids and hydrocinnamides used in the preparation of these amines as well as the syntheses of many of the intermediates used in their preparation. The hydrolysis and methylation of an hydroxy-4-methylcoumarin always gave the *trans* form of the resulting dimethoxy- β -methylcinnamic acid.

KALAMAZOO, MICHIGAN

RECEIVED AUGUST 1, 1942

[CONTRIBUTION FROM THE SANDERS LABORATORY OF CHEMISTRY, VASSAR COLLEGE]

The Reaction of *n*-Butylmagnesium Bromide with Some Aromatic Ketones^{1,2}

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Since *n*-butyl bromide can be prepared by students in good yield and reacts readily with magnesium to give a Grignard reagent, we had hoped to work out a series of student preparations by adding this Grignard reagent to a ketone and dehydrating the resulting tertiary alcohol to the corresponding unsaturated compound. This purpose was not achieved, but several new compounds were prepared in the course of the studies. Four ketones were selected for study: acetophenone, benzophenone, benzil and desoxybenzoin.

A. Acetophenone.—The reaction of acetophenone and *n*-butylmagnesium bromide gave good yields (72–80%) of the expected tertiary alcohol, 2-phenylhexanol-2 (I). This tertiary alcohol was very resistant to complete dehydration, but was finally transformed into the unsaturated hydrocarbon, 2-phenylhexene-2 (II), by heating with Lucas reagent. The position of the double bond was established by oxidation to acetophenone and *n*-butyric acid. The same results were obtained whether the oxidizing agent was potassium permanganate in sulfuric acid or chromium trioxide in acetic acid.

B. Benzophenone.—The reducing action of aliphatic Grignard reagents on benzophenone has

(1) Presented before the Organic Division of the American Chemical Society, Buffalo, September 7, 1942.

(2) Abstracted from the theses submitted by Mary Elizabeth Saeger and Florence E. Warneke in partial fulfillment of the requirements for the degree of Master of Arts at Vassar College.

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been studied by several workers.⁵ Schlenk and Bergmann⁶ obtained impure diphenyl-*n*-butylcarbinol by the reaction of phenylmagnesium bromide on ethyl *n*-valerate. It was mixed with the dehydration product and was easily converted into the unsaturated hydrocarbon. The two reactions which we carried out gave no tertiary alcohol and no unsaturated hydrocarbon. Benzohydrol (17 and 30%) was obtained. The remaining oils were distilled under reduced pressure and a yield of 5.6% of dibenzylhydril ether separated from the residue (above 270°, 42 mm.). Analyses of this compound agreed closely with the calculated values. Dibenzhydril ether had previously been reported by Kharasch and Weinhouse⁵ as resulting from the reaction of allylmagnesium bromide on benzophenone.

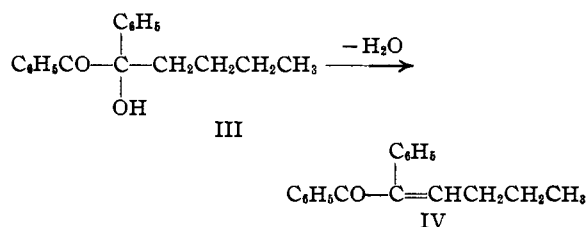
C. Benzil.—The reaction of *n*-butylmagnesium bromide on benzil gave small yields of solid products regardless of the variations in procedure. Both addition and reduction occurred. The reduction product, benzoin, was obtained in seven of the ten reactions in yields varying from 0.5 to 13.0%. The mono-addition product 1,2-diphenylhexanol-2-one-1 (II) was obtained in all ten reactions in yields varying from 0.5 to 5.6%. A solid which was possibly the di-addition product (V) was obtained twice in very small yields. Benzoic acid was obtained after the oily

(5) Blicke and Powers, *THIS JOURNAL*, **51**, 3378 (1929); Noller and Hilmer, *ibid.*, **54**, 2503 (1932); Kharasch and Weinhouse, *J. Org. Chem.*, **1**, 209 (1936).

(6) Schlenk and Bergmann, *Ann.*, **479**, 42 (1930).

mixtures were exposed to the light for some time. Under these conditions benzil decomposes to form benzoic acid.⁷ The only generalization which can be drawn from the results of the ten reactions is that the yield of mono-addition product (III) was smaller when a large excess of *n*-butylmagnesium bromide was used. The highest yields were obtained when 0.2 mole of benzil was added to 0.5 mole of *n*-butylmagnesium bromide.

Dehydration of the mono-addition product (III) by refluxing with Lucas reagent gave a liquid unsaturated ketone (IV) whose structure was established by oxidation to benzil and *n*-butyric acid.



Attempts to prepare the di-addition product by the reaction of *n*-butylmagnesium bromide on the mono-addition product were not successful.

D. Desoxybenzoin.—No addition products were obtained from the reaction of *n*-butylmagnesium bromide on desoxybenzoin, but various reduction products were isolated in very small yields. The product obtained in the largest amounts was stilbene, which would result from reduction of the desoxybenzoin followed by the loss of a molecule of water. It was obtained in three of the four reactions in yields of 2.5, 5.3 and 7.4%. Desoxybenzoin pinacol (m. p. 175°) was obtained in two reactions, but the total yield was only 0.3 g. It was identified by a mixed melting point with a known sample of the pinacol. A compound thought to be the pinacolone (VI) was obtained in two reactions, the total yield being 1%. All attempts to rearrange the pinacol were unsuccessful and the amount of the compound VI available was too small to make structure proof possible. The formation of a pinacolone would be interesting, for, although the pinacol has been known since 1870, no mention of the pinacolone could be found. Orechoff⁸ dehydrated the pinacol by boiling it with acetyl chloride, a treatment known to rearrange many pinacols, and recorded the formation of 1,2,3,4-tetraphenylbutadiene-1,3 and other products.

(7) Klinger, *Ber.*, **19**, 1864 (1886).

(8) Orechoff, *ibid.*, **47**, 91 (1914).

Experimental

General Procedure.—Since the variations in length of time of heating the reaction mixtures, variations in the kind and amount of solvent used to dissolve the ketones and decomposition of the magnesium complex with dilute sulfuric acid or with ammonium chloride solution seemed to have no effect on the kind or amount of resulting products, the individual experiments will not be described.

n-Butylmagnesium bromide was prepared in the usual way from 0.5 mole of *n*-butyl bromide. Slightly less than the calculated amount of the ketone was dissolved in either benzene or ether and dropped slowly into the Grignard solution. After standing or being heated for varying lengths of time the magnesium complex was decomposed, the organic material was extracted with ether, and most of the solvent was removed on the steam-bath. If solid separated on standing, it was filtered and recrystallized from appropriate solvents. When no more solid formed, the oils were distilled under reduced pressure. Solid which formed in any of the fraction was then removed and recrystallized. Many of the fractions have not solidified after standing for over a year.

2-Phenylhexanol-2, I.—One refractionation gave the pure alcohol, b. p. 123–124° (9 mm.); *d*₂₅ 0.954. It was colorless and decomposed partially when distilled at atmospheric pressure.

Anal. Calcd. for C₁₂H₁₈O: C, 80.85; H, 10.18; mol. wt., 178. Found: C, 80.67; H, 10.15; mol. wt., 178.

2-Phenylhexene-2, II.—Many attempts were made to dehydrate 2-phenylhexanol-2 and none of them were entirely successful. Distillation at atmospheric pressure resulted in the partial decomposition of the alcohol. Samples of the alcohol (20–25 g.) were refluxed for two hours with 75 ml. of 20% sulfuric acid and with 20 g. of fused potassium bisulfate, for four hours with 10 g. of fused zinc chloride and with 50 g. of acetic anhydride, and for eight hours with a trace of iodine. The alcohol was dropped on anhydrous cupric sulfate at 230°. Analyses of the products from all of these reactions showed a percentage of carbon intermediate between the values calculated for the alcohol and for the unsaturated hydrocarbon. The best results were obtained by refluxing the alcohol with an equal weight of Lucas reagent for thirty minutes. After separation, washing with water and drying, the product boiled 210–230° with the main fraction at 223–226°. It decolorized bromine readily.

Anal. Calcd. for C₁₂H₁₆: C, 89.94; H, 10.06; mol. wt., 160. Found: C, 87.13; H, 9.87; mol. wt., 161.

1,2-Diphenylhexanol-2-one-1, III.—This compound is a white solid melting at 124°. When crystallized from a benzene-petroleum ether mixture or from 50% alcohol it forms long fine needles. The dehydration is described below. The starting material was recovered unchanged after attempts to prepare the di-addition product by treating 0.004 mole of this mono-addition product with 0.04 mole of *n*-butylmagnesium bromide. The reaction was forced by refluxing the reactants in *n*-butyl ether for five hours.

Anal. Calcd. for C₁₈H₂₀O₂: C, 80.56; H, 7.51; mol. wt., 268. Found: C, 80.13; H, 8.44; mol. wt., 273.

1,2-Diphenylhexene-2-one-1, IV.—This compound was prepared by the dehydration of 1,2-diphenylhexanol-2-

one-1. Treatment of the alcohol with gaseous hydrochloric acid and refluxing it with a trace of iodine in glacial acetic acid failed to bring about the expected dehydration. After repeated trials had failed to produce any solid material from the products of the reaction of the alcohol with Lucas reagent, the resulting liquid was distilled at atmospheric pressure. In an actual preparation of the unsaturated compound, 2 g. of the alcohol was boiled for six hours with 30 ml. of Lucas reagent. After washing with water and drying, the yield was almost 2 g. of a liquid boiling 288–290°. It decolorized bromine readily.

Anal. Calcd. for $C_{13}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.28; H, 7.23.

5,6-Diphenyldecandiol-5,6, V.—A total of about 0.5 g. of solid thought to be this di-addition product was obtained in two of the ten reactions between *n*-butylmagnesium bromide and benzil. It was only slightly soluble in benzene but after recrystallization from alcohol it melted at 184°.

Anal. Calcd. for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26; mol. wt., 326. Found: C, 81.87, 81.49; H, 6.24, 5.79; mol. wt., 339, 318.

Preparation of Desoxybenzoin Pinacol.—A very small yield (5%) of the pinacol was obtained by the reduction of benzoin by the method of Ballard and Dehn,⁹ and no pinacol was obtained by the method of Wislicenus and Blank.¹⁰ Desoxybenzoin pinacol was obtained in 97% yield by exposing a solution of 6 g. of desoxybenzoin in 50 ml. of isopropyl alcohol to the sunlight for several days. This is an adaptation of the method described by Fieser¹¹ for the preparation of benzopinacol from benzophenone. The pinacol melted at 172° and was identical with the small amount of material obtained from the reaction of *n*-butylmagnesium bromide on desoxybenzoin. Molecular weight determinations and analyses for carbon and hydrogen agreed well with the calculated values.

Attempts to Rearrange the Pinacol to the Pinacolone.—When 2 g. of the pinacol was refluxed for five minutes with a few crystals of iodine in 15 ml. of glacial acetic acid, only starting material was recovered. Increasing the time of heating to one and one-half hours caused no rearrangement and the pinacol was recovered. When the time of heating was increased to eight hours, dark gummy ma-

terial was formed which would not crystallize. Refluxing for six hours with hydriodic acid in glacial acetic acid gave dark non-crystalline material. Two grams of the pinacol was added to 70 ml. of cold, concd. sulfuric acid and the resulting bright green solution was poured over ice after standing for two hours at room temperature. The pinacol was recovered. Refluxing for two hours with dilute sulfuric acid caused no rearrangement and the pinacol was recovered. Finally, *n*-butylmagnesium bromide was prepared from 5 g. of *n*-butyl bromide and 1 g. of the pinacol was added to the Grignard reagent. The ether was refluxed for one hour, then the solvent was removed and the mixture was heated overnight on the steam-bath. After decomposition with ice and ammonium chloride solution, the pinacol was recovered.

Desoxybenzoin Pinacolone, VI.—The compound thought to be the pinacolone was obtained in one reaction from a fraction boiling 242–252° (53 mm.) and from the residue, above 226° (64 mm.), in another reaction. It was crystallized from alcohol and melted at 133°. The amount available was too small to determine whether the phenyl or the benzyl group had migrated.

Anal. Calcd. for $C_{22}H_{30}O$: C, 89.32; H, 6.42; mol. wt., 377. Found: C, 89.23, 89.21; H, 6.07, 6.19; mol. wt., 376.

Summary

1. The reaction of *n*-butylmagnesium bromide on acetophenone resulted in addition to form a new tertiary alcohol. This alcohol was dehydrated to form the corresponding new olefin.
2. Benzophenone was reduced by *n*-butylmagnesium bromide to form benzohydrol and di-benzhydrol ether.
3. The reaction of *n*-butylmagnesium bromide on benzil resulted in reduction to benzoin and addition to form a new hydroxy ketone. The hydroxy ketone was dehydrated to form the corresponding unsaturated ketone.
4. Desoxybenzoin was reduced by *n*-butylmagnesium bromide to form stilbene, desoxybenzoin pinacol and a compound thought to be desoxybenzoin pinacolone.

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RECEIVED AUGUST 6, 1942

(9) Ballard and Dehn, *THIS JOURNAL*, **54**, 3970 (1932).

(10) Wislicenus and Blank, *Ann.*, **248**, 9 (1888).

(11) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Company, Boston, Mass., 1935, p. 202.