branched alkyl radical to tetrachloroethylene in the liquid phase proceeds almost as efficiently as the addition of methyl radicals to ethylene in the gas phase.

The fact that Szwarc[1b] has found that the addition of methyl radicals to tetrachloroethylene does not proceed efficiently might be due to the unsuitability of his measuring technique in a system containing tetrachloroethylene. The method developed by Szwarc uses the thermal decomposition of acetyl peroxide as a source of methyl radicals. The methyl radicals abstract hydrogen from the solvent (isooctane), forming methane. In the presence of solutes consuming methyl radicals, a net decrease in the amount of methane formed is observed. The difference in methane formed in the presence and absence of a solute constitutes a measure of its affinity toward methyl radicals. In the particular case of tetrachloroethylene, a chain reaction between the solvent radicals and tetrachloroethylene could ensue, similar to the reaction observed in this work. The formation of HCl in the system might induce decomposition of the acetyl peroxide, resulting in an increased rate of methyl radical generation. The enhanced rate of methyl radicals formation could thus mask their disappearance by interaction with the solute. Under such circumstances, a fortuitously low value for methyl radical addition to tetrachloroethylene could be obtained.

Our results would imply, assuming comparable rates for the addition of radicals to olefins in the liquid and gaseous phase, that the steric hindrance caused by the presence of the bulky chlorine atoms in tetrachloroethylene is almost completely offset by the inductive effect of the halogen substituents.

Acknowledgment. The authors wish to thank Dr. N. Danieli of the Weizman Institute of Science for the mass spectrometer analyses.

Kinetics of the Addition of Methylmagnesium Bromide to 4-Methylmercaptoacetophenone in Diethyl Ether[1]

James Billet[2] and Stanley G. Smith

Contribution from the Department of Chemistry, University of Illinois, Urbana, Illinois 61801. *Received January 5, 1968*

Abstract: The ultraviolet spectrum of reacting solutions of 4-methylmercaptoacetophenone in ether solutions of methylmagnesium bromide at 25.0° has been found to exhibit an absorbance, $\lambda_{\max}$ 336 mμ (ϵ 1.5×10^4), corresponding to complex formation with an apparent equilibrium constant of 15 l./mol. The pseudo-first-order rate constant for the addition of methylmagnesium bromide to the carbonyl group increases from 0.3 to 1.3 sec^{-1} with an increase in the Grignard concentration from 0.05 to 0.6 *M*. Reaction schemes involving conversion of the complex to product which provide a descriptive summary of these data are outlined. A twofold decrease in pseudo-first-order rate constant with an increase in ketone concentration by a factor of *ca.* 10, esr signals, and an absorption spectrum, $\lambda_{\max}$ 334 and 560 mμ, observed during the reaction of methylmagnesium bromide with benzophenone, as well as the formation of benzopinacol in 14% yield from 9.6×10^{-3} *M* ketone and 2 *M* Grignard, suggest the presence of a ketyl-like side reaction in this system.

Recent studies[3] have suggested that formation of a complex between Grignard reagents and ketones is fast[4–6] on the time scale of conversion of reactants to products. However, the nature of the reactive species in the Grignard reagent and details of the product-forming steps require further clarification. The early suggestion of Meisenheimer and Casper[7] that a complex between the Grignard reagent and ketone is converted to product by a unimolecular process has received substantial support.[4–6,8–10] Other data[11–13] have been interpreted as inidicating that in the product-forming step, the complex reacts with a second molecule[14] of organomagnesium reagent.

In a previous spectroscopic and kinetic study of the reaction of methylmagnesium bromide with 2,4-dimethyl-4′-methylmercaptobenzophenone in diethyl ether,[4] below *ca.* 0.3 *M* methylmagnesium bromide, data were found to be quantitatively consistent with unimolecular conversion of complex to product, while above *ca.* 0.3 *M* the reaction was found to be faster

---

(1) Research supported by a grant from the National Science Foundation.

(2) Sinclair Oil Predoctoral Fellow.

(3) For reviews see: (a) B. J. Wakefield, *Organometal. Chem. Rev.*, **1**, 131 (1966); (b) W. Tochtermann, *Angew. Chem.*, **5**, 351 (1966); (c) R. E. Dessy and W. Kitching, *Advan. Organometal. Chem.*, **4**, 280 (1966); (d) E. C. Ashby, *Quart. Rev.* (London), **2**, 259 (1967).

(4) (a) S. G. Smith, *Tetrahedron Lett.*, **7**, 409 (1963); (b) S. G. Smith and G. Su, *J. Amer. Chem. Soc.*, **86**, 2750 (1964); (c) *ibid.*, **88**, 3995 (1966).

(5) S. G. Smith and J. Billet, *J. Amer. Chem. Soc.*, **89**, 6948 (1967).

(6) (a) T. Holm, *Tetrahedron Lett.*, **28**, 3329 (1966); (b) T. Holm, *Acta Chem. Scand.*, **19**, 1819 (1965); (c) *ibid.*, **20**, 1139 (1966); (d) *ibid.*, **20**, 2821 (1966).

(7) J. Meisenheimer and J. Casper, *Chem. Ber.*, **54B**, 1655 (1921).

(8) H. O. House and D. D. Traficante, *J. Org. Chem.*, **28**, 355 (1963).

(9) (a) J. Miller, G. Gregoriou, and H. S. Mosher, *J. Amer. Chem. Soc.*, **83**, 3966 (1961); (b) D. O. Cowan and H. S. Masher, *J. Org. Chem.*, **27**, 1 (1962).

(10) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963).

(11) C. G. Swain and H. B. Boyles, *J. Amer. Chem. Soc.*, 73, 870 (1951).

(12) (a) M. Anteunis, *J. Org. Chem.*, 26, 4214 (1961); (b) *ibid.*, 27, 596 (1962); (c) M. Anteunis, *Bull. Soc. Chim. Belg.*, 73, 655 (1964).

(13) E. C. Ashby, R. Duke, and H. M. Neumann, *J. Amer. Chem. Soc.*, **89**, 1964 (1967).

(14) P. Pfeiffer and H. Blank, *J. Prakt. Chem.*, **153**, 242 (1939).

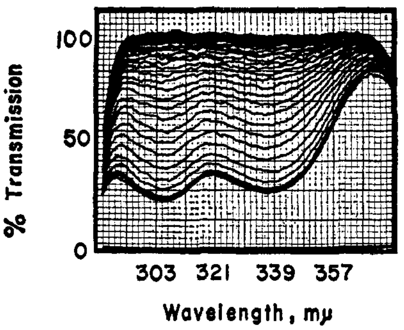


Figure 1. Absorption spectrum of 5.9×10^{-5} *M* 4-methylmercaptoacetophenone in 0.093 *M* recrystallized methylmagnesium bromide in diethyl ether at 25.0° recorded 18.2 times/sec. The first recorded spectrum was obtained under continuous-flow conditions.

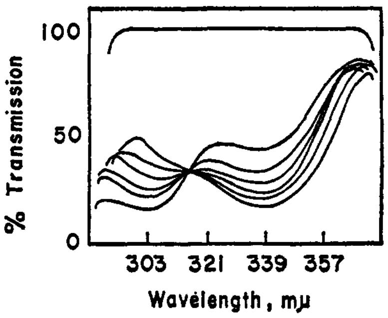
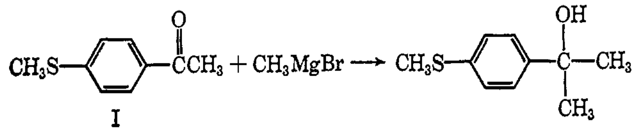


Figure 2. Absorption spectrum constructed from the first recorded spectra of 4-methylmercaptoacetophenone in 0.0392 to 0.386 *M* methylmagnesium bromide in diethyl ether at 25.0°, exhibiting an isosbestic point at 316 mμ.

than predicted on this basis. General medium effects, changes in the gross nature of the organomagnesium reagent with concentration, and/or higher order kinetic terms had to be invoked to quantitatively fit the kinetic data. However, in the reaction of dimethylmagnesium with 4-methylmercaptoacetophenone in diethyl ether,[5] the simple picture of rapid complex formation followed by unimolecular formation of products was found to be consistent with kinetic and spectroscopic data over the concentration range studied (0.01 to 0.6 *M* Me_2Mg). This paper describes a subsequent spectroscopic and kinetic study of the reaction of methylmagnesium bromide with the relatively unhindered ketones, 4-methylmercaptoacetophenone (I) and benzophenone, in diethyl ether at 25.0°.



I

Results

4-Methylmercaptoacetophenone. Stopped-flow, rapid-scan spectrophotometry[5,15] indicates that 4-methylmercaptoacetophenone in the presence of methylmagnesium bromide in diethyl ether exhibits an absorbance at 336 mμ in addition to the free ketone absorbance at 300 mμ.[16a] The additional absorbance is formed essentially instantaneously[16b] on the time scale of conversion to products, as in previous studies,[4-6] and is attributed to a complex between the ketone and methylmagnesium bromide. In the spectrum illustrated in Figure 1, 0.0275 sec was required to sweep through and record the indicated wavelength region. The absorption spectrum was recorded 18.2 times/sec. The first recorded spectrum in Figure 1 corresponds to continuous-flow conditions, making relative absorbance at various wavelengths independent of the time required to sweep through the spectral region. The remaining traces were obtained after the mixed reagents stopped flowing through the spectroscopic cell. It is evident from Figure 1 that both ketone and complex decrease at the same rate to the methylmagnesium bromide base line. An isosbestic point at 316 mμ is illustrated in Figure 2, which was constructed from the spectrum of ketone I under continuous-flow conditions in diethyl ether solutions of various concentrations of methylmagnesium bromide.

The apparent equilibrium constant for 1:1 complex formation, *K*, eq 1, and the extinction coefficient of the complex at its absorbance maximum, $\epsilon_c{}^c$, may be calculated directly from the spectroscopic data by application of the Scott[17,18] procedure since at the highest methylmagnesium bromide concentration employed only 4% reaction has occurred before the spectrum is recorded. This procedure, Figure 3, gives a least-squares intercept and slope corresponding to an equilibrium constant,[19] *K*, of 19 l./mol and an extinction coefficient, $\epsilon_c{}^c$, for the complex at its absorbance maximum (336 mμ)[16a] of 1.4×10^4.

Because of the reactivity of the system and the sensitivity of the slope and intercept of the Scott plot to errors in measurement,[17b-d] the spectroscopic data were subjected to an additional analysis. The equilibrium constant, *K*, for 1:1 complex formation, eq 1, may be calculated at various Grignard concentrations using eq 2, where $A_c{}^c$ is the absorbance of the complex at its maximum, $\epsilon_c{}^c$ is the extinction coefficient of the complex at its maximum, $A_k{}^k$ is the absorbance of the

$$\text{ketone} + \text{MeMgBr} \overset{K}{\rightleftarrows} \text{complex} \tag{1}$$

$$K = \frac{A_c{}^c/\epsilon_c{}^c}{(A_k{}^k/\epsilon_k{}^k)[\text{MeMgBr}]} \tag{2}$$

---

(15) For reviews of flow methods and detailed descriptions of typical experimental apparatus, see: (a) F. J. W. Roughton and B. Chance in "Investigation of Rates and Mechanisms of Reaction," Part II, S. L. Friess, E. S. Lewis, and A. Weissberger, Ed., Interscience Publishers, New York, N. Y., 1963, Chapter 14; (b) E. F. Caldin, "Fast Reactions in Solution," John Wiley and Sons, Inc., New York, N. Y., 1964, Chapter 3.

(16) (a) Since both absorbance maxima exhibit small bathochromic shifts with increasing methylmagnesium bromide concentration, the absorbance maxima reported were obtained by extrapolation of plots of apparent maximum *vs.* methylmagnesium bromide concentration to zero concentration. (b) The ultraviolet absorbance attributed to the complex is present at the first spectrophotometric measurement, *ca.* 0.03 sec after mixing equal volumes of the reagents.

(17) (a) R. L. Scott, *Rec. Trav. Chim.*, **75**, 787 (1956); (b) K. Conrow, G. D. Johnson, and R. E. Bowen, *J. Amer. Chem. Soc.*, **86**, 1025 (1964); (c) W. B. Person, *ibid.*, **87**, 167 (1965); (d) N. J. Rose and R. S. Drago, *ibid.*, **81**, 6138 (1959).

(18) The rapidity of the reaction of 4-methylmercaptoacetophenone with dimethylmagnesium recently reported[5] precluded the Scott treatment, since a substantial fraction of the reaction occurred before the first spectroscopic observation, *ca.* 0.16 sec after mixing. The lower reactivity of 4-methylmercaptoacetophenone and methylmagnesium bromide and the use of a modified stopped-flow apparatus with an elapsed time between mixing and spectroscopic observation of *ca.* 0.03 sec permitted measurement before a significant amount of reaction had occurred.

(19) See ref 4c for a discussion of the significance of the equilibrium constants calculated from these data.

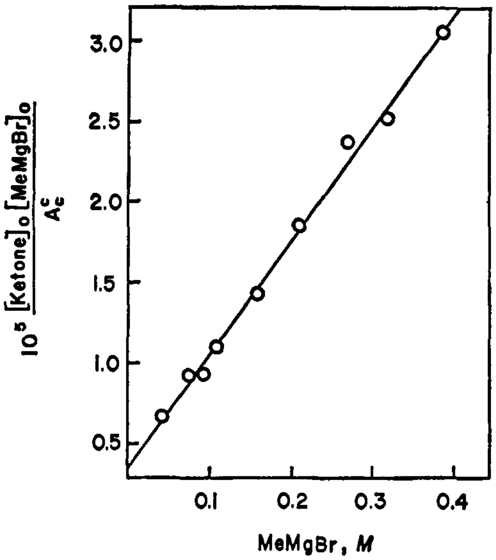


Figure 3. Scott plot for the absorbance of the complex of 4-methylmercaptoacetophenone, A_c^c, in diethyl ether solutions of methylmagnesium bromide at 25.0°.

ketone at its maximum,[16a] ϵ_k^k is the extinction coefficient of the ketone at its maximum, and [MeMgBr] the concentration of Grignard reagent.

Although 4-methylmercaptoacetophenone is transparent at the absorbance maximum of its methylmagnesium bromide complex, contribution by the complex to the total absorbance, A_k^{k+c}, at the ketone maximum must be considered. As indicated in eq 3 and 4, the

$$\frac{A_k^{k+c}}{A_c^c} = \frac{[\text{ketone}]\epsilon_k^k + [\text{complex}]\epsilon_k^c}{[\text{complex}]\epsilon_c^c} \tag{3}$$

$$\frac{A_k^{k+c}}{A_c^c} = \frac{1}{[\text{MeMgBr}]}\left[\frac{\epsilon_k^k}{K\epsilon_c^c}\right] + \frac{\epsilon_k^c}{\epsilon_c^c} \tag{4}$$

ratio of the extinction coefficient of the complex at the ketone absorbance maximum to the extinction coefficient of the complex at the complex absorbance maximum, $\epsilon_k^c/\epsilon_c^c$, may be obtained by a plot of the ratio of the total absorbance at the ketone maximum to the absorbance at the complex maximum, A_k^{k+c}/A_c^c, *vs.* 1/[MeMgBr]. The data plotted in Figure 4 yield a slope of $\epsilon_k^k/\epsilon_c^c K$ and an intercept of $\epsilon_k^k/\epsilon_c^c$, the desired extinction coefficient ratio, 0.25.

The apparent extinction coefficient of the complex at its absorbance maximum, ϵ_c^c, is then calculated from the absorbance at the complex maximum, A_c^c, the flow-cell path length, 1.00 cm, and the equilibrium concentration of complex. The equilibrium concentration of complex is equal to the difference between the initial and equilibrium concentration of ketone before any reaction has occurred, the equilibrium concentration of ketone being calculated from the difference between the total absorbance at the ketone maximum, A_k^{k+c}, and the absorbance at the ketone maximum contributed by the complex, $0.25A_c^c$.

Table I summarizes values of the extinction coefficient of the methylmagnesium bromide complex of 4-methylmercaptoacetophenone in diethyl ether at its absorbance maximum, ϵ_c^c, and the apparent equilibrium constant for 1:1 complex formation, K, calculated from eq 2 using the spectroscopic data obtained at various concentrations of methylmagnesium bromide. The average values of K, 15 l./mol, and ϵ_c^c, 1.5×10^4 l./mol cm, agree reasonably well with the values obtained using the Scott procedure based on data at a single wavelength.

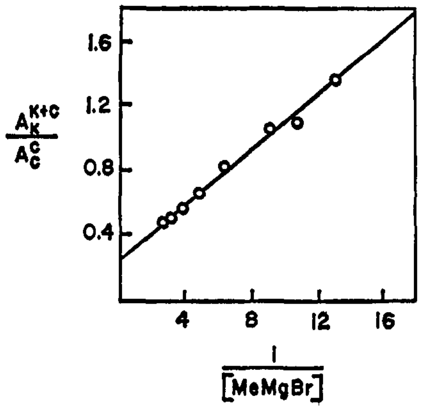


Figure 4. Plot of A_k^{k+c}/A_c^c *vs.* 1/[MeMgBr], from eq 4 and the spectrum of 4-methylmercaptoacetophenone in diethyl ether solutions of methylmagnesium bromide at 25.0°.

Table I. Equilibrium Constants for 1:1 Complex Formation between 5.921×10^{-5} *M* 4-Methylmercaptoacetophenone and Methylmagnesium Bromide in Diethyl Ether at 25.0° [a]

[MeMgBr], M[b]	A_c^c	A_k^{k+c}	A_k^k	$10^{-4}\epsilon_c^c$, l./mole cm	K, l./mol[c]
0.0392	0.339	0.808	0.723	1.45	15.8
0.0759	0.484	0.659	0.538	1.47	15.7
0.0927	0.585	0.648	0.502	1.71	16.6
0.110	0.588	0.628	0.481	1.66	14.7
0.158	0.644	0.540	0.379	0.59	14.3
0.210	0.660	0.443	0.278	1.45	14.9
0.273	0.678	0.390	0.220	1.40	14.9
0.319	0.746	0.390	0.203	1.52	15.2
0.386	0.744	0.366	0.180	1.48	14.1
			Av	1.53 ± 0.09	15.1 ± 0.6

[a] See text for definition of symbols. [b] Total base. [c] Calculated using eq 2 and a value for ϵ_k^k of 2.02×10^4 and an average value for ϵ_c^c of 1.53×10^4.

Although the apparent equilibrium constant (Table I) is relatively constant over the Grignard concentration range investigated, the exact nature of the complex or complexes inevitably depends upon the nature of the organomagnesium species contributing to the constitution of the Grignard reagent. A mixture of complexes formed from monomeric and dimeric Grignard reagents can, with appropriate values of the equilibrium constants, appear deceptively simple. In addition, some contribution to the spectrum by complexes of the ketone with dimethylmagnesium and magnesium bromide cannot be excluded.

The rate of disappearance of the complex between 4-methylmercaptoacetophenone and methylmagnesium bromide was spectrophotometrically determined by a stopped-flow[15] technique. While the concentration of ketone was varied from 10^{-4} to 10^{-2} *M*, the use of at least a tenfold excess of methylmagnesium bromide provided pseudo-first-order kinetics. First-order rate constants were calculated by reproducing transmittance *vs.* time oscillographs with an analog computer programmed for electronic simulation of the first-order rate equation.

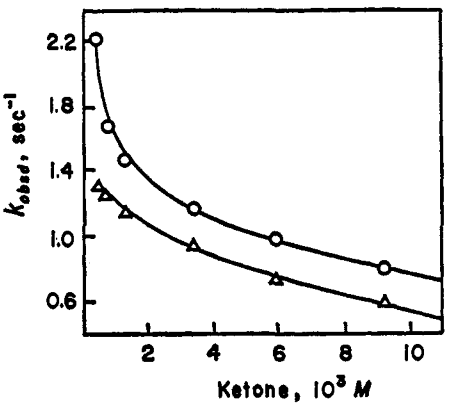


Figure 5. Plot of k_{obsd} *vs.* ketone concentration for the reaction 4-methylmercaptoacetophenone (I) with 0.158 M methylmagnesium bromide in diethyl ether at 25.0°: ○, ketone I; △, *ca.* 10^{-2} M acetone added to ketone I (Table II).

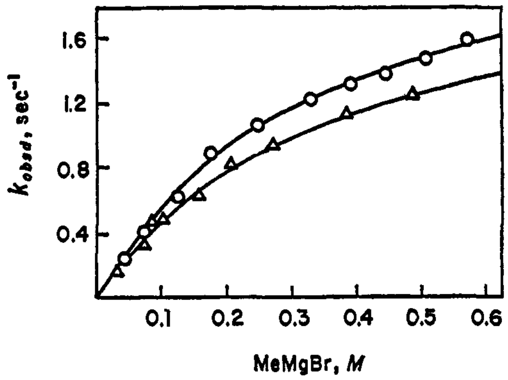


Figure 6. Plot of k_{obsd} *vs.* concentration of methylmagnesium bromide in the reaction with 4-methylmercaptoacetophenone in diethyl ether at 25.0°: ○, methylmagnesium bromide and 1.05×10^{-2} M ketone I; △, recrystallized methylmagnesium bromide and 2.98×10^{-3} M ketone I (Table III).

The observed first-order rate constant, k_{obsd}, is not independent of the initial ketone concentration. The data summarized in Table II and illustrated in Figure 5 indicate that increasing the initial ketone concentration from 5×10^{-4} to 10^{-2} M decreases the pseudo-first-order rate constant for reaction with, *e.g.*, 0.16 M methylmagnesium bromide from 2.2 to 0.7 sec^{-1}.

Table II. Effect of Ketone Concentration on the Pseudo-First-Order Rate Constant for the Reaction of Methylmagnesium Bromide with 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

Crude MeMgBr^a			Recrystallized MeMgBr^b	
Initial ketone, 10^3M	k_{obsd}, sec^{-1}		Initial ketone, 10^3M	k_{obsd}, sec^{-1}
0.463	2.23	1.31^c	0.669	1.19
0.784	1.69	1.27^c	0.719	1.14
1.34	1.48	1.15^c	1.19	1.14
3.39	1.18	0.935^c	3.04	1.11
5.89	0.993	0.728^c	5.44	1.13
9.23	0.801	0.573^c	7.59	1.14
			8.58	1.10

[a] Crude MeMgBr, 0.158 M base, 0.160 M halide. [b] Recrystallized MeMgBr, 0.323 M base, 0.339 M halide. [c] Acetone, 10^{-2} M, mixed with ketone I.

A similar but considerably less pronounced phenomenon was previously observed in the reaction of methylmagnesium bromide with 2,4-dimethyl-4′-methylmercaptobenzophenone.[4b,c] In that study, with 10^{-5} M ketone, pseudo-first-order rate constants tended to lack reproducibility, due to a marked ketone dependence of the rate constant at low ketone concentrations; but the use of 10^{-4} to 10^{-3} M ketone or a mixture of 10^{-5} M ketone and 10^{-3} M acetone gave reproducible rate constants which were appropriately independent of ketone concentration under pseudo-first-order conditions. The use of 10^{-2} M acetone added to 4-methylmercaptoacetophenone solutions decreases the high rates observed with methylmagnesium bromide and *ca.* 10^{-4} M ketone, but the addition of acetone is not effective in completely removing the ketone concentration dependence (Table II, Figure 5).

However, the ketone concentration dependence in the reaction of 4-methylmercaptoacetophenone with methylmagnesium bromide was effectively removed for ketone concentrations from 10^{-3} to 10^{-2} M by recrystallization of the Grignard reagent (Table II) the observed pseudo-first-order rate constant being unchanged from 0.7×10^{-3} to 9×10^{-3} M initial ketone concentrations. These observations suggest that methylmagnesium bromide as prepared under the conditions of these experiments contains a low concentration of a reactive species which can be at least partially removed by recrystallization.

The effect of methylmagnesium bromide concentration on the rate of reaction with 4-methylmercaptoacetophenone is illustrated in Figure 6 and summarized in Table III. While recrystallized methylmagnesium bromide is less reactive than the reagent as prepared, at the ketone concentrations employed, the kinetic data relating k_{obsd} *vs.* methylmagnesium bromide concentration for both reagents are qualitatively similar.

Table III. Reaction of Methylmagnesium Bromide with 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

MeMgBr,^{a} M	k_{obsd}, sec^{-1}	Recryst MeMgBr,^{b} M	k_{obsd}, sec^{-1}
0.0525	0.243	0.0392	0.172
0.0806	0.402	0.0759	0.344
0.131	0.618	0.0927	0.466
0.182	0.850	0.110	0.502
0.252	1.06	0.158	0.642
0.334	1.24	0.210	0.835
0.396	1.32	0.273	0.935
0.452	1.38	0.386	1.16
0.513	1.51	0.488	1.28
0.574	1.60		

[a] Ketone, 1.05×10^{-2} M. [b] Ketone, 2.98×10^{-3} M.

The products of the reaction of 3.53 mmol of 4-methylmercaptoacetophenone with 80 mmol of methylmagnesium bromide in 100 ml of diethyl ether were determined after work-up with sulfuric acid and dehydration in benzene with *p*-toluenesulfonic acid. The nmr and ir spectra of the crude products were identical with the spectra of a mixture of 4% 4-methylmercaptoacetophenone and 96% 2-(4-methylmercaptophenyl)propene, the products of enolization and the dehydration of the expected tertiary alcohol addition product, respectively.

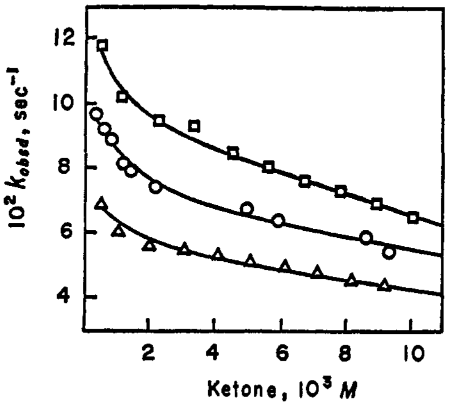


Figure 7. Plot of K_{obsd} *vs.* ketone concentration for the reaction of benzophenone with methylmagnesium bromide in diethyl ether at 25.0°: ○, methylmagnesium bromide, 0.085 *M;* □, recrystallized methylmagnesium bromide, 0.123 *M;* △, recrystallized methylmagnesium bromide, 0.123 *M*, and acetone, 8.6 × 10^{-3} *M* (Table V).

Benzophenone. The rates of reaction of methylmagnesium bromide and benzophenone in diethyl ether at 25.0° were also measured under pseudo-first-order conditions. For faster reactions (half-life less than 10 sec) the stopped-flow technique was used. For slower reactions, an ether solution of benzophenone was injected through a silicon-rubber seal into thermostated ultraviolet cells containing methylmagnesium bromide reagent. A continuous plot of absorbance at a selected wavelength *vs.* time was obtained. From these data rate constants were calculated using a least-squares digital computer technique with data weighed in proportion to the absolute magnitude of the absorbance. A typical kinetic run is illustrated in Table IV.

Table IV. Reaction of 0.123 *M* Recrystallized Methylmagnesium Bromide with 5.10 × 10^{-4} *M* Benzophenone in Diethyl Ether at 25.0°

Time, sec	Rel absorb, 300 mμ	$10^2 k_{obsd}$,[a] sec^{-1}
2.50	0.970	
3.75	0.872	11.7
5.00	0.783	11.4
6.25	0.682	12.0
7.50	0.625	11.5
8.75	0.560	11.6
10.00	0.501	11.8
11.25	0.452	11.8
12.50	0.413	11.8
13.75	0.380	11.8
15.00	0.352	11.7
17.50	0.298	11.9
50.00	0.161	11.8
	Weighted least-squares	11.8

[a] Integrated.

The rate of reaction of benzophenone with methylmagnesium bromide in diethyl ether under pseudo-first-order conditions also exhibits a ketone concentration dependence. The pseudo-first-order rate constant for the reaction of 0.085 *M* methylmagnesium bromide with benzophenone decreases by a factor of 2 as the initial ketone concentration is increased from 3.8 × 10^{-4} to 10^{-2} *M* (Table V, Figure 7). In these experiments, recrystallization of the methylmagnesium bromide reduced but did not eliminate the ketone concentration dependence of the first-order rate constant at low benzophenone concentrations. The ketone concentration dependence illustrated in Table V and Figure 7 was investigated by repetitive additions of benzophenone to a methylmagnesium bromide solution. Thus the ketone concentration listed in Table V is actually the sum of incremental additions of ketone, while the corresponding rate constant refers to the rate of reaction of the last increment.

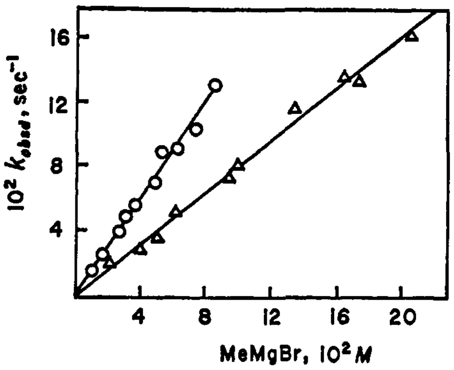


Figure 8. Plot of k_{obsd} *vs.* concentation of methylmagnesium bromide for the reaction with benzophenone in diethyl ether at 25.0°: ○, 0.5 × 10^{-3} *M* ketone; △, 5 × 10^{-3} *M* ketone (Table VI).

Table V. Effect of Ketone Concentration[a] on the Pseudo-First-Order Rate Constant for the Reaction of Methylmagnesium Bromide with Benzophenone in Diethyl Ether at 25.0°

MeMgBr[b]		Recryst MeMgBr[c]			
Initial ketone, 10^3 *M*	$10^2 \times k_{obsd}$, sec^{-1}	Initial ketone, 10^3 *M*	$10^2 \times k_{obsd}$, sec^{-1}	Initial ketone, 10^3 *M*	$10^2 \times k_{obsd}$,[d] sec^{-1}
0.384	9.62	0.510	11.8	0.508	6.86
0.576	9.20	1.12	10.1	1.02	5.99
0.778	8.89	2.24	9.56	2.04	5.66
1.17	8.15	3.36	9.23	3.06	5.50
1.45	7.93	4.48	8.52	4.08	5.30
2.17	7.41	5.60	8.04	5.10	5.15
5.02	6.80	6.72	7.59	6.12	4.98
5.94	6.47	7.84	7.25	7.14	4.82
8.62	5.87	8.96	6.91	8.16	4.57
9.38	5.47	10.1	6.43	9.18	4.43

[a] Ketone concentration represents the sum of incremental additions; rate constant was measured on last increment. [b] 0.0848 *M* MeMgBr. [c] Recrystallized 0.123 *M* MeMgBr. [d] Acetone, 8.61 × 10^{-3} *M* added.

The effect of using *ca.* 0.5 × 10^{-3} *M* or 5 × 10^{-3} *M* benzophenone on the rate constant for reaction of benzophenone with methylmagnesium bromide is given in Table VI and Figure 8, the lower ketone concentration giving rise to higher rate constants over a *ca.* tenfold change in concentration of the Grignard reagent. The change in observed pseudo-first-order rate constant at *ca.* 5 × 10^{-3} *M* benzophenone and methylmagnesium bromide concentrations ranging from 0.02 to 0.8 *M* are summarized in Table VII and plotted in Figure 9.

The product of the reaction of 4.14 mmol of benzophenone with 80 mmol of methylmagnesium bromide in diethyl ether was determined after work-up with sulfuric acid and dehydration in benzene with *p*-toluene-

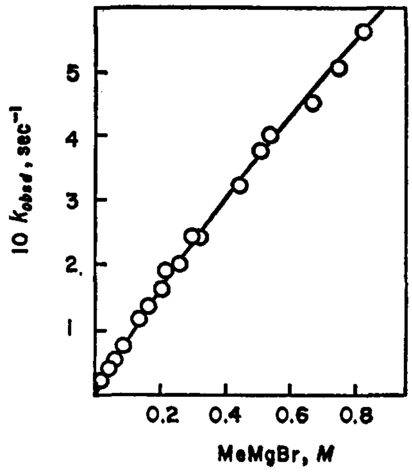


Figure 9. Plot of k_{obsd} *vs.* concentration of methylmagnesium bromide in the reaction with 5 × 10^{-3} *M* benzophenone in diethyl ether at 25.0° (Table VII).

Table VI. Reaction of Methylmagnesium Bromide with Benzophenone in Diethyl Ether at 25.0°

MeMgBr, 10^2 *M*	Initial ketone, 10^3 *M*	10^2 × k_{obsd}, sec^{-1}	MeMgBr, 10^2 *M*	Initial ketone, 10^3 *M*	10^2 × k_{obsd}, sec^{-1}
0.925	0.504	1.50	2.02	4.82	2.01
1.70	0.524	2.56	3.92	4.82	2.87
2.76	0.616	4.04	5.11	5.52	3.58
3.13	0.464	4.48	6.22	5.52	5.33
3.67	0.604	5.52	9.45	6.42	7.55
4.91	0.584	6.98	0.0	4.82	8.14
5.15	0.430	9.10	13.6	4.82	11.7
6.25	0.516	9.06	16.7	5.52	13.8
7.45	0.634	10.4	17.5	6.42	13.5
8.65	0.597	13.2	20.8	4.82	16.4

Table VII. Reaction of Methylmagnesium Bromide with Benzophenone in Diethyl Ether at 25.0°

MeMgBr,[a] *M*	Initial ketone, 10^3 *M*	10 × k_{obsd}, sec^{-1}	MeMgBr,[a] *M*	Initial ketone, 10^3 *M*	10 × k_{obsd}, sec^{-1}
0.0202	4.82	0.201	0.306	6.42	2.47
0.0511	5.52	0.358	0.328	4.82	2.48
0.0622	5.52	0.533	0.448	4.82	3.25
0.0945	6.42	0.755	0.514	6.42	3.79
0.136	4.82	1.17	0.541	6.42	4.03
0.167	5.52	1.38	0.667	6.42	4.50
0.208	4.82	1.64	0.752	4.82	5.12
0.219	5.86	1.93	0.825	6.42	5.69
0.273	6.42	2.07			

[a] Total base titer.

sulfonic acid. The nmr and infrared spectra of the crude product were identical with the spectra of an authentic sample of 1,1-diphenylethylene. Quantitative vapor phase chromatography, using 9-fluorenone as internal standard, indicated the product to be 99% 1,1-diphenylethylene, the dehydration product of the expected tetriary alcohol.

The products of the reaction of 2.38 mmol of benzophenone with 500 mmol of methylmagnesium bromide in diethyl ether were similarly determined after work-up with sulfuric acid and dehydration in benzene with *p*-toluenesulfonic acid. The nmr and infrared spectra of the crude products were identical with the spectra of a mixture of 14% benzopinacol and 86% 1,1-diphenylethylene. Quantitative vapor phase chromatography, using 9-fluorenone as internal standard, indicated the products to be 14% benzopinacol and 85% 1,1-diphenylethylene.

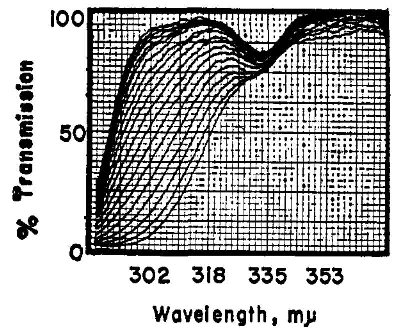


Figure 10. Absorption spectrum of 10^{-3} *M* benzophenone in 0.3 *M* recrystallized methylmagnesium bromide in diethyl ether at 25.0°, recorded 1.1 times/sec.

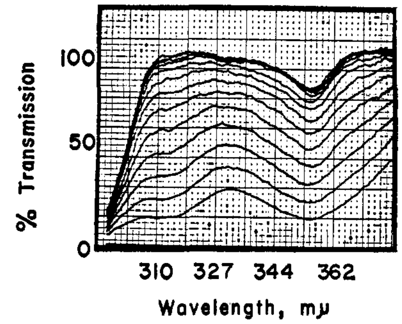


Figure 11. Absorption spectrum of *ca.* 10^{-3} *M* 4-methylmercaptobenzophenone in 0.3 *M* recrystallized methylmagnesium bromide in diethyl ether at 25.0°, recorded 1.1 times/sec.

Rapid-scan spectroscopy (Figure 10) indicates that during the reaction of methylmagnesium bromide with benzophenone in diethyl ether an absorbance is produced, λ_{max} 334 mμ, which persists for several minutes after the disappearance of ketone. An additional band is also observed at 560 mμ. Reacting solutions are pink and exhibit an unresolved esr signal[20] at 3400 G only while the color persists. Recrystallization of the methylmagnesium bromide reagent decreases the intensity of the absorption spectrum of the pink species.

Since the substituted ketone 4-methylmercaptobenzophenone absorbs at longer wavelengths than benzophenone it is possible to record the disappearance of the ketone, λ_{max} 312 mμ, and the Grignard–ketone complex, λ_{max} 354 mμ. As illustrated in Figure 11, an absorbance, λ_{max} 354 mμ, remains after the ketone and the complex absorbance have disappeared. The remaining absorbance subsequently decays to the base line. In one preparation of 0.3 *M* methylmagnesium bromide this decay was observed to exhibit a first-order rate constant of 0.022 sec^{-1} at room temperature, *ca.* 23°. The same reaction mixture displays an esr signal which decays with essentially the same rate constant, 0.018 sec^{-1}.

---

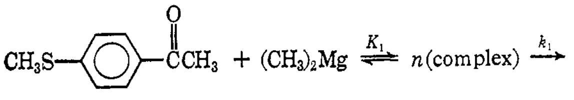
(20) Reports of esr signals during the course of Grignard reactions have appeared: (a) G. A. Russel, E. G. Janzen, and E. T. Strom, *J. Amer. Chem. Soc.*, **86**, 1807 (1964); (b) K. Maruyama, *Bull. Chem. Soc. Jap.*, 37, 897 (1964). The reaction of phenylmagnesium bromide with benzophenone in tetrahydrofuran[20b] is accompanied by an esr signal similar in hyperfine structure to the magnesium ketyl of benzophenone. The reacting solution also exhibits visible absorbance, λ_{max} 555 mμ.

The reduction of benzophenone to benzopinacol in diethyl ether with a mixture of magnesium and magnesium bromide also gives rise to red solutions, an unresolved esr signal at 3400 G, and absorbance maxima at 334 and 560 mμ.

Since it is likely that the benzophenone reduction proceeds by way of a ketyl, the similarity of the uv spectrum of the slowly decaying components of the Grignard reaction suggests the presence of a magnesium ketyl in the Grignard reaction. The ketone concentration dependence of the reaction rate and the observance of a significant fraction of benzopinacol only when a large excess of Grignard reagent is employed suggest that methylmagnesium bromide, as normally prepared, contains a small amount of a component capable of inducing ketyl formation.

Discussion

4-Methylmercaptoacetophenone. The reaction of 4-methylmercaptoacetophenone (I) with dimethylmagne-

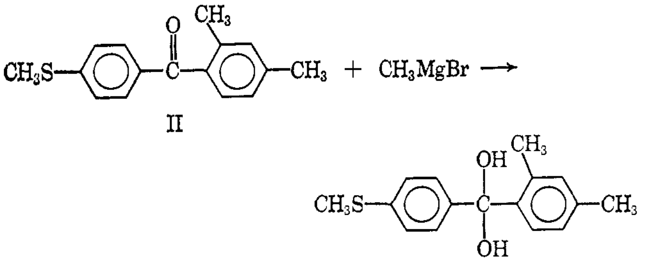


I

addition + enolization (5)

sium in diethyl ether at 25.0° was previously found[5] to be adequately described by the relatively simple scheme in eq 5. Direct spectroscopic measurements yield a value of 6.2 l./mol for the equilibrium constant, K_1, and kinetic studies are consistent with a first-order rate constant for conversion of complex(s) to products, k_1, of 19.5 sec^{-1} from 0.01 to 0.6 *M* dimethylmagnesium.

In contrast to this relatively simple result, the reaction of 2,4-dimethyl-4′-methylmercaptobenzophenone with methylmagnesium bromide[4c] is faster than predicted on the basis of eq 5, above a concentration of *ca.* 0.3 *M* methylmagnesium bromide, using measured equilibrium constants. Although the data allow a variety of interpretations, two general types of modification of the simple scheme have been explicitly considered.[4c] For example, the data are consistent with complex formation followed by first-order conversion to product, eq 6, if



$$\text{ketone} + \text{Grignard} \overset{K_2}{\rightleftarrows} \text{complex} \xrightarrow{k_2} \text{product} \qquad (6)$$

the rate constant, k_2, is assumed to increase because of a medium effect which is linear in the concentration of titratable Grignard reagent, *G*. The observed pseudo-first-order rate constant is then given by eq 7 where *b* is a

$$k_{\text{obsd}} = \frac{K_2k_2G(1 + bG)}{K_2G + 1} \qquad (7)$$

measure of the sensitivity of the reaction to medium effects. An alternative interpretation of this formulation, of course, assigns the specific function of the second term to a reaction between the complex and a second Grignard molecule to form product. Recently Ashby[3d,13] suggested that only the second-order term is important in the reaction of benzophenone with methylmagnesium bromide.

Taking explicit account of the indications that monomeric Grignard, G_1, is converted to a dimeric reagent,[21] G_2, with increasing concentration and allowing each of these species to react in a characteristic way give the scheme outlined in eq 8–10.[4] This scheme, because of

$$K + G_1 \overset{K_3}{\rightleftarrows} C_1 \xrightarrow{k_3} P \qquad (8)$$

$$2G_1 \overset{K_4}{\rightleftarrows} G_2 \qquad (9)$$

$$K + G_2 \overset{K_5}{\rightleftarrows} C_2 \xrightarrow{k_5} P \qquad (10)$$

the large number of parameters, describes the available data for ketone II.

Since the kinetic and spectroscopic data in the relatively unhindered ketone, I, and dimethylmagnesium are adequately summarized by the scheme (eq 6) it is of interest to subject the data for the reaction of this ketone with methylmagnesium bromide to the treatment outlined above. The results, as illustrated by the dashed line in Figure 12, are not consistent with eq 7, the observed rate constants being substantially larger than calculated using the measured equilibrium constant of 15 l./mol and a first-order rate constant for unimolecular conversion of complex to products of 0.70 sec^{-1}. However, invoking an additional factor, linear in the concentration of titratable Grignard reagent, results in a good fit to the observed data. The solid line in Figure 12 was calculated from eq 7 using a value for *b* of 2.3. This value is larger than that required to describe the data for ketone II by a factor of 4, suggesting a compound-dependent sensitivity.

The scheme involving dimerization of the methylmagnesium bromide reagent, eq 8–10, may also be applied to the data for the reaction of ketone I with methylmagnesium bromide. While the large number of parameters inevitably allows the use of a family of [illegible] of equilibrium constants and rate constants, two parameters impose boundary conditions. The apparent equilibrium constant for 1:1 complex formation is 15 l./mol and the order of magnitude of K_3, estimated from the degree of association of ethylmagnesium bromide,[21] is *ca.* 10 l./mol. A satisfactory description of the experimental data is obtained using values of K_3 and K_5 of 20 and 23 l./mol, respectively, and rate constants k_3 and k_5 of 0.14 and 2.2 sec^{-1}, respectively. As summarized in Table VIII, these parameters reproduce the observed rate constants and yield a relatively constant value for gross complex formation within experimental error of the observed value. It is of interest to note that, as with the previous example,[4c] to the extent that this scheme represents the actual chemical system, the complex containing the dimeric Grignard yields product *ca.* ten times faster than the complex between ketone and monomeric Grignard. Thus, the formation of a more reactive complex between the ketone and

---

(21) (a) E. C. Ashby and F. Walker, *J. Organometal. Chem.* (Amsterdam), 9, 17 (1967); (b) J. Toney and G. Stucky, *Chem. Commun.*, 1168 (1967).

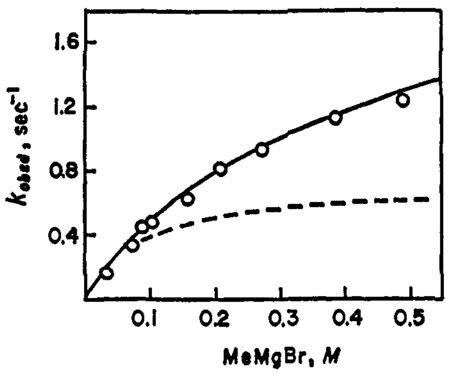


Figure 12. Plot of k_{obsd} *vs.* concentration of recystallized methylmagnesium bromide for the reaction with 4-methylmercaptoacetophenone in diethyl ether at 25.0°. The dashed line was calculated from eq 6 with an equilibrium constant, K_1, of 15 l./mol and a rate constant, k_1, of 0.70 sec^{-1}. The solid line was calculated from eq 7, with a valve for b of 2.3.

dimeric Grignard can account for the observed pseudo-first-order rate constant being larger than predicted on the basis of the scheme outlined in eq 6. Additional compensation for medium effects and refinements in the estimated degree of association of the Grignard reagent and equilibrium constants for complex formation will, of course, affect the absolute magnitude of the derived parameters. It should be further noted[8] that, because of the high reactivity of dimethylmagnesium relative to methylmagnesium bromide, only a small amount of dimethylmagnesium present in equilibrium with the Grignard reagent is adequate to account for the observed rate level with ketone I in diethyl ether.

Table VIII. Comparison of Calculated and Observed Pseudo-First-Order Rate Constants and Equilibrium Constants for the Reaction of 4-Methylmercaptoacetophenone with Methylmagnesium Bromide in Diethyl Ether at 25.0°

MeMgBr,[a] M	$(MeMgBr)_2$,[a] M	Stoich Grignard, M	k, sec^{-1} Calcd[b]	Interpolated[c]	K_{calcd},[b,d] l./mol
0.05	0.025	0.100	0.54	0.50	16
0.075	0.056	0.188	0.81	0.78	15
0.100	0.100	0.300	1.00	1.0	14
0.125	0.156	0.437	1.16	1.2	14
0.140	0.196	0.532	1.22	1.3	14

[a] Calculated with a K_3 of 10 l./mol. [b] Calculated with k_3 and k_5 of 0.14 and 2.2 sec^{-1}, respectively, and a K_3 of 20 and K_5 of 23 l./mol. [c] Interpolated from Figure 12. [d] Experimental value is 15 l./mol.

Benzophenone. Recently Ashby and coworkers[13] reported kinetic data on the reaction of benzophenone with methylmagnesium bromide in diethyl ether at 25°. These data were obtained with dilute Grignard solutions under conditions where the disappearance of ketone followed pseudo-first-order kinetics. It was found that a plot of the observed first-order rate constant *vs.* concentration of the Grignard reagent is a straight line over the concentration region investigated; however, it is reported that the line does not extrapolate through the origin. These data were taken as evidence for the mechanism given in eq 11–12.

$$G + K \overset{K}{\rightleftarrows} C \qquad (11)$$

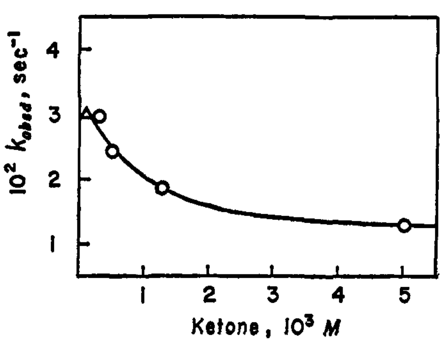


Figure 13. Plot of pseudo-first-order rate constant, k_{obsd}, *vs.* ketone concentration for the reaction of benzophenone with 1.7 × 10^{-2} M methylmagnesium bromide in diethyl ether at 25.0°, interpolated from plots of k_{obsd} *vs.* methylmagnesium bromide concentration: △, Ashby, *et al.*;[13] ○, this study.

$$C + G \overset{k}{\rightleftarrows} P \qquad (12)$$

$$k_{obsd} = \frac{kKG^2}{1 + KG} \qquad (13)$$

Because of the appearance of a ketyl uv–visible spectrum, λ_{max} 334 and 560 mμ, as well as an esr signal from reacting solutions and a radical coupling product, benzopinacol, in 14% yield in the present work, it is important to compare the rate levels reported by Ashby and coworkers[21] with the data in Table VII. Because of the marked decrease in observed rate constant with increasing ketone concentration, such a comparison is accomplished by plotting the observed first-order rate constants *vs.* ketone concentration at constant Grignard concentration. Such a plot is given in Figure 13 for 0.017 M methylmagnesium bromide. The data were obtained from plots of k *vs.* Grignard at various concentrations of ketone and interpolating rate constants from a line through the data at 0.017 M Grignard. The result indicates that the two sets of data are in substantial agreement, placing Ashby's results[13] on the steep part of the ketone concentration dependence curve.

Because of the formation of what appears to be a radical species in the reaction of benzophenone with methylmagnesium bromide under the conditions used in these kinetic studies and our failure, to date, to completely eliminate the coupling reaction with dilute ketone solutions, a quantitative treatment of these data does not seem justified at this time. Qualitatively, however, with data obtained for 10^{-2} M ketone and methylmagnesium bromide (Figure 9) there seems to be nothing unique about the kinetic phenomenology for the addition reaction, and it seems reasonable that benzophenone would fit the mechanistic rationales developed for similar systems.[4c]

Experimental Section

Ketones. 4-Methylmercaptoacetophenone was prepared as previously described.[5] The procedures of Bnn-Hoi and Hoan were used to prepare 4-methylmercaptobenzophenone, mp 78–79° (lit.[22] 76°). Benzophenone was crystallized from n-pentane and zone refined before use.

Grignard Reagents. Methylmagnesium reagents were prepared and analyzed as previously described.[5] When appropriate, methylmagnesium bromide was repeatedly recrystallized from diethyl ether by cooling a filtered solution to −78° for *ca.* 1 hr, followed by

---

[22] N. P. Bnn-Hoi and N. Hoan, *J. Org. Chem.*, 17, 350 (1952).

removal of solvent by filtration and dissolution of the crystalline reagent in freshly distilled solvent at room temperature.

Kinetics and Spectroscopy. Rapid-scan spectroscopy and stopped-flow kinetic experiments were performed as previously described.[5] Base-line control of the single-beam rapid-scan spectrum was accomplished with programmed modulation of the deuterium source. The stopped-flow apparatus used in these experiments consisted of a stainless steel block appropriately machined for valves, syringe reservoirs, and thermostated water circulation, a Gibson-Chance[15] eight-jet stainless steel mixer, a 1.00-cm flow cell with quartz windows, a stop syringe, and a manually operated hydraulic drive. An elapsed time between mixing and spectroscopic observation of *ca.* 0.03 sec is conveniently accessible with this apparatus.

Esr spectra of freshly mixed reacting solutions of methylmagnesium bromide and ketones in diethyl ether at room temperature were obtained using a stopped-flow apparatus and a 2-mm quartz esr flow cell positioned in the sample cavity of a Varian V4502 spectrometer.

Product Analyses. To 100 ml of 0.8 *M* methylmagnesium bromide (80 mmol) in diethyl ether was slowly added with rapid stirring 0.5858 g (3.53 mmol) of 4-methylmercaptoacetophenone dissolved in 20 ml of diethyl ether. A yellow color immediately formed and rapidly disappeared. The reaction mixture was vigorously stirred for 20 min and then hydrolyzed with just enough 0.5 *M* sulfuric acid to dissolve all the magnesium salts. The ether portion was subsequently washed with two portions each of saturated sodium bicarbonate and distilled water. After removal of ether by distillation, 50 ml of benzene and 50 mg of *p*-toluenesulfonic acid were added. The benzene was removed by distillation and the residue dissolved in ether and washed successively with saturated sodium bicarbonate and distilled water. The product solution was then dried with magnesium sulfate and the solvents were carefully removed by mild heating, followed by evacuation at room temperature to 0.5-mm pressure for 2 hr. The product was then melted in a nitrogen atmosphere, cooled, and again evacuated to 0.5-mm pressure for 2 hr, yielding a white solid (0.5800 g).

The infrared and nmr spectra of the crude product mixture were identical with a synthetic mixture of 4% 4-methylmercaptoacetophenone and 96% 2-(4-methylmercaptophenyl)propene. Quantitative vapor phase chromatography using a 6-ft column of 10% Ucon fluid on Chromosorb W at 195°, following calibration with authentic compounds[5] and benzophenone as internal standard, indicated the products to be 4% 4-methylmercaptoacetophenone and 96% 2-(4-methylmercaptophenyl)propene, the products of enolization and dehydration of the expected tertiary alcohol, respectively.

Benzophenone (Eastman) was recrystallized from *n*-pentane and purified in a Fisher zone refiner. To 100 ml of 0.8 *M* methylmagnesium bromide (80 mmol) in diethyl ether was slowly added, with rapid stirring, 0.7525 g (4.14 mmol) of benzophenone in 20 ml of diethyl ether, affording a MeMgBr/ketone ratio of 20. A yellow color formed immediately and rapidly disappeared, leaving a pink color which persisted for several minutes after the addition of ketone. Work-up as described above yielded a colorless liquid (0.735 g) exhibiting one component by vapor phase chromatography (4.0 min) using a 6-ft column of 10% Ucon fluid on Chromosorb W at 200°. The nmr and infrared spectra of the crude product were identical with spectra of authentic 1,1-diphenylethylene. Quantitative vapor phase chromatography, using 9-fluorenone as internal standard, indicated the product to be 98.8% 1,1-diphenylethylene, the dehydration product of the expected tertiary alcohol.

The addition of 0.4324 g (2.38 mmol) of benzophenone to 250 ml of 2 *M* methylmagnesium bromide (500 mmol) in diethyl ether, affording a MeMgBr/ketone ratio of 200, yielded upon work-up a colorless liquid (0.4311 g). The product exhibited two components by vapor phase chromatography, using a 6-ft column of 10% Ucon fluid on Chromosorb W at 200°, with retentions of 4.0 and 6.0 min. The infrared and nmr spectra of the crude product mixture were identical with a synthetic mixture of 86% 1,1-diphenylethylene and 14% benzopinacol. Quantitative vapor phase chromatography, following calibration with authentic compounds and 9-fluorenone (10.8 min) as internal standard, indicated the products to be 84.5% 1,1-diphenylethylene (4.0 min) and 13.8% benzopinacol (6.0 min).

The addition of 1.371 g (6.01 mmol) of 4-methylmercaptobenzophenone to 100 ml of 0.8 *M* methylmagnesium bromide (80 mmol) in diethyl ether, affording a MeMgBr/ketone ratio of 13, yielded 1.320 g of a pale yellow solid, mp 64–64.5°. The product exhibited one component by vapor phase chromatography (9.1 min), using a 6-ft column of 10% Ucon fluid on Chromosorb W at 240°.

Recrystallization of *ca.* 0.5 g of crude product from *n*-pentane yielded a pale yellow solid, mp 67–67.5°. The melting point of a mixture of crude and recrystallized product was 66.5–67°. The nmr and infrared spectra of the crude product were identical with the spectra of recrystallized product. The nmr and infrared spectra are that expected for 1-(4-methylmercaptophenyl)-1-phenylethylene, the dehydration product of the expected tertiary alcohol. The nmr spectrum exhibits singlets at τ 7.61 (3.1) and 4.65 (2.0) and an aromatic multiplet centered at τ 2.81 (8.9).

Anal. Calcd for $C_{15}H_{14}S$: C, 79.60; H, 6.23; S, 14.17. Found: C, 79.32; H, 6.34; S, 14.17.

Coupling Products. Benzophenone was reduced to benzopinacol, mp 185–186° (lit.[23] 186), by reaction with a mixture of magnesium and magnesium bromide in diethyl ether as described by Gomberg.[23] Samples of the pink reaction mixture were rapidly filtered into silicone rubber sealed uv cells and an esr tube cooled to −78°. These solutions exhibited an absorbance λ_{max} 334 and 560 mμ which disappeared within 10 min at room temperature and an unresolved esr signal at 3400 G at −130° which disappeared rapidly upon warming to room temperature.

Using the same procedure,[23] 4-methylmercaptobenzophenone was reduced to the corresponding pinacol, in 97% yield, mp 158–159°. The reacting solution is orange and exhibits an unresolved esr signal at 3400 G at −130°, which disappears within minutes after warming to room temperature.

Acknowledgment. The assistance of R. W. Anderson, W. D. Winegardner, D. M. O'Brien, and associates in the design and construction of apparatus is gratefully acknowledged. Professor H. O. House provided helpful discussion.

---

(23) M. Gomberg and W. E. Bachman, *J. Amer. Chem. Soc.*, **49**, 236 (1927).