

DIALKYL MAGNESIUMS AS THE PRINCIPAL ACTIVE REAGENTS IN GRIGNARD ATTACK

AT CARBONYL OXYGENS OF o-QUINOL ACETATES¹

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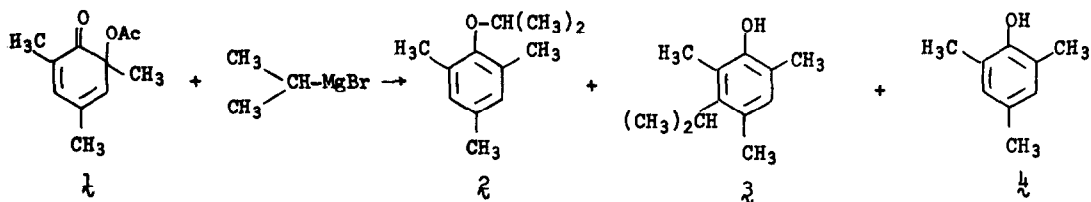
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In previous communications, one of us reported that Grignard and lithium reagents attack the oxygen atoms of carbonyl groups in o-quinol acetates (6-acetoxycyclohexa-2,4-dien-1-ones) to give alkyl aryl ethers, as well as the expected products of reduction of the quinol acetates to phenols and of normal and conjugate addition to the carbonyl groups.² While ether formation largely superseded conjugate addition in reactions with tertiary and benzylic Grignard and lithium reagents, primary Grignard reagents gave only traces of products resulting from attack at carbonyl oxygens - a result which accounts for the fact that attack at oxygen was previously considered to occur only in a single exceptional reaction of an o-quinol diacetate.³

We have now found that dialkylmagnesiums react with o-quinol acetates to give exceptionally high ratios of yields of ethers to yields of products of conjugate addition, even when primary dialkylmagnesiums are employed. Furthermore, in reactions employing Grignard reagents, the ratio of attack at carbonyl oxygens to conjugate addition is markedly increased by a decrease in the concentration of the Grignard reagent - an effect which seems best explained by the assumption that formation of ethers by Grignard reagents (as well as reduction by those reagents) occurs in large part through the reactions of dialkylmagnesiums, rather than of the Grignard reagents themselves.

The reaction of diisopropylmagnesium with 6-acetoxy-2,4,6-trimethylcyclohexa-2,4-dien-1-one (1) yields isopropyl mesityl ether (2), the conjugate addition product meta-isopropylmesitol (3), and the reduction product mesitol (4).

The ratio of the yield of products from attack by the Grignard reagent at the carbonyl oxygen to the yield of products from conjugate addition is markedly affected by the concentration of the Grignard reagent (although not by the relative concentrations of the Grignard reagent and of the quinol acetate). At high (>0.5 M) concentrations of isopropylmagnesium bromide the ratio of 2 to 3



obtained from the reaction with 1 is essentially invariant with changes in the Grignard concentration. At low concentrations of isopropylmagnesium bromide, however, the relative yield of 2 increases rapidly as the Grignard concentration decreases. This is illustrated in the Figure below. (The initial ratio of Grignard concentration to concentration of 1 in each run was at least 10 to 1, so that the concentration of Grignard reagent was essentially constant throughout each run.)

In contrast to the pronounced effect of Grignard concentration on the ether/meta-isopropylphenol yield ratio, the ether/mesitol yield ratio remained at an essentially constant value of ca. 1.0 over the entire range of Grignard concentrations.

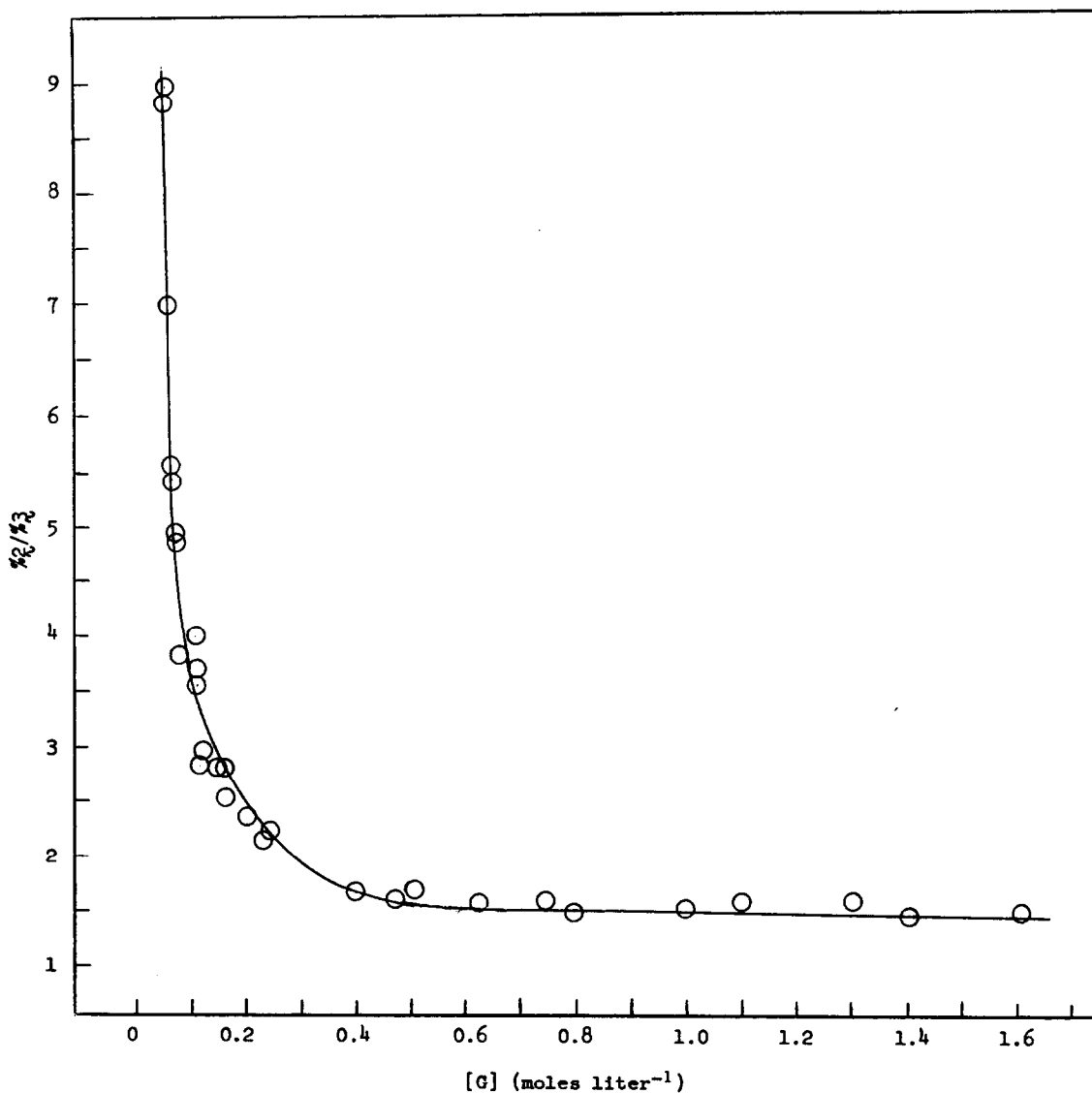
When isopropylolithium was employed as the carbanionoid reagent, the relative yields of all three products were essentially unaffected by changes in concentration of either reagent.

For the reaction of 1 with isopropylmagnesium bromide, linear correlations ($r = 0.97-0.98$) are obtained by plotting the ratio $\%2/\%3$ vs. $[G]^{-(1.5-2.0)}$, where $[G]$ is the concentration of the Grignard reagent. This dependency can be accounted for by the assumption that the ether 2 is formed by reaction of the quinol acetate with both the monomeric Grignard reagent, G_1 , and the polymeric Grignards $G_{2.5-3.0}$,⁴ while the conjugate addition product 3 is formed almost entirely from the polymeric Grignards. This hypothesis would give the rate laws:

$$\frac{d[2]}{dt} = k[1][G_1] + k'[1][G_{2.5-3.0}]$$

$$\frac{d[3]}{dt} = k''[1][G_{2.5-3.0}]$$

The same rate laws, however, would be obtained if the ether is formed principally by reaction of the quinol acetate with diisopropylmagnesium (obtained from the Grignard reagent by the Schlenk equilibrium) rather than directly with the Grignard reagent, provided that diisopropylmagnesium exists largely as its monomer over the entire range of Grignard concentrations.⁶ The hypothesis that diisopropylmagnesium would react with 1 to give 2 but little, if any, 3 was tested by adding 10% (by volume) of dioxane to the ethereal Grignard solution ($[G] = 0.42$ M). This resulted in a remarkable increase in the $\%2/\%3$ ratio from the normal 1.5/1 to 21/1. In contrast, the $\%2/\%4$ ratio remained essentially unchanged by addition of dioxane, as well as by changes in Grignard concentration. When isolated diisopropylmagnesium was reacted with quinol acetate 1 in ether, in the absence



of dioxane, the $\%_2/\%_3$ ratio was 15/1. However, the $\%_2/\%_4$ ratio dropped to 0.5 (compared to ca. 1.0 with the Grignard reagent), possibly due to formation of magnesium hydride by partial decomposition of diisopropylmagnesium during removal of solvent.¹ Changes in the concentration of diisopropylmagnesium had no effect on the product composition.

Other dialkylmagnesiums similarly gave high yields of ethers on reaction with quinol acetates. Reaction of $\frac{1}{2}$ with diethylmagnesium, for instance, gave an ether/"ethylmesitol" ratio of 1.4, while the ratio from reaction of $\frac{1}{2}$ with ethylmagnesium bromide was only 0.08.²

The invariance of the k_2/k_4 ratio throughout most of these reactions suggests that formation of these two molecules, whether from diisopropylmagnesium or isopropylmagnesium bromide, proceeds by the same rate limiting steps, which precede the product forming steps. Since ethers appear to be formed in these reactions by combination of phenoxy and alkyl radicals,^{2,8} we suggest that reduction occurs predominantly by a disproportionation reaction between these two radicals.

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References

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- (2) B. Miller, J. Am. Chem. Soc., **95**, 8458 (1973).
- (3) F. Wessely and J. Kotlan, Monatsh. Chem., **84**, 124 (1953).
- (4) No evidence appears to be available in regard to the degree of association of isopropylmagnesium bromide. However, the degrees of association of both ethylmagnesium bromide and *t*-butylmagnesium bromide increase from 1.0 to ca. 2.5-2.7 as the concentration increases.⁵
- (5) F. Walker and E.C. Ashby, J. Am. Chem. Soc., **91**, 3845 (1969).
- (6) While dimethylmagnesium appears to be polymerized in ether solution, diethylmagnesium exists in essentially monomeric form at all concentrations.⁵
- (7) e.g. E.C. Ashby, T.L. Wiesemann, J.S. Bowers, Jr., and J.T. Laemmle, Tetrahedron Lett., 21 (1976)
- (8) B. Miller, Chem. Comm., 751 (1974).