

as in the product of lower quality. The former contains approximately twice as much stearin as the latter.

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

THE REDUCTION OF AROMATIC KETONES AND BENZILS BY TRIPHENYLMETHYLMAGNESIUM BROMIDE

By W. E. BACHMANN

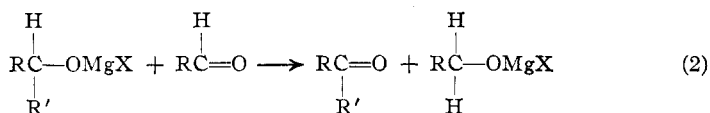
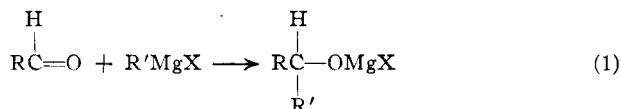
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It is clear that the reduction which so frequently occurs in the Grignard reaction may be occasioned in several ways.¹ It has long been known that aliphatic Grignard reagents can exercise a reducing action toward certain compounds; as a rule an unsaturated hydrocarbon is formed in addition to the reduction product.

The work of Gomberg and Bachmann² on the reducing action of a mixture of magnesium and magnesium iodide has made it obvious that the Grignard reagent must be filtered from unused magnesium if reduction by this system is to be avoided. A number of instances have been reported in which reduction occurred when unused magnesium was allowed to remain in the Grignard reagent.³

Marshall⁴ discovered that a mutual oxidation and reduction reaction may occur between excess of an aldehyde and the normal addition compound which is formed by the action of a Grignard reagent on the aldehyde. The reaction which occurs may be formulated as follows



The reaction involves a transfer of H and MgX from a molecule of the secondary alcohol to a molecule of aldehyde; the products are a ketone and a primary alcohol. The importance of this mode of reduction has been overlooked to a great extent; its applicability has been indicated by

¹ See Noller, *THIS JOURNAL*, **53**, 635 (1931).

² Gomberg and Bachmann, *ibid.*, **49**, 236 (1927); **49**, 2584 (1927); **50**, 2762 (1928); **52**, 4967 (1930).

³ See for example Boyd and Hatt, *J. Chem. Soc.*, 898 (1927); Hatt, *ibid.*, 1623 (1929); Barnett, Cook and Nixon, *ibid.*, 505 (1927); Lagrave, *Ann. chim.*, [10] **8**, 363 (1927).

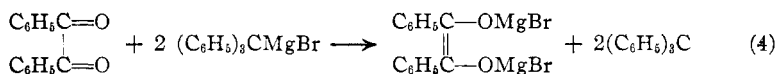
⁴ Marshall, *J. Chem. Soc.*, **105**, 527 (1914); **107**, 509 (1915); **127**, 2184 (1925).

¹¹ Schmidlin, *Ber.*, **39**, 4198 (1906), was the first to obtain benzopinacol from the interaction of triphenylmethylmagnesium chloride and benzophenone; however, he attributed the reduction to the magnesium which was present in the mixture. Gilman

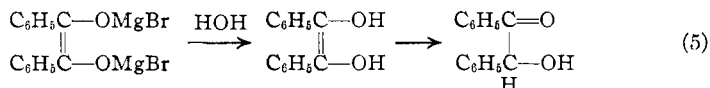
and a practically quantitative yield of triphenylmethyl are obtained. Not only benzophenone but also *p*-chloro-, *p*-phenyl- and *p,p'*-diphenylbenzophenone in addition to fluorenone and xanthone have been found to be reduced to pinacols by triphenylmethylmagnesium bromide.

This type of reduction takes place to a slight extent in the reaction between phenylmagnesium bromide and benzophenone. If a filtered solution of the Grignard reagent is added to a solution of benzophenone in a nitrogen atmosphere, the red color of the bromomagnesium ketyl becomes visible. If diphenylbenzophenone is employed, the characteristic deep blue color of the corresponding ketyl appears. Indeed, the colors which have been observed by others¹² in the course of the Grignard reaction are attributed to the formation of ketyl radicals, albeit in minute amounts. Whether other types of reduction or whether even the normal addition reaction of the Grignard reagent takes place through the intermediate formation of radicals¹³ is left undecided.

It has further been found that benzil is reduced by triphenylmethylmagnesium bromide. Two molecules of the Grignard reagent react with one molecule of the benzil and there is formed the bromomagnesium salt of stilbene-diol¹⁴ (II) and triphenylmethyl.



Hydrolysis of the reaction mixture gives benzoin in addition to triphenylmethyl



The presence of the bromomagnesium salt of stilbene-diol prior to hydrolysis was indicated by the color of the mixture during the reaction and was proved by the formation of stilbene-diol dibenzoate,¹⁴ $\text{C}_6\text{H}_5\text{C}(\text{OOC}\text{C}_6\text{H}_5)=\text{C}(\text{C}_6\text{H}_5\text{COO})\text{C}_6\text{H}_5$, when the reaction mixture before hydrolysis was and Fothergill, *THIS JOURNAL*, **51**, 3149 (1929), likewise, reported the formation of some pinacol (22–31% yields). Compare also the reaction of thio-ketones with the Grignard reagent [Schönberg and Schütz, *Ber.*, **60**, 2351 (1927)].

¹² Of these, Davies, Dixon and Jones, *J. Chem. Soc.*, 1916 (1930), report not only that the red color of the ketyl is produced on the addition of benzophenone to amyl Grignard reagents but also that small yields (4–9%) of benzopinacol were isolated. As Noller, *Ref. 1*, points out, however, these investigators siphoned or decanted but did not filter their solutions from excess of magnesium. Noller subsequently was unable to find any benzopinacol among the products of the action of isobutylmagnesium bromide on benzophenone.

¹³ Späth, *Monatsh.*, **34**, 1967 (1913); Schlubach and Goes, *Ber.*, **55**, 2897 (1922); Blicke and Powers, *THIS JOURNAL*, **51**, 3378 (1929).

¹⁴ Gomberg and Bachmann, *ibid.*, **49**, 2584 (1927); Gomberg and Van Natta, *ibid.*, **51**, 2238 (1929).

treated with benzoyl chloride. Dimethylbenzil and dichlorobenzil react with triphenylmethylmagnesium bromide in the same manner as benzil. The reaction of this Grignard reagent with benzil is analogous to the reaction that occurs between iodomagnesium hydrazobenzene, $C_6H_5N(MgI)-(IMg)NC_6H_5$, and benzil in which azobenzene¹⁵ and the iodomagnesium salt of stilbene-diol are produced.

Experimental

All operations, including the preparation of the Grignard reagent and its reactions with ketones and benzils, were carried out in an atmosphere of nitrogen.

Triphenylmethylmagnesium Bromide + Benzophenone.—The Grignard reagent was prepared from 16.2 g. of triphenylmethyl bromide in a mixture of 30 cc. of ether and 60 cc. of benzene according to the directions of Gomberg and Bachmann.¹⁶ The filtered solution of triphenylmethylmagnesium bromide was treated with 9.1 g. of benzophenone. The solution immediately became deep red in color. After three hours of refluxing, the solution was hydrolyzed with ice and dilute acetic acid. Air was passed into the orange-yellow solution until oxidation of triphenylmethyl was complete; by using a sintered-glass distributor, this result was attained in less than an hour. The triphenylmethyl peroxide which had precipitated was filtered off and washed with benzene and with acetone: wt., 10.3 g.; m. p. 186°.

The ether-benzene filtrate was allowed to evaporate to dryness. The solid residue was digested with warm petroleum ether (40–60°) in order to remove unreacted benzophenone; only traces of this compound were found in the filtrate. The crude pinacol was then dissolved in 140 cc. of cold acetone; this treatment left 0.5 g. of peroxide undissolved. Evaporation of the acetone solution gave a solid which after treatment with alcohol consisted of practically pure benzopinacol: wt., 8.5 g.; m. p. 186–188°.

In another experiment, the crude pinacol which was obtained on evaporation of the acetone solution was rearranged to β -benzopinacolin by heating it for a few minutes with 40 cc. of glacial acetic acid which contained a few crystals of iodine.¹⁷ In this manner 7.5 g. of pinacolin was obtained. The yield of peroxide was again 10.8 g.

The results obtained from the interaction of triphenylmethylmagnesium bromide and a number of ketones are given in Table I. In each case one mole of Grignard reagent was employed for one mole of ketone.

Triphenylmethylmagnesium Bromide + Benzil.—A solution of 5.2 g. of benzil in 30 cc. of benzene was added to a solution of triphenylmethylmagnesium bromide prepared from 16.2 g. of triphenylmethyl bromide. An opaque dark brown color was formed but this disappeared as the reaction proceeded; at the end of the reaction the solution was transparent orange in color. These color phenomena are entirely analogous to those observed in the reduction of benzil by the binary system $Mg + MgI_2$. After the solution had been refluxed for two and one-half hours, it was hydrolyzed. Air was passed into the solution in order to oxidize the triphenylmethyl. The peroxide was filtered off and the filtrate was evaporated to dryness. The solid residue was extracted with ether in a Soxhlet extractor in order to dissolve the benzoin and leave peroxide undissolved. In this manner there was obtained 11.5 g. of triphenylmethyl peroxide and 4.2 g. of benzoin.

Reaction with Benzoyl Chloride.—After refluxing a mixture of 5.2 g. of benzil and the Grignard reagent from 16.2 g. of triphenylmethyl bromide for two hours, the solution

¹⁵ Bachmann, *THIS JOURNAL*, **53**, 1524 (1931).

¹⁶ Gomberg and Bachmann, *ibid.*, **52**, 2455 (1930).

¹⁷ Gomberg and Bachmann, *ibid.*, **49**, 246 (1927).

TABLE I
 REDUCTION OF KETONES BY TRIPHENYLMETHYLMAGNESIUM BROMIDE

Ketone	Ketone, g.	Yields of products			
		Pinacol		Peroxide	
		G.	%	G.	%
Benzophenone	9.1	8.5	93	10.8	83 ^a
4-Chlorobenzophenone	5.41	4.2	78	5.2	80
4-Phenylbenzophenone ^b	6.5	5.6	86	4.5	70
4,4'-Diphenylbenzophenone ^c	8.35	8.0	98	5.0	77
Fluorenone ^d	4.5	3.6	80	4.8	74
Xanthone ^e	4.9	4.1	84	5.0	77

^a Since solutions of pure triphenylmethyl give only 80–85% yields of triphenylmethyl peroxide, this yield represents practically a quantitative formation of triphenylmethyl.

^b The color of the reaction mixture was green (from the blue of the ketyl and the orange-yellow of triphenylmethyl). Since the pinacol is little soluble, hydrolysis was carried out in a nitrogen atmosphere and the pinacol which precipitated was filtered off; the triphenylmethyl in the filtrate was then oxidized to peroxide. A portion of the pinacol was rearranged to pinacolin by heating it with acetic acid and iodine; there was obtained the pinacolin, benzoyl-4,4'-diphenyl-triphenylmethane, of m. p. 198°. For descriptions of these and related compounds see Gomberg and Bachmann, *THIS JOURNAL*, **49**, 236 (1927).

^c The mixture was refluxed for one hour. The solution was intense greenish-blue and then intense green in color. The same procedure was employed here as is given under phenylbenzophenone.

^d Part of the pinacol (1.7 g.) precipitated on hydrolysis of the reaction mixture. For purposes of identification a portion of the pinacol was warmed with 70% sulfuric acid; it gave the expected 9-diphenylenephenanthrone of m. p. 255°.

^e Most of the xanthopinacol (3.2 g.) precipitated on hydrolysis. A sample when warmed with 70% sulfuric acid gave dixanthylene; m. p. 312°.

was cooled and treated with a solution of 7 cc. of benzoyl chloride in 30 cc. of benzene. After being kept warm for two hours, the mixture was allowed to stand at room temperature for twelve hours. Hydrolysis of the mixture, followed by oxidation of the triphenylmethyl, gave 6.0 g. of stilbenediol dibenzoate of m. p. 158° and 10.5 g. of triphenylmethyl peroxide.

In Table II are listed the results obtained from the interaction of two moles of triphenylmethylmagnesium bromide and one mole of the benzil.

Phenylmagnesium Iodide (2 Moles) + Benzaldehyde (1 Mole).—A filtered solution of phenylmagnesium iodide which had been prepared from 42 g. of iodobenzene in 75 cc. of ether was added drop by drop in the course of an hour to a warm solution of 10.6 g. of freshly distilled benzaldehyde in 30 cc. of benzene. After the addition, the mixture was warmed for one hour and was then allowed to stand overnight. The mixture was hydrolyzed, washed and dried. The solvents were removed by distillation and the mixture was then distilled on a steam-bath under a pressure of 1 mm. The benzyl alcohol which distilled was freed from biphenyl by extraction with water. From the aqueous extract was obtained 2.7 g. (25%) of benzyl alcohol (identified as the phenyl urethan, m. p. 76°, and as the *p*-nitrobenzoic acid ester, m. p. 84–85°).

The residue in the distilling flask was warmed with 40 cc. of ligroin (60–80°); this dissolved the benzohydrol and left 3.5 g. of triphenylcarbinol in the form of large crystals. From the ligroin filtrate there were obtained 8 g. of benzhydrol and an additional 1.0 g. of triphenylcarbinol.

TABLE II
REDUCTION OF BENZILS BY TRIPHENYLMETHYLMAGNESIUM BROMIDE

Benzil	Benzil, g.	Yields of products			
		Benzoin		Peroxide	
		G.	%	G.	%
Benzil	5.2	4.2	80	11.5	88
Benzil	5.2	6.0 ^a		10.5	80
4,4'-Dichlorobenzil	3.5	3.4	95	5.3	81
4,4'-Dichlorobenzil	3.5	4.0 ^b		3.6	56
4,4'-Dimethylbenzil	3.0	2.3 ^c		2.9	44

^a Stilbene-diol dibenzoate.

^b Dichloro-stilbene-diol dibenzoate [Gomberg and Van Natta, *THIS JOURNAL*, **51**, 2238 (1929)] produced by treating the reaction mixture with 4 cc. of benzoyl chloride.

^c Dimethyl-stilbene-diol dibenzoate. After recrystallization from alcohol it melted at 137–138° and was identical with the dibenzoate prepared from the benzil through the MgI reaction.

Summary

A number of aromatic ketones have been reduced to pinacols by means of the Grignard reagent, triphenylmethylmagnesium bromide. The reduction proceeds through the intermediate formation of radicals according to the following formulation: $\text{RRC=O} + (\text{C}_6\text{H}_5)_3\text{CMgBr} \longrightarrow \text{RRC}\cdot + \text{OMgBr} + (\text{C}_6\text{H}_5)_3\text{C}\cdot$. The ketyl radicals then associate to the pinacolate: $2\text{RRC}\cdot + \text{OMgBr} \rightleftharpoons \text{RRC}(\text{OMgBr})(\text{OMgBr})\text{CRR}$.

Benzils are reduced by triphenylmethylmagnesium bromide to the bromomagnesium salt of stilbene-diols: $\text{RCOCOR} + 2(\text{C}_6\text{H}_5)_3\text{CMgBr} \longrightarrow \text{RC}(\text{OMgBr})=\text{C}(\text{OMgBr})\text{CR} + 2(\text{C}_6\text{H}_5)_3\text{C}\cdot$.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

SOME NEW LOCAL ANESTHETICS CONTAINING THE MORPHOLINE RING¹

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In view of the very pronounced local anesthetic activity of the aromatic esters of the dialkylamino alcohols, such as procaine and butyn, it has seemed of interest to study the preparation and physiological properties of an analogous series in which the dialkylamino group is replaced by a morpholine ring. It is not to be expected that the morpholine ring as such should have any particular effect but it is possible that the ether linkage in the ring might serve to increase the solubility of the morpholine derivatives in lipoids and so increase the anesthetic powers.

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