difficult in the melt than in acetonitrile.[2] Solvation of the resultant radical cation should make the oxidation potential more negative (i.e., easier) in the more highly solvating medium. Thus, it is apparent that these room-temperature tetrachloroaluminate melts are not particularly strong solvating media when compared to polar organic solvents for organic cations.

The rate of dimerization of the triphenylmethyl radical in the $AlCl_3$ melt appears to be reasonably consistent with the reported stability of this radical in organic solvents. Cyclic voltammetric data reported on 5 mM triphenylmethyl perchlorate in dimethyl sulfoxide indicated chemical reversibility at 1.1 V s^{-1}.[31] However, a latter report states that the reoxidation of the triphenylmethyl radical to the carbonium ion became significant only at scan rates greater than 1.0 V s^{-1}.[30a] Although the scan rate is not reported, a more recent publication on the triphenylmethyl anion/radical couple in tetrahydrofuran reports a cyclic voltammetric peak current ratio of 1.06 for the couple, which indicates complete chemical reversibility.[35] Concentration effects on the rate of dimerization are important in any of the above data and need to be taken into account for comparison purposes.

The reasonably good fit of the kinetic data to an irreversible dimerization model (Figure 6) indicates a large equilibrium constant for reaction 4. An attempt was made to calculate the magnitude of this equilibrium constant from ESR data. The 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) was used as a stable radical standard. Integration of peak areas was carried out on a known quantity of DPPH radical vs. the triphenylmethyl radical produced in the melt as a result of electrolysis of the carbonium ion. Upon addition of 1 faraday/mol of charge to a 10^{-2} M solution of carbonium ion, ESR peak integration of the resultant solution indicated a radical concentration of 5×10^{-4} M after a 24-h equilibration. Thus, the equilibrium constant for reaction 4 is on the order of 10^4 L mol^{-1}. The relatively low equilibrium concentration of triphenylmethyl radicals in the melt is consistent with the adequacy of an irreversible second-order EC model to calculate the rate constant for the dimerization reaction.

The rate of formation of triphenylmethyl carbonium ions in this melt was too slow to measure with transient electrochemical techniques. Rates of acid–base reactions in the low-temperature $AlCl_3$ melts in previous reports have apparently been too slow to quantitatively determine rate constants by cyclic voltammetry.[2,3] Further work on other carbonium ions including acylium ions is in progress and will be subsequently reported.

Acknowledgment. We thank Helen M. Jacoby, a National Science Foundation Undergraduate Participant, for conducting electrochemical experiments on the triphenylmethyl hexafluorophosphate salt and acid–base chemistry studies of **3** and **4**. The support of the University of North Dakota Graduate Research Committee is acknowledged with gratitude.

Registry No. 1, 13948-08-8; **2**, 2216-49-1; **3**, 18909-18-7; **4**, 3416-63-5; triphenylmethyl chloride, 76-83-5.

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[35] B. Jaun, J. Schwarz, and R. Breslow, *J. Am. Chem. Soc.*, **102**, 5741 (1980).

Mechanism of the Reaction between Benzylmagnesium Chloride and Carbonyl Compounds. A Detailed Study with Formaldehyde

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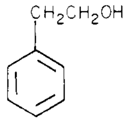
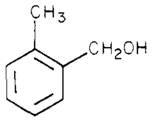
The reaction of benzylmagnesium chloride in THF with monomeric formaldehyde has been studied in detail. A mechanism is presented which accounts for the formation of the products, 2-phenylethanol, *o*-tolylcarbinol, and *o*-(2-hydroxyethyl)benzyl alcohol. A change in technique for Grignard titration and formaldehyde addition results in a much-improved mass balance than achieved previously. The decreased yield of the major product, *o*-tolylcarbinol, with increased reaction time is explained in terms of a hitherto unsuspected equilibrium influenced by the polymerization of monomeric formaldehyde. An intermediate organometallic species which could lead to some of the diol product, *o*-(2-hydroxyethyl)benzyl alcohol can be trapped as the trimethylsilyl derivative, but the quantity is insufficient to account for the amount of diol when an excess of formaldehyde is employed. An ene or Prins reaction is invoked for the formation of most of the diol. Deuterium tracer studies suggest competition between a proton abstraction pathway leading to the trimethylsilyl-trapped organometallic species and a base-catalyzed, stereospecific 1,3 hydrogen shift.

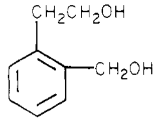
Ever since Grignard[1] first examined the reaction of benzylmagnesium chloride with formaldehyde, there has been considerable disagreement regarding the nature of the products formed in this reaction.[2-4] The most recent work[5] on the subject has clearly shown that three products, I–III, are all formed in varying amounts, depending upon the reaction conditions.



I



II



III

2-Phenylethanol (I), which normally would be the expected product, is found instead to be a consistently minor component of the final product mixture. The so-called "abnormal" *o*-tolylcarbinol (II) appears as the major product when low concentrations of formaldehyde are used. The amount of "abnormal" diol III [*o*-[2-hydroxyethyl)benzyl alcohol] increases from trace quantities at low formaldehyde concentration to a major component at high

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[1] Grignard, V *Bull. Soc. Chim. Fr.* **1903**, *29*, 953.

[2] Tiffeneau, M.; Delange, R. *C. R. Hebd. Seances Acad. Sci.* **1903**, *137*, 573.

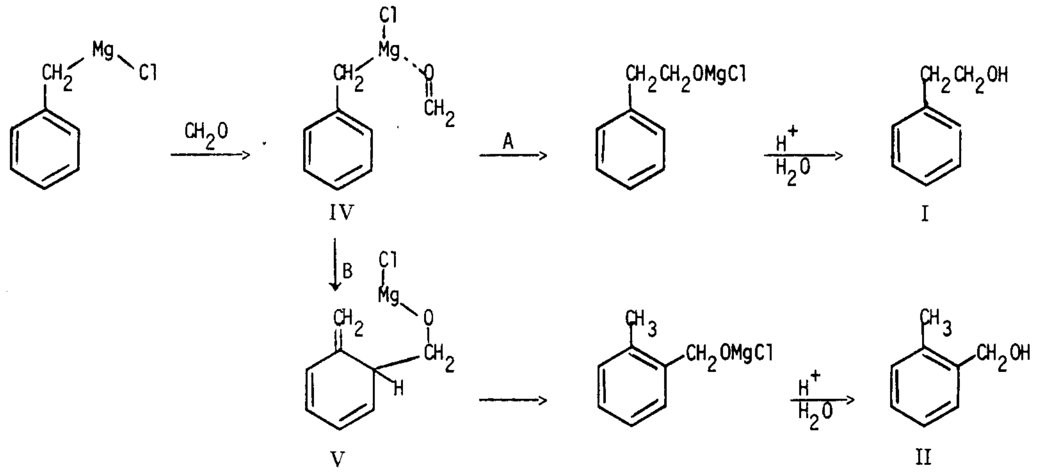
[3] Tiffeneau, M.; Delange, R. *J. Chem. Soc.* **1904**, *86*, 48.

[4] Mousseron, M.; Du, N. P. *Bull. Soc. Chim. Fr.* **1948**, *15*, 91.

[5] (a) Benkeser, R. A.; DeTalvo, W.; Darling, D. *J. Org. Chem.* **1979**, *44*, 225. (b) Benkeser, R. A.; Johnston, T. E. *J. Am. Chem. Soc.* **1966**, *88*, 2220.

0022-3263/82/1947-1243$01.25/0 © 1982 American Chemical Society

Scheme I



formaldehyde concentrations, while the yield of II varies inversely to the yield of III.

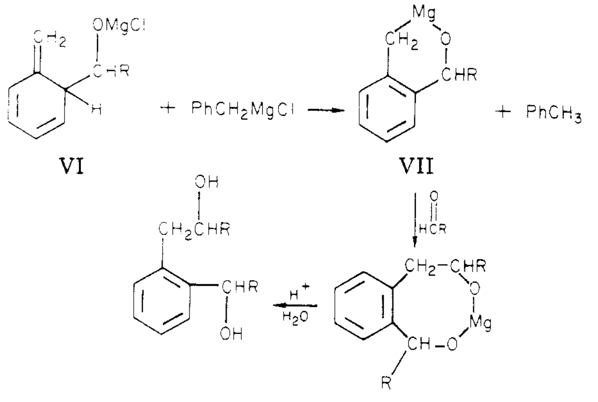
Johnson[6] was the first to propose a detailed mechanism for the formation of II. Although not aware of the existence of diol (III), he did recognize *o*-tolylcarbinol (II) as the major product under certain conditions and suggested the latter was formed via a six-centered transition state from an initial Grignard–formaldehyde complex (IV, Scheme I).

The mechanism was adequate since complex IV either could yield I by transfer of the benzyl group in a four-centered manner generally accepted at that time for the addition of simple Grignards to carbonyl-containing species[7,8] (path A, Scheme I) or could yield II by a six-centered route (path B, Scheme I). Although it was suggested[6] that triene, V, quickly rearomatized *before* hydrolysis, there was no specific suggestion as to how this isomerization might occur.

Later work[9b] showed that higher aliphatic aldehydes would react with the benzyl Grignard reagent to give products corresponding to I and III but not II. A modification of Johnson's mechanism was proposed[9] as shown in Scheme II to explain the formation of the abnormal diol product. This involved abstraction of an allylic proton from triene VI by a molecule of benzyl Grignard reagent, resulting in the formation of toluene and organometallic VII. Compound VII could then react further with a second molecule of aldehyde to form the diol (Scheme II).

The curious discrepancy of why formaldehyde gave only II as the abnormal product instead of III, while other aldehydes gave only diols rather than products similar to II, was partially cleared by the discovery that formaldehyde did give III.[5a] Later[5b] it was shown that products similar to II could also be found in the cases of acetaldhyde and trifluoroacetaldehyde, indicating that likely there was no fundamental difference between the mechanism of the reactions of formaldehyde and other aldehydes. When the earlier mechanism[9a] was considered for formaldehyde,[5] it was thought that if triene V was being converted to a new organometallic, the formation of III would indeed be favored by a large concentration of formaldehyde. Conversely, if there was insufficient formaldehyde available, simple protonation of the organometallic upon hydrolysis would yield II. Some evidence[5a] for the existence of such an organometallic species was found when a small quantity of [*o*-(hydroxymethyl)benzyl]trimethylsilane was isolated from a benzyl Grignard–formaldehyde reaction mixture by the addition of trimethylchlorosilane before hydrolysis. If the earlier mechanism[9a] is extended to include formaldehyde, the stoichiometry requirement that each equivalent of abnormal product uses 2 equiv of Grignard reagent provides some explanation for the customarily low overall yield of the reaction.

Scheme II



While some of the facts supported the Young–Siegel mechanism,[9a] other data were not entirely satisfactory. The quantity of [*o*-(hydroxymethyl)benzyl]trimethylsilane was disquietingly small, and unpublished experiments[10] utilizing tritium labeling at the ortho position gave results which would indicate little allylic proton abstraction. In order to clear up these questions, we initiated a more detailed study of the formaldehyde reaction.

Results and Discussion

The classic method[9b,11] for adding monomeric formaldehyde to a Grignard solution has been to decompose paraformaldehyde thermally, condense the vapor in a cold trap, and then allow the liquid monomer to vaporize at room temperature in a stream of nitrogen through an inlet tube positioned *above* the surface of the Grignard solution. In this way, the formaldehyde passes over the Grignard solution and does not clog the end of the tube by polymerizing at this point as a result of its contact with the basic Grignard solution. However, we found that this method

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(6) Johnson, J. R. *J. Am. Chem. Soc.* **1933**, *55*, 3029.

(7) (a) Hess, K.; Rheinboldt, H. *Chem. Ber.* **1921**, *54*, 2043. (b) Meisenheimer, J. *Justus Liebigs Ann. Chem.* **1925**, *442*, 180.

(8) For an excellent review on the mechanism of Grignard additions to ketones see: Ashby, E. C. *Pure Appl. Chem.* **1980**, *52*, 545.

(9) (a) Young, W. G.; Siegel, S. *J. Am. Chem. Soc.* **1944**, *66*, 354. (b) Siegel, S.; Boyer, W. M.; Jay, R. R. *Ibid* **1951**, *73*, 3237.

(10) Kharasch, M. S.; Reinmuth, O. "Grignard Reactions of Nonmetallic Substances"; Prentice-Hall: New York, 1954; p 1142.

(11) Gilman, H.; Breuer, F. *J. Am. Chem. Soc.* **1934**, *56*, 1127.

Table I. Reaction of Benzylmagnesium Chloride with Monomeric Formaldehyde at Varying Time Intervals

$$C_6H_5CH_2MgCl \xrightarrow[\text{time}]{CH_2O} \xrightarrow[H_2O]{NH_4Cl} C_6H_5CH_3 + I^a + II^b + III^c$$

			% yield				
expt	ratio of $C_6H_5CH_2MgCl/CH_2O$	reaction time, h	$C_6H_5CH_3$	I[a]	II[b]	III[c]	overall
1	1:1	1	39	7	51	3	>99
2	1:2.5	1	[f]	8	28	16	52
3	1:1 (+1.5)[d]	1 (+1)	[f]	5	45	8	58
4	1:1	1[e]	38	6	50	5	99
5	1:1	2	36	7	49	2	94
6	1:1	4	56	4	35	1	96
7	1:1	8	55	7	35	2	99

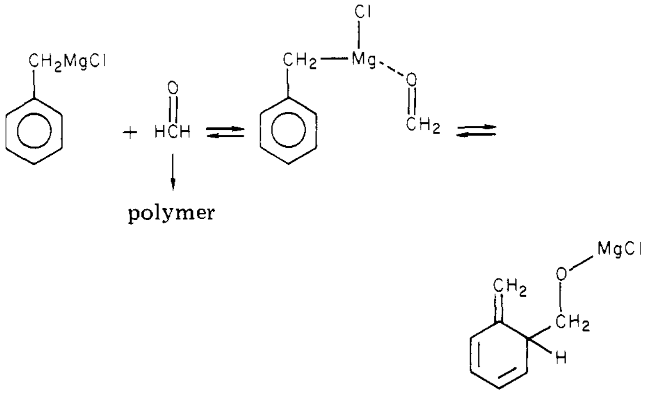
[a] 2-Phenylethanol. [b] *o*-Tolylcarbinol. [c] *o*-(2-Hydroxyethyl)benzyl alcohol. [d] CH_2O (1.5 equiv) added 1 h after the addition of the first equivalent. [e] Hydrolysis with 2 N HCl. [f] Toluene not isolated.

permitted the escape of considerable quantities of unreacted formaldehyde from the system, making any quantitative study of the reaction impossible. This difficulty was obviated by using THF as the solvent for the benzyl Grignard reagent and employing a specially modified wide-mouthed inlet tube. In this way, the desired quantity of monomeric formaldehyde could be added by thermally decomposing a weighed amount of paraformaldehyde and forcing the vapor by a nitrogen stream directly *through* the Grignard–THF solution. By positioning the mouth of the inlet tube *below* the surface of the solution virtually no formaldehyde escaped, and excellent material balances could be realized.

In the first series of experiments, 0.1 mol of benzylmagnesium chloride in 200 mL of THF was treated with gaseous formaldehyde for varying time periods as depicted in Table I. It can be seen that forcing even a single equivalent of formaldehyde through the Grignard solution rather than over it raises the yield of products I–III from the usual 15–20% to over 60% after 1 h. This immediately casts doubt on the modified[9] Johnson mechanism. If every molecule of II and III requires a second molecule of benzyl Grignard acting as a base (Scheme II), an amount of toluene equal to the combined yields of II and III should have been isolated. This is clearly not the case. It is also apparent that, by increasing the reaction time from 2 to 4 h (entries 5 and 6, Table I), the yield of II decreases substantially while the amount of toluene increases. Since we had established that no formaldehyde was escaping, we feel this result can best be explained in terms of an equilibrium between the formaldehyde and the benzyl Grignard reagent which is displaced in favor of the starting materials as shown in Scheme III. The triene intermediate (Y) finds it increasingly difficult to locate more monomeric formaldehyde (because of its ever-diminishing concentration) with which to react to form III. Hence, the equilibrium continues to shift to the left because the monomeric formaldehyde is prone to polymerization to a form which is relatively unreactive toward the Grignard reagent. The latter is converted to toluene upon hydrolysis. The reaction shows the same concentration effect as reported previously,[5] where III increases and II decreases with increasing amounts of starting formaldehyde (compare entries 1 and 2, Table I). Entries 2 and 3 (Table I) are enlightening. In entry 2, 2.5 equiv of formaldehyde are added all at once during the first hour of reaction. In entry 3, only 1 equiv of formaldehyde is added during the first hour, followed by an additional 1.5 equiv during the second hour of reaction. It is clear that the species which leads to III is not present in large amounts after 1 h of reaction.

While the toluene which was isolated from the various reactions (Table I) could have formed from excess Grignard during hydrolysis, there is nothing in Table I to either prove or disprove that at least some of it might not have formed prior to hydrolysis. To test this possibility, we treated the benzyl Grignard bearing deuteriums in place of the ortho hydrogens with formaldehyde and then hydrolyzed it with a protonic medium. The products were then analyzed to determine the fate of the deuterium removed in the formation of the abnormal products. Also, the undeuterated benzyl Grignard was similarly treated with formaldehyde and hydrolyzed with an exclusively deuterated medium. The results are shown in Table II.

Scheme III



Y

The existence of a small quantity of species VIII, which could form only *prior* to hydrolysis, is evidence that some deuterium abstraction by Grignard reagent does take place during the reaction, probably as indicated in Scheme II. Similarly, the undeuterated toluene (XIII) in Table II can be taken as evidence of the same mechanistic pathway, since it too must have formed prior to hydrolysis. (Blank experiments showed that no more than 5% of XIII could have formed by trace amounts of water introduced from the thermal decomposition of the initial paraformaldehyde.)[12] The difference between the amounts of VIII and XIII is substantial and may reflect a deuterium isotope effect. It is clear from the data that replacement of the ortho hydrogens with deuterium caused some change, as evidenced by the variation in the relative ratios of normal to abnormal products.

The *o*-tolyl species X and XV could have been formed by protonation (or deuteration) of organometallic species during hydrolysis or by protonation (or deuteration) of the corresponding triene intermediates (like compound V in

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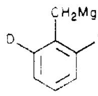
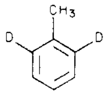
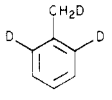
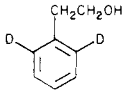
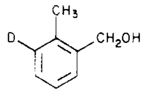
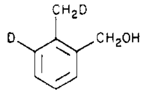
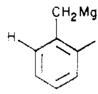
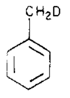
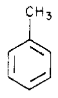
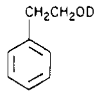
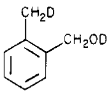
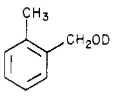
[12] Paraformaldehyde contains some chemically bound water which would be introduced into the system by our present procedure. We determined this would be no more than 5% by treating (4-methylphenyl)magnesium bromide in THF with gaseous formaldehyde and then hydrolyzing with DCl/D_2O. See the Experimental Section for details.

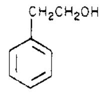
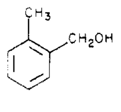
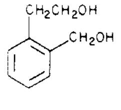
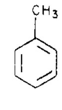
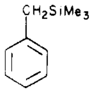
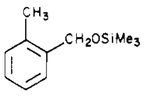
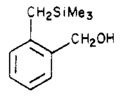
Table II. Deuterium Labeling in the Reaction of the Benzyl Grignard with Monomeric Formaldehyde[a]

reaction	reactant	reagents	products (% yield)				
1		(1) CH_2O; (2) NH_4Cl, H_2O	 VII (37)	 VIII (3)	 IX (18)	 X (13)	 XI (13)
2		(1) CH_2O; (2) 20% DCl, D_2O	 XII (13)	 XIII (19)	 XIV (5)	 XV (13)	 XVI (40)

[a] No attempt was made to isolate diols in these experiments.

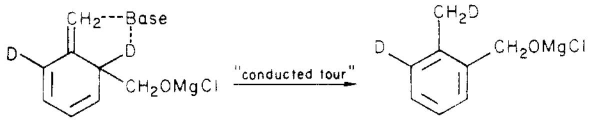
Table III. Trapping of Intermediates with Trimethylchlorosilane

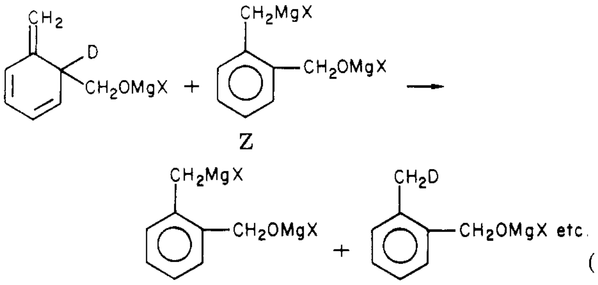
$$C_6H_5CH_2MgCl \xrightarrow[\text{time}]{CH_2O} \xrightarrow{(CH_3)_3SiCl} \xrightarrow{24\text{ h}} \xrightarrow{2\text{ N HCl}} \text{I} + \text{II} + \text{III}^a + \text{XIII} + \text{XVII}^b + \text{XVIII}^c + \text{XIX}^d$$

reaction time, h	% yield						
							
reaction time, h	I	II	III	XIII	XVII	XVIII	XIX
0	2	22	3	5	55	5	6
1	3	37	3	5	24	16	6
4	1	20	2	7	46	11	7

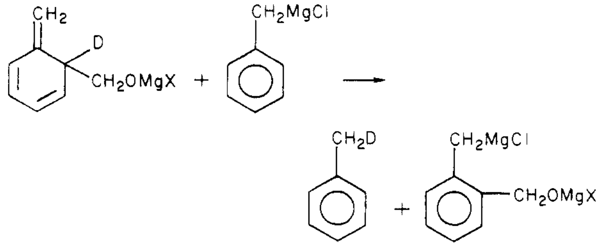
[a] See ref 5a. [b] Bygden, A. *Chem. Ber.* 1912, *45*, 707. [c] Anal. Calcd for $C_{11}H_{18}OSi$: C, 68.04; H, 9.28; Si, 14.43. Found: C, 68.27; H, 9.19; Si, 14.25. [d] See ref 5a.

Scheme I) if the latter survived until hydrolysis. It would be impossible to distinguish between these possibilities on the basis of the data in Table II. However, the *o*-tolyl species XI and XVI could have formed only before hydrolysis, possibly by an intramolecular stereospecific transfer of the allylic hydrogen (or deuterium) of the triene to the *exo*-methylene position. Such a process would result in rearomatization without the formation of any new organometallic species, similar to the isomerization originally envisioned by Johnson.[6] While stereospecific 1,3 hydride shifts are thermally forbidden by orbital-symmetry considerations,[13] Cram[14] and other workers[15] have demonstrated several cases of intramolecular 1,3 hydrogen shifts in analogous systems which take place via base catalysis. Since the benzyl Grignard–formaldehyde reaction mixture would have free Grignard reagent as well as various alkoxide bases present, it is not difficult to visualize XI and XVI as arising from their trienes by such a "conducted tour"[16] process. It is recognized that one cannot preclude an intermolecular hydrogen transfer to account for the formation of compounds XI and XVI. All that would be required to initiate such a chain process would be the formation of just one molecule of Z (eq 1), which could conceivably come about through the auspices of one molecule of benzyl Grignard reagent (eq 2). If such were the case, however, it is not immediately apparent why species Z should be more successful in perpetuating the chain than the benzyl Grignard reagent itself. Regardless, it is clear that some of the ortho hydrogen in V does find its way onto the methyl group of the *o*-tolyl product.





(1)



(2)

Z

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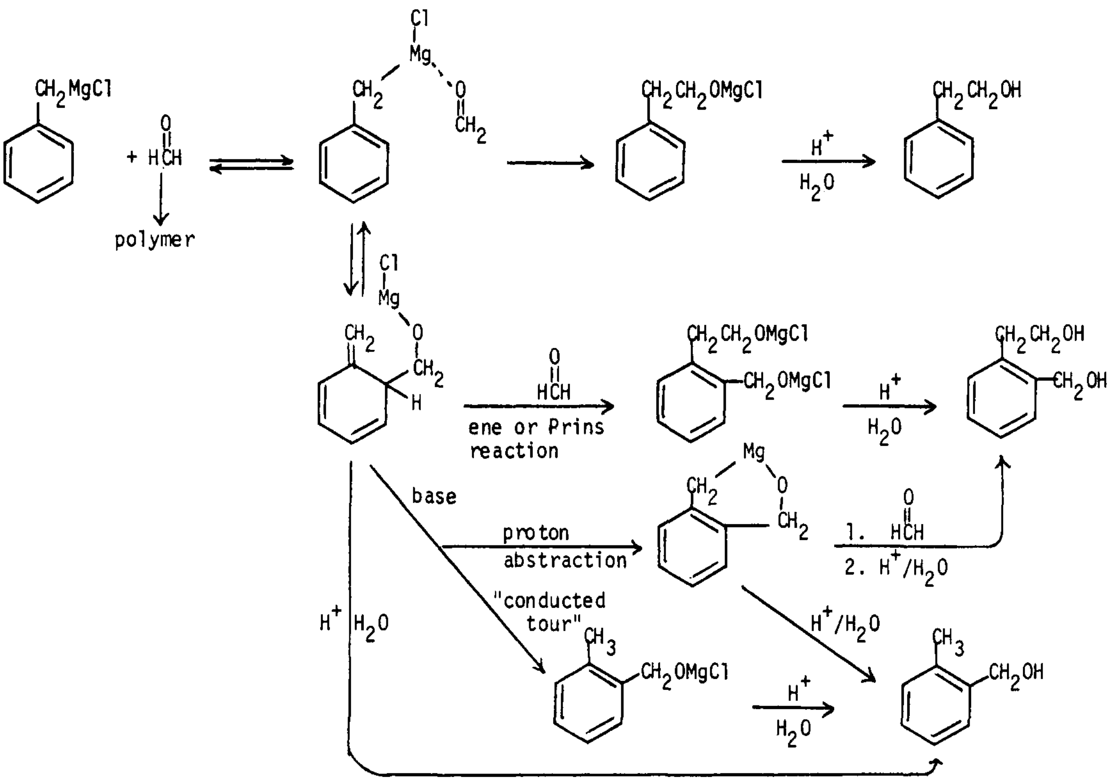
[13] Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Academic Press: Weinheim, Germany, 1970.

[14] For leading references see: Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1965; p 176.

[15] Bank, S.; Rowe, C. A., Jr.; Schriesheim, A. *J. Am. Chem. Soc.* **1963**, *85*, 2115. Bergson, G.; Weidler, A. M. *Acta Chem. Scand.* **1963**, *17*, 862, 1798, 2691, 2724.

[16] See ref 14, p 190.

Scheme IV

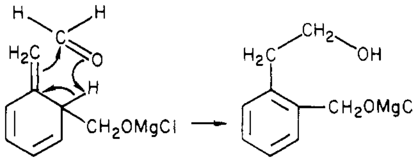


The data in Table III from the trapping experiments with trimethylchlorosilane confirm the conclusions drawn from Tables I and II. As the reaction time is increased from 1 to 4 h, more benzyl Grignard is trapped as its trimethylsilyl derivative (XVII). This fits nicely with the concept of an equilibrium involving the Grignard reagent which is shifted to its starting components with time. The small amount of XIX found could be considered as evidence for the regenerated organometallic suggested by earlier workers.[9] This conclusion must be considered tentative, however, since it is not known whether triene V might not be able in some way to react with trimethylchlorosilane to yield XIX without the intervention of an intermediate organometallic.[17] Species XVIII merely represents the Me_3Si-protected alcohol of II which was not completely hydrolyzed in the workup.

On the basis of the data presented herein, a reasonable mechanism for the reaction of the benzyl Grignard with formaldehyde can now be proposed as shown in Scheme IV. It is similar to Johnson's original mechanism in that the same four-centered and six-centered pathways are available. It should be stressed, however, that both the formation of the Grignard–formaldehyde complex and the formation of the triene must be considered reversible to explain the decrease in yield of the *o*-tolylcarbinol with increasing reaction time. Some recent elegant work[18] with [(1-naphthyl)methyl]magnesium chloride and formaldehyde lends additional evidence for the postulated equilibria. In the naphthyl case, it was possible to isolate the triene intermediate akin to V, and it could be shown that it did revert to starting materials under the proper conditions.

The proton abstraction concept[5,9] does not appear to be a major process in the reaction. Utilizing the idea of a base-assisted "conducted tour",[16] it can be seen that complete proton abstraction to yield an organometallic species could be viewed as simply the extreme case where the base removes the allylic proton rather than assisting in its transport. Even if some alkoxide species functioned as the base, the abstracted proton would eventually become bound to any free Grignard reagent which might be present due to the large difference in the pk_a values between the possible bases. The organometallic species which would be formed by proton abstraction is shown in Scheme IV in a closed, cyclic form to explain the fact that, if it does react with additional formaldehyde, it does so only at the benzylic position to give diol III. If the organometallic were not restricted in some manner, it might be expected to react with excess formaldehyde at the other available ortho position. No such trisubstituted diol has ever been found.

Scheme V



Since the regenerated organometallic species does not appear to form in large quantities, there must exist some other pathway to give the increasing amounts of diol III when greater concentrations of formaldehyde are available for reaction. A logical pathway for such diol formation would be via an ene[19,20] reaction as shown in Scheme V. Ene reactions with carbonyl compounds generally require more stringent conditions than those used in the benzyl Grignard–formaldehyde reaction.[20] However, the stabilization gained by restoring the aromatic system would be a powerful driving force in this case.

The feasibility of such an ene reaction was demonstrated previously[21] in this laboratory wherein the mixture re-

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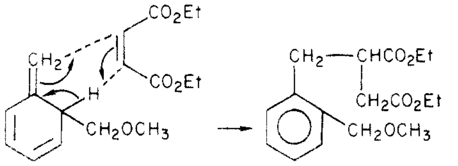
[17] To our knowledge, however, this would be a new reaction in organosilicon chemistry.

[18] Bernardon, C.; Deberly, A. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2631.

[19] (a) Alder, K.; Pascher, F.; Schmitz, A. *Chem. Ber.* **1943**, *76*, 27. (b) Alder, K.; von Brachel, H. *Justus Liebigs Ann. Chem.* **1962**, *651*, 141.

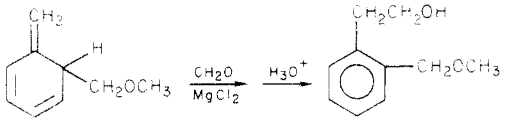
[20] Hoffman, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556.

sulting from the reaction of benzylmagnesium chloride with chloromethyl methyl ether was found to react with diethyl maleate in what was viewed as a four-centered cyclic process (eq 3). It was further demonstrated[21] that



(3)

this same triene intermediate would undergo the well-known Prins reaction with monomeric formaldehyde and anhydrous magnesium chloride (eq 4). The hydrocarbon analogue of V, 5-methylene-1,3-cyclohexadiene, has been shown to undergo ene reactions.[22]



(4)

A similar reaction between the intermediate derived from the 1-naphthylmethyl Grignard and formaldehyde to give a diol analogous to III has also been invoked.[18] In this case the reaction was referred to as a "Prins" since it was catalyzed by magnesium salts. In the more reactive benzyl systems, one cannot say whether diol III results from a concerted ene reaction or a very fast multistep Prins reaction. However, a direct reaction between triene V and formaldehyde does explain why more of the diol III is formed with increasing concentrations of formaldehyde. With more formaldehyde available in the initial stages of the reaction, triene V can react to form diol before it can rearomatize by a 1,3 hydrogen transfer or a proton abstraction. If triene V were still present at the time of hydrolyis, it might well form II at that time.

The mechanism presented in Scheme IV is quite consistent with all experimental observations. It explains such diverse phenomena as the competition between proton abstraction, the apparently forbidden 1,3 hydride shift, the deuterium isotope results, and the reversibility of the reactions leading to abnormal products. While the present study has dealt exclusively with the reaction of the benzyl Grignard reagent with monomeric formaldehyde, the mechanistic picture[23] presented in Scheme IV should be general for all benzylic systems which react with carbonyl reagents to give products akin to I–III.

Experimental Section

Benzylmagnesium Chloride in THF. A 1.0-L flask with an addition funnel was charged with magnesium turnings (60.67 g, 2.5 mol) and flame dried under a stream of N_2. The magnesium turnings were covered with 150 mL of dry THF, and the flask was immersed in a cold water bath at 20–23 °C. The addition funnel was charged with a solution of benzyl chloride (75.9 g, 0.60 mol) in 350 mL of THF. A small portion of the halide solution was added to the flask to initiate the reaction. Once the reaction had begun, the magnesium was stirred at a moderate rate, and the remaining halide solution was added dropwise over a period of 48 h. The mixture was kept continuously under N_2. The resulting gray-black solution was transferred to a dry bottle and stored in the cold under N_2 where it was stable for a minimum of several weeks. Titration by addition of an aliquot of the Grignard to a known quantity of acid and back-titrating with standardized base indicated a yield of 90–95%. Titration by the Eastham method,[24,25] which determines only active Grignard, indicated a yield of 75–80%.

Benzylmagnesium Chloride in THF with Monomeric Formaldehyde. General Procedure. A dry 50-mL flask was charged with paraformaldehyde (3.2 g, 0.107 mol) which had been dried for several days in a desiccator over P_2O_5. The flask was sealed with a glass stopper that contained both a glass inlet and a glass outlet tube. Nitrogen gas was passed through the inlet tube. The outlet tube was connected by a minimum length of Tygon tubing to a wide-mouth glass tube which had been fitted by a rubber septum onto the neck of 300-mL flask equipped with a magnetic stirrer. A needle leading to a water-filled bubbler was fitted through the septum, thus providing an outlet for the nitrogen. The 300-mL flask was charged with a solution of 0.1 mol of benzylmagnesium chloride (Eastham titration) in 200 mL of THF and cooled in an ice bath. The gas-inlet tube was positioned so that its mouth was well below the surface of the Grignard solution. The connection between the flasks was heated with electric heating tape, and an oil bath heated to 180–200 °C was applied to the flask containing the paraformaldehyde. The stream of N_2 introduced into this flask swept the gaseous formaldehyde directly from the cracking vessel *through* the cold Grignard solution.

After the formaldehyde had been added, the connection was broken, the inlet tube raised above the surface, and the flask sealed under N_2. The ice bath was removed and the reaction mixture stirred at room temperature for 1 h before hydrolysis with a minimum of saturated ammonium chloride solution. Examination of the gas-inlet tube revealed only 0.2 g of paraformaldehyde which failed to reach the solution. Analysis of the water in the pressure relief bubbler by Tollens reagent indicated that no formaldehyde had escaped via this route. The precipitated salts were removed by filtration and washed with 25 mL of diethyl ether. The filtrate was dried over $MgSO_4$ and distilled through a 30-cm Widmer column over a period of 6 h to remove most of the THF solvent. When the distillation had noticeably slowed, the solution was transferred to a 50 mL flask and 0.05 g of anhydrous K_2CO_3 added. The Widmer column was replaced with a short-path microhead, and all of the material which could distill at or below 110 °C at atmospheric pressure was collected in two fractions, a and b. The pressure was reduced and the distillation continued to give the remaining three fractions, c–e: (a) 90–108 °C (760 mm), and (b) 108–112 °C (760 mm), both mixtures of THF and toluene; (c) 64–74 °C (0.25 mm) and (d) 80–130 °C (0.25 mm), mixtures of I, II, benzyl alcohol and bibenzyl; (e) 130–150 °C (0.25 mm), mixture of III and bibenzyl. The fractions were analyzed by VPC by using a 5 ft × $^1/_4$ in. 5% FFAP and HMDS-treated Chrom W column: a and b at 50 °C, c and d at 125 °C, e at 225 °C. In addition to the small amounts of benzyl alcohol and bibenzyl which were formed in the preparation of the Grignard reagent, the following products were found: toluene (3.6 g, 39%), 2-phenylethanol (I; 0.9 g, 7%), *o*-tolylcarbinol (II; 6.2 g, 51%), *o*-(2-hydroxyethyl)benzyl alcohol (III; 0.4 g, 3%). The same techniques were used for all of the reactions listed in Table I.

2,6-Dideuterio-4-nitrotoluene. By use of the procedure of Corn,[26] a 500-mL flask was charged with 4-nitrotoluene (97.3 g, 0.71 mol) and D_2SO_4 (200 g, 2 mol) which had been prepared previously by the reaction of SO_3 and D_2O. The flask was heated to 85–90 °C for 36 h. After cooling, the brown solution was poured over 500 g of crushed ice. As the ice melted, a large quantity of a brown solid precipitated. The solid was collected by filtration and dissolved in 200 mL of diethyl ether, and the solution was shaken in a separatory funnel with the aqueous filtrate. The layers were separated, and the aqueous phase was extracted again with 100 mL of ether. The organic extracts were combined and dried over $MgSO_4$, and the solvent was removed in vacuo to give 90.6

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[21] Benkeser, R. A.; DeTalvo, W. *J. Am. Chem. Soc.* **1967**, *89*, 2141.

[22] Kopecky, K. R.; Lau, M.-P. *J. Org. Chem.* **1978** *43*, 525.

[23] It must be emphasized that Scheme IV does not reflect the influence of more subtle features like solvation effects, Schlenk equilibria, and molecular aggregation of the Grignard reagent (monomeric, dimeric, etc.).

[24] Eastham, J. F.; Watson, S. C. *J. Organomet. Chem.* **1967**, *9*, 165.

[25] It is quite likely that all previous workers who employed the benzyl Grignard reagent used less concentrated solutions than they realized, since simple acid titration was used to determine its titer.

[26] Corn, J., unpublished studies, Purdue University, 1970. See also: Renaud, R. N.; Kovachic, D.; Leitch, L. C. *Can. J. Chem.* **1961**, *39*, 21.

g of a brown solid whose NMR spectrum showed slightly greater than 75% deuterium incorporation at the positions ortho to the methyl group. The solid was heated with an additional 150 g of D_2SO_4 for 72 h and worked up in the same fashion to give 89.8 g of brown solid. The NMR of the material showed, by integration, greater than 95% replacement of the protons ortho to the methyl group with deuterium. The yield of 2,6-dideuterio-4-nitrotoluene formed in the two exchanges was 90%.

2,6-Dideuterio-4-aminotoluene.[26] A 2-L flask equipped with a mechanical stirrer, addition funnel, and condenser was charged with 2,6-dideuterio-4-nitrotoluene (57.0 g, 0.41 mol) and granulated (approximately 3 mesh) tin (97.0 g, 0.82 mol). The addition funnel was charged with 202 mL of concentrated HCl solution (38%) which was added dropwise until the heat generated by the reaction liquified the deuterated aminotoluene. Once the initial exotherm had subsided slightly, the remaining HCl solution was added over 1 h. The mixture was then heated to 75 °C for 0.5 h. The solution was cooled and made basic by the careful addition of NaOH (150 g, 3750 mmol) in 250 mL of H_2O. The resulting solution was steam-distilled until 500 mL of distillate had been collected. The distillate was extracted three times with 100-mL portions of diethyl ether. The organic extracts were combined and dried over $MgSO_4$, and the solvent was removed in vacuo to give 30 g (68%) of 2,6-dideuterio-4-aminotoluene as pale orange crystals, mp 41–43 °C. The NMR spectrum showed no change in the percent of deuterium incorporation.

2,6-Dideuteriotoluene.[26] A 2-L flask equipped with a mechanical stirrer, addition funnel, and thermometer was charged with 2,6-dideuterio-4-aminotoluene (46.6 g, 0.43 mol), 530 mL of deionized water, and 84.7 mL of concentrated HCl solution. The flask was cooled in an ice bath to approximately 5 °C and the addition funnel charged with a solution of $NaNO_2$ (30.62 g, 0.43 mol) in 60 mL of deionized H_2O. The $NaNO_2$ solution was added dropwise to the reaction flask over a period of 4 h so that the temperature did not rise above 8 °C. It was stirred in the cold for an additional 0.5 h before being quickly poured into a 2-L flask containing 472 mL of 50% H_3PO_2 at 5 °C. The resulting orange solution began to evolve N_2 and was placed under a mercury bubbler in a cold room for 24 h. It was then warmed to room temperature, and the orange layer which had formed was separated. The aqueous phase was extracted three times with 100-mL portions of diethyl ether and saturated with NaCl to force out any remaining organic materials. The organic layers was combined, washed with 1.0 M NaOH, and dried over $MgSO_4$. The solvent was removed by slow distillation at atmospheric pressure through a 30-cm Widmer column. The residue was distilled at atmospheric pressure through a 15-cm, glass bead packed column to give 29.4 g (73%) of 2,6-dideuteriotoluene as a clear liquid, bp 107–109 °C (760 mm). The NMR spectrum showed no change in the deuterium labels.

2,6-Dideuteriobenzyl Chloride.[26] A 100-mL flask equipped with a thermometer, condenser, and gas-inlet tube was wrapped in aluminum foil. It was charged with 2,6-dideuteriotoluene (29.4 g, 0.3 mol) and *tert*-butyl hypochlorite[27] (22.0 g, 0.2 mol) and purged by bubbling a stream of N_2 through the solution for 0.5 h. The N_2 flow was reduced to a minimal rate, the foil removed, and the flask illuminated by a 60-W light as a distance of 10 cm. After 5 min, the temperature began to rise until the solution refluxed at 80 °C. The light was removed to a distance of 20 cm, and the illumination was continued at intervals to control the reflux. After 45 min the yellow color of the *tert*-butyl hypochlorite had disappeared, and the temperature dropped. The reaction mixture was distilled at atmospheric pressure through a 30-cm Widmer column to give a fraction of *tert*-butyl alcohol collected from 78 to 80 °C and 13.9 g of unreacted 2,6-dideuteriotoluene collected from 105 to 108 °C. The Widmer column was replaced with a splash guard and the distillation continued to give 14.0 g (55%) of 2,6-dideuteriobenzyl chloride as a clear liquid, bp 178–183 °C (760 mm). The NMR spectrum showed the material to be the desired monochlorinated product with the deuterium labels undisturbed.

Reaction of (2,6-Dideuteriobenzyl)magnesium Chloride in THF with Formaldehyde. By use of the General Procedure (vide supra), a solution of 0.082 mol of (2,6-dideuteriobenzyl)-magnesium chloride in 200 mL of THF was prepared and gaseous formaldehyde (2.46 g, 0.082 mol) added. After being stirred for 1 h at room temperature, the mixture was hydrolyzed with saturated NH_4Cl solution. The workup was as described previously. The toluene and *o*-tolylcarbinol were collected pure by preparative VPC and analyzed on a Varian A-60 NMR spectrometer. The deuterium content of each species was determined by integration of the appropriate NMR peaks. The results are shown in Table II, reaction 1.

Reaction of Benzylmagnesium Chloride in THF with Formaldehyde. Hydrolysis with DCl/D_2O. By use of the General Procedure, 0.1 mol of gaseous formaldehyde was added to 0.1 mol of benzyl Grignard in 200 mL of THF. This solution was stirred for 1 h at room temperature before being hydrolyzed with a minimum of 20% $DCl-D_2O$ (Columbia Chemicals). Filtration and distillation as before gave the results shown in Table II, reaction 2.

Trapping with Trimethylchlorosilane. By use of the previous procedure, monomeric formaldehyde (3.0 g, 0.1 mol) was added to a solution of 0.1 mol of benzylmagnesium chloride in 200 mL of THF at 0 °C. After the solution had stirred for the desired period of time (0, 1, and 4 h) at room temperature, trimethylchlorosilane (54.32 g, 0.5 mol) was added in one portion by a syringe. The solution was stirred under N_2 for 24 h, during which time the flask became filled with a solid mass of white precipitate. The flask was cooled in a water bath and 75 mL of 2 N HCl added. The solid dissolved in several minutes to give a two-phase system which was stirred for 0.5 h. The mixture was extracted twice with 100-mL portions of diethyl ether. The aqueous phase was saturated with NaCl and extracted with 50 mL of diethyl ether. The organic extracts were combined, dried over $MgSO_4$, and distilled. The following fractions were collected and analyzed by VPC (5% FFAP column): (a) 70–90 °C (760 mm) and (b) 90–95 °C (760 mm), mixture of THF, hexamethyldisiloxane, and toluene; (c) 40–80 °C (16 mm), mixture of XVII and XVIII; (d) 55–85 °C (0.3 mm), mixture of XVII, XVIII, I, and II; (e) 90–110 °C (0.3 mm), mixture of XVIII, II, and XIX; (f) 120–160 °C (0.3 mm), mixture of XIX and II. The yields of the products are given in Table III.

Determination of Water Content of Monomeric Formaldehyde. By use of the General Procedure (vide supra), gaseous formaldehyde (3.0 g, 0.1 mol) was added directly to a solution of 0.1 mol of (4-methylphenyl)magnesium bromide in 100 mL of THF. After the resulting solution had stirred for 1 h at room temperature it was hydrolyzed with a minimum of 20% DCl in D_2O. The solids were removed, and the filtrate was distilled in the usual manner to permit isolation of the toluene together with all other reaction products. The major fraction of 9.1 g of clear liquid was collected, boiling at 70–75 °C (0.25 mm). This distillate solidified to white crystals melting at 57–58 °C. An NMR spectrum of the crystals showed them to be the oxygen-deuterated 4-methylbenzyl alcohol with only traces of the protonated alcohol. The yield of the alcohol was 75%. A 15% yield of toluene was isolated. An NMR analysis of a VPC-collected sample of this toluene showed it was a mixture of 70% toluene monodeuterated at the *p*-position and 30% undeuterated. Hence a maximum of 5% (15% × 30%) of any proton source like water could have been introduced accidentally or by cracking of the formaldehyde.

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Registry No. I, 60-12-8; II, 89-95-2; III, 6346-00-5; VII, 80515-60-2; VIII, 80515-61-3; IX, 53907-52-1; X, 80515-62-4; XI, 80515-63-5; XII, 1861-00-3; XIII, 108-88-3; XIV, 49681-79-0; XV, 80515-64-6; XVI, 80515-65-7; XVII, 770-09-2; XVIII, 80515-66-8; XIX, 57754-01-5; benzyl chloride, 100-44-7; formaldehyde, 50-00-0; 2,6-dideuterio-4-nitrotoluene, 80515-67-9; 2,6-dideuterio-4-aminotoluene, 80515-68-0; 2,6-dideuteriobenzyl chloride, 80515-69-1.

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(27) Teeter, H. M.; Bell, E. W. "Organic Syntheses"; Wiley; New York, 1963; Collect. Vol. IV, p 125.