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COMPARISON OF THE REACTIVITY OF METHYLMAGNESIUM CHLORIDE AND DIMETHYLMAGNESIUM TOWARD 4-METHYLMERCAPTOACETOPHENONE IN DIETHYL ETHER

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Kinetic and spectroscopic studies of the reactions of methylmagnesium bromide with substituted benzophenones[1] and 4-methylmercaptoacetophenone[2] in diethyl ether indicate mechanisms for the Grignard addition reaction involving rapid complex formation followed by relatively slow conversion of complex to product. However, the unambiguous assignment of mechanistic roles to various organomagnesium species is difficult because of the lack of definitive knowledge of the nature of the Grignard reagent[3] over the concentration ranges employed. Dialkylmagnesium has frequently been suggested as contributing to the composition of Grignard reagents[3] and invoked as a major reactive species in the reaction of many Grignard reagents with ketones.[4] Comparison of the rates of reaction of dimethylmagnesium[5] and methylmagnesium chloride with 4-methylmercaptoacetophenone in diethyl ether, presented in this communication, provides for this system some experimental evaluation of these proposals.

Stopped-flow, rapid-scan spectrophotometry[2,5] indicates that reacting solutions of methylmagnesium chloride and 4-methylmercaptoacetophenone (I) in diethyl ether at 25.0° exhibit absorbance, λ_{max} 308 mμ, which is attributed to free ketone I and an additional absorbance, λ_{max} 332 mμ, formed essentially instantaneously on the time scale of conversion to products, which is attributed to organomagnesium complexation of ketone I. The apparent equilibrium constant,* $\bar{K}$, for 1:1 complex formation is ca. 20 l./mole. The absorbance maxima subsequently disappear at identical rates. The observed pseudo-first-order rate constant, $\underline{k}_{obsd}$, is

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*Ketone I exhibits similar complexation with dimethylmagnesium,[5] λ_{max} 337, $\bar{K}$ 6.2 ± 0.7 l./mole and methylmagnesium bromide,[2] λ_{max} 336, $\bar{K}$ 15.1 ± 0.6 l./mole.

appropriately independent of the initial concentration of ketone I from 10^{-3} to 10^{-2} M and increases from 2.3 to 15 sec^{-1} as the methylmagnesium chloride reagent concentration is increased from 0.06 to 0.6 M (Figure 1). Pseudo-first-order rate constants for various concentrations of methylmagnesium chloride are summarized in Table I.

Table I. Reaction of Methylmagnesium Chloride[a] with 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

MeMgCl,[b] M	k_{obsd}, sec^{-1}	MeMgCl,[b] M	k_{obsd}, sec^{-1}
0.056	2.25	0.278	9.92
0.099	4.03	0.316	11.2
0.125	5.67	0.424	13.2
0.164	6.28	0.456	13.7
0.170	7.57	0.518	13.9
0.186	7.65	0.530	14.5
0.236	9.00	0.594	15.4

[a] Total base. [b] Ketone, 3×10^{-3} M.

The effect of organomagnesium reagent concentration on the rates of reaction of methylmagnesium chloride and dimethylmagnesium[5] with ketone I in diethyl ether at 25.0° are illustrated in Figure 1. A comparison of the relative rates of reaction with ketone I suggests that Me_2Mg is not the only reactive species in the methylmagnesium chloride reagent. For example, at 0.30 M, methylmagnesium chloride exhibits a pseudo-first-order rate constant of 11 sec^{-1}. A 0.30 M methylmagnesium chloride reagent is, in the limit, stoichiometrically equivalent to a mixture of 0.15 M Me_2Mg and 0.15 M $MgCl_2$. If Me_2Mg were the only reactive species in the methylmagnesium chloride reagent, then a methylmagnesium chloride rate constant of 11 sec^{-1} would require a Me_2Mg concentration of 0.22 M. This result* is incompatible with both the stoichiometry of Me_2Mg formation from a Grignard reagent and the known solubility of magnesium chloride in diethyl ether,[6] *ca.* 10^{-3} M.

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*It is assumed that any gross medium effects upon reactivity toward ketone I in diethyl ether are comparable for both the methylmagnesium chloride and dimethylmagnesium reagents.

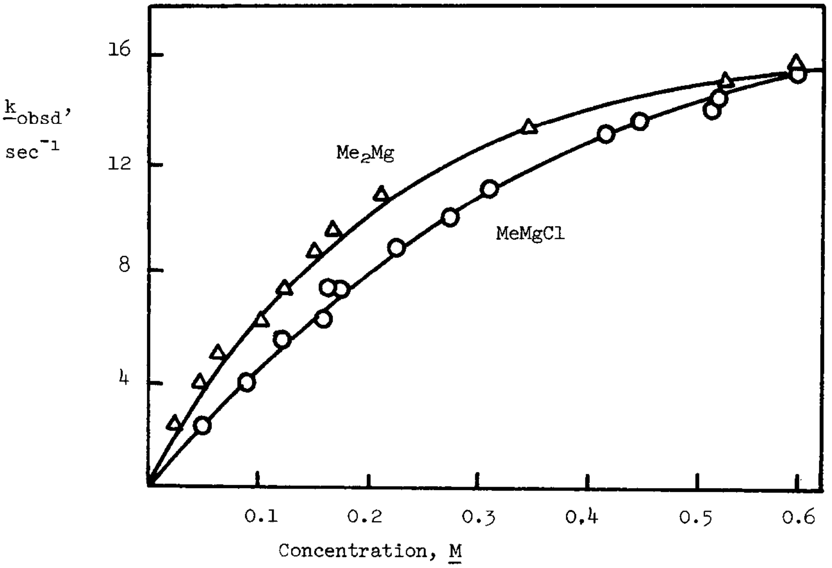

Figure 1. Plot of $\underline{k}_{obsd}$ vs. Concentration of Methylmagnesium Chloride and Dimethylmagnesium in Reaction with 4-Methylmercaptoacetophenone in Diethyl Ether at 25.0°

The state of aggregation of the Grignard reagent may contribute to the observed relative rates.[1] For example, alkylmagnesium chlorides have been reported[7] to exist as dimers, and methylmagnesium bromide, which is ca. ten times less reactive than dimethylmagnesium in this system,[2] displays[7] an apparent general increase in association with concentrations in diethyl ether. Because of the relatively large rate difference between dimethylmagnesium and methylmagnesium bromide with ketone I, a small amount of dimethylmagnesium in equilibrium with methylmagnesium bromide could, as noted earlier,[2] account for the observed rate level with the bromide reagent.

Because both the structure of the alkyl group and the nature of the halide affect the degree of association of the Grignard reagent and the relative reactivity toward carbonyl compounds, generalization of these results is not justified without additional data.

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