On the Reaction of Methylmagnesium Bromide with Benzophenone: the Effect of Magnesium Metal Purity on Kinetic Data

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Summary Previously reported complications in the interpretation of kinetic data of Grignard–ketone reactions due to by-product formation and dependence of rate constant on ketone concentrations have been eliminated by use of ultra-pure magnesium for the preparation of the Grignard reagent; however, a further previously unobserved complication involving a non first-order disappearance of ketone has been observed.

THE mechanism of Grignard compound addition to ketones, although under intense scrutiny for several years in a number of laboratories, has turned out to be an unusually involved and complicated problem. Further serious implications in the interpretation of kinetic data were recently reported[1] when it was found that benzopinacol is formed in substantial amount (14%) when methylmagnesium bromide is treated with benzophenone in diethyl ether under pseudo-first-order conditions. Because of the appearance of a ketyl u.v. visible spectrum and an e.s.r. signal for reacting solutions and the inability to eliminate the formation of benzopinacol in the reaction, previous workers[1] have concluded that a quantitative treatment of kinetic data was not justified.

We report evidence that: (i) the formation of benzopinacol is a function of the purity of the magnesium used to prepare the Grignard compound and that this by-product can be essentially eliminated by using an ultra-pure source of magnesium; (ii) the previously reported dependence of the rate constant on the initial concentration of benzophenone disappears when methylmagnesium bromide is prepared from ultra-pure magnesium; and (iii) a further complication concerning the mechanism of this reaction has arisen with the observation that the disappearance of benzophenone under pseudo-first-order conditions using an excess of methylmagnesium bromide prepared from the purest magnesium is still not clearly a simple first-order process. Implications of these findings on the mechanism of methylmagnesium bromide addition to benzophenone are suggested.

With respect to point (i), we have found that the amount of benzopinacol formation increases as the Grignard to ketone ratio increases (Table) when the Grignard compound is prepared from Dow triply-sublimed magnesium. A similar increase in the e.s.r. signal indicative of an increase in free radical concentration has also been observed in the reaction of aromatic ketones with Grignard reagents.[2] The increase in by-product formation with an increase in Grignard to ketone ratio leads us to believe that benzopinacol formation is caused by small amounts (p.p.m.) of transition metal impurities known to exist in triply-sublimed magnesium. Such transition metal impurities are believed to produce organo-transition metal compounds which decompose at room temperature to free radical species that catalyse the formation of benzopinacol from benzophenone. The by-product can be suppressed (from 20 to 6% at comparable Grignard to ketone ratios) by preparing the methylmagnesium bromide from triply-sublimed magnesium using an excess of methyl bromide which is removed prior to reaction with benzophenone (the yield of Grignard was unaffected by the excess of methyl bromide). The most dramatic results were obtained when ultra-pure magnesium† was used with an excess of methyl bromide for the preparation of the Grignard compound since reaction with benzophenone results in the formation of the normal addition product from 98·5—100%, depending on the Grignard to ketone ratio.

TABLE

Product analysis and pseudo-first-order rate constants (k_{obs}) *from the reaction of methylmagnesium bromide prepared from triply-sublimed magnesium with benzophenone in diethyl ether at* 25·0°

$G_0 \times 10^3$ M	$K_0 \times 10^5$ M	$G_0:K_0$	% Side reaction	% Addition	$k_{obs} \times 10^3$(sec^{-1}) (Initial slope value)	$k_{obs} \times 10^3$(sec^{-1}) (Average slope) value)
8·38	11·8	71 : 1	13	87	12·8	9·90
8·38	6·28	133 : 1	22	78	16·1	11·5
8·38	3·72	225 : 1	25	75	12·6	12·4
8·38	2·40	350 : 1	28	72	14·1	14·1

The complication reported earlier[1] concerning the dependence of the rate constant on initial ketone concentration was also eliminated by the use of methylmagnesium bromide prepared from ultra-pure magnesium (Figure 1). However, a further complication has arisen in these studies that was not noticed earlier[3] and apparently has gone unnoticed by other workers[4] since first-order rate constants have been reported for several Grignard–ketone systems. Reference to Figure 2 shows that the reaction of methylmagnesium bromide and benzophenone under pseudo-first-order conditions (an excess of methylmagnesium bromide) is not clearly first-order in ketone. Thus, elimination of the by-product decreases the curvature at comparable Grignard–ketone ratios (Figure 2) but it is not eliminated. In addition to reducing the curvature in the first-order plots, the most striking result of eliminating the side-reaction is the reduction of the rate of reaction by approximately 2/3.

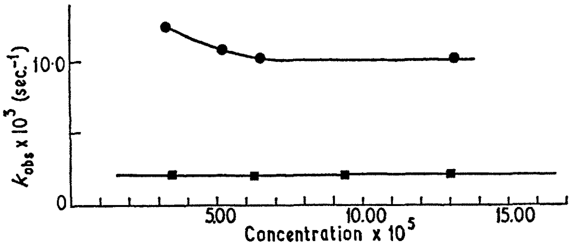

FIGURE 1. *Variation of the pseudo-first-order rate constant* (k_{obs}, *from extrapolated initial slope in first-order plot*) *with initial benzophenone concentration at a constant methylmagnesium bromide concentration.* ● = *Triply-sublimed magnesium* (*methylmagnesium bromide concentration* $M_g{}^0 = 6{\cdot}45 \times 10^{-3}$M) ■ = *Ultra-pure magnesium* ($M_g{}^0 = 2{\cdot}43 \times 10^{-3}$M).

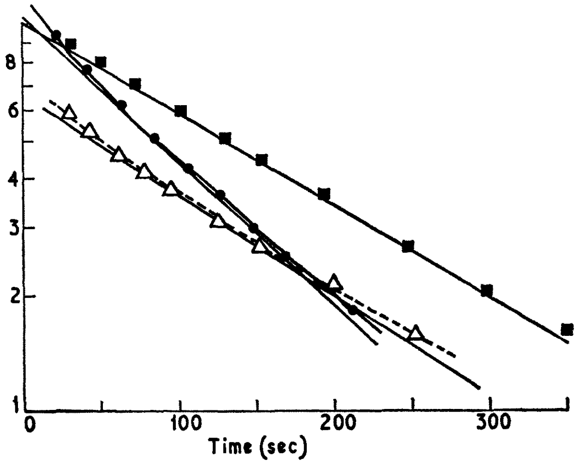

FIGURE 2. *Illustration of line curvature in the pseudo-first-order plot of disappearance of benzophenone.* ■ = *Ultra-pure magnesium* (*methylmagnesium bromide concentration*, $M_g{}^0 = 6{\cdot}42 \times 10^{-3}$M; *initial benzophenone concentration*, $M_K{}^0$, *from extrapolated initial slope* $= 5{\cdot}92 \times 10^{-5}$M; $M_g{}^0 : M_K = 108:1$). ● = *Triply-sublimed magnesium* ($M_g{}^0 = 6{\cdot}45 \times 10^{-3}$M; $M_K{}^0 = 6{\cdot}50 \times 10^{-5}$M; $M_g{}^0 : M_K{}^0 = 99:1$). ▲ = *Ultra pure magnesium* ($M_g{}^0 = 7{\cdot}42 \times 10^{-3}$M; $M_K{}^0 = 3{\cdot}95 \times 10^{-4}$M; $M_g{}^0 : M_K{}^0 = 19:1$).

As the data in the Table show, the values for the rate constants with by-product formation depend not only on the initial ketone concentration, but also on the portion of the curve used to determine the values. Thus, failure to eliminate the side-reaction in the previous investigations[1,4] and failure to report line curvature in the first-order plots has led to a situation where none of the previous data can be interpreted or compared with confidence.

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† We are indebted to Professor Royal W. Stark for the sample of ultra-pure magnesium. The residual resistance ratios of *ca.* 5×10^6 compared with the best Dow triply-sublimed magnesium of 10^3. No impurities could be detected using an AEI, MS-7 spark source mass spectrometer. All evidence indicates $< 10^{-8}$ impurity.

In the case of the ultra-pure Grignard system where by-product formation has been essentially eliminated, the line curvature in the first-order plot is consistent with the behaviour expected if the reacting species in solution is Me_2Mg and its reaction upsets the Schlenk equilibrium. Thus, as the Grignard to ketone ratio decreases, the concentration of Me_2Mg (by far the minor component in the Schlenk equilibrium) becomes an important factor in agreement with increased line curvature in the first-order plot (Figure 2) at lower Grignard to ketone ratios (still under pseudo-first-order conditions). In addition to being consistent with the kinetic data in hand, this suggestion is also supported by two additional pieces of information: (i) $MeMg\cdot OCPh_2Me$ (the intermediate expected for Me_2Mg reaction) has been observed as the major component of the reaction mixture at −110° by 100 MHz n.m.r.) and (ii) the equilibrium constant calculated for the Schlenk equilibrium from the kinetic data is 670 (for ethylmagnesium bromide $K = 480$). Further studies are in progress.

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