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Rate-Determining Electron Transfer from Allylic Grignard Reagents to Benzophenone

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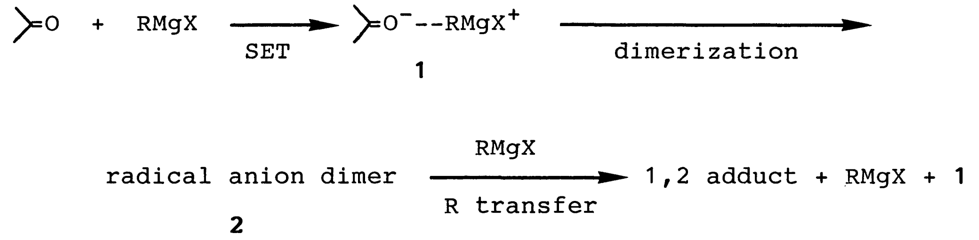
The reactions of allyl magnesium bromide and crotyl magnesium bromide with benzophenone were determined to proceed via a rate-determining electron transfer mechanism by means of the isotope effect and substituent effect technique.

The Grignard reaction is one of the most important reactions in synthetic organic chemistry, and extensive mechanistic investigations have been carried out.[1] It is now widely accepted that the reactions of Grignard reagents with aromatic ketones proceed via single electron transfer (SET) from the reagents to the ketones.[2-4] Recent attention has been focused on the characterization of intermediates involved and the identification of the rate-determining step of the reaction. In 1981, Ashby proposed that two kinds of intermediates are involved in the Grignard reaction, one to give a 1,2-addition product and the other to give 1,4- and 1,6-adducts and pinacol.[2a] Later, Maruyama and coworkers presented spectroscopic and kinetic evidences which suggest that the initial radical ion pair (**1**) formed by SET dimerizes very quickly to **2** before yielding a 1,2 adduct (Eq. 1).[3c,d] They also indicated on the basis of kinetic analysis of their ESR data that the R transfer step is slowest among the sequence of steps for the reactions of benzophenone with alkyl and phenyl Grignard reagents.[3e]



(1)

We have recently shown that the reaction of MeMgI with benzophenone gave a normal carbon kinetic isotope effect (KIE) of 1.054. This together with the substituent effect on reactivity allowed us to conclude that the R transfer step is rate determining in the reaction.[5] In the present paper, we report experimental evidence which suggests that the rate-determining step of the Grignard reaction differs depending on the reagent and that the reactions of allylic Grignard reagents with benzophenone involve SET as the rate-determining step.

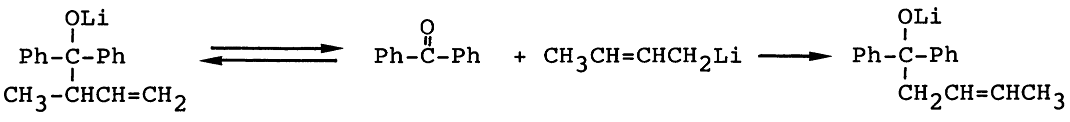
Table 1. Kinetic Isotope Effects in the Reactions of Benzophenone with **3** and **4**[a)]

Reaction of **3**			Reaction of **4**		
$\underline{f}^{b)}$	$\underline{A}_f^{b)}$	$^{12}\underline{k}/^{14}\underline{k}$	$\underline{f}^{b)}$	$\underline{A}_f^{b)}$	$^{12}\underline{k}/^{14}\underline{k}$
0.0	0.5155±0.0004		0.0	0.4817±0.0004	
22.0	0.5157±0.0004	1.002	22.4	0.4819±0.0010	1.002
30.7	0.5141±0.0008	0.993	29.1	0.4816±0.0012	0.999
32.3	0.5155±0.0002	1.000	30.4	0.4806±0.0003[c)]	0.999
40.4	0.5151±0.0013	0.999	38.2	0.4804±0.0010[c)]	0.998
48.7	0.5155±0.0013	1.000	40.2	0.4806±0.0003	0.996
		0.999±0.003			0.999±0.002

a) Reactions were carried out in diethyl ether at 0.0±0.1 °C. Error limits are the standard deviations. b) $\underline{f}$ is the fraction of reaction (%) and $\underline{A}_f$ is the molar radioactivity (mCi/mol) of the ketone at the fraction of reaction, $\underline{f}$. c) Different batch of benzophenone ($\underline{A}_0$ = 0.4808±0.0004 mCi/mol) was used.

The reactions of allyl magnesium bromide (**3**) and crotyl magnesium bromide (**4**) with benzophenone-carbonyl-$^{14}\underline{C}$ were carried out in diethyl ether at 0 °C and the ^{14}C KIEs were determined by the method reported previously.[6)] These reactions gave the sole 1,2-addition product quantitatively. The KIEs were calculated from the variation in radioactivity of recovered benzophenone. As shown in Table 1, it is clear that both reactions gave the KIE of unity. These KIEs indicate that there is no bonding change at the carbonyl carbon in the TSs of these reactions. Substituent effects for the reactions of substituted benzophenones with **3** were determined by the competition method as described previously.[7)] The Hammett plot in Fig. 1a shows a very small ρ value of -0.03.[8)] Furthermore, the reactivity differences between the ortho- and para-substituted derivatives are much smaller than those for the reaction of MeMgI shown in Fig. 1b for comparison. The results in Table 1 and Fig. 1a are similar to those reported for the reaction of benzophenone with MeLi,[7)] and consistent with the mechanism, in which SET occurs as the rate-determining step followed by the fast C-C bond formation.[9)]

The reactions of the allylic lithium and magnesium reagents with ketones are known to be reversible.[10)] For example, the reaction of benzophenone with crotyl lithium, the kinetically controlled methallyl adduct, $CH_2=CHCH(CH_3)C(C_6H_5)_2OLi$, was shown to be converted through the equilibrium to the more stable crotyl adduct, $CH_3CH=CHCH_2C(C_6H_5)_2OLi$, on standing at 162 °C for 144 h in diglyme (Eq. 2).[10)] Thus, although the reactions of **3** and **4** with benzophenone yield exclusively 1,1-diphenyl-3-butenol (**5**) and 1,1-diphenyl-2-methyl-3-butenol (**6**) respectively, the observed negligible KIEs and the value may be deteriorated by such an equilibrium. In order to check whether the observed values are totally of



$$\underset{\mathrm{CH_3\text{-}CHCH{=}CH_2}}{\overset{\mathrm{OLi}}{\mathrm{Ph\text{-}C\text{-}Ph}}} \rightleftarrows \overset{\mathrm{O}}{\mathrm{Ph\text{-}C\text{-}Ph}} + \mathrm{CH_3CH{=}CHCH_2Li} \longrightarrow \underset{\mathrm{CH_2CH{=}CHCH_3}}{\overset{\mathrm{OLi}}{\mathrm{Ph\text{-}C\text{-}Ph}}} \qquad (2)$$

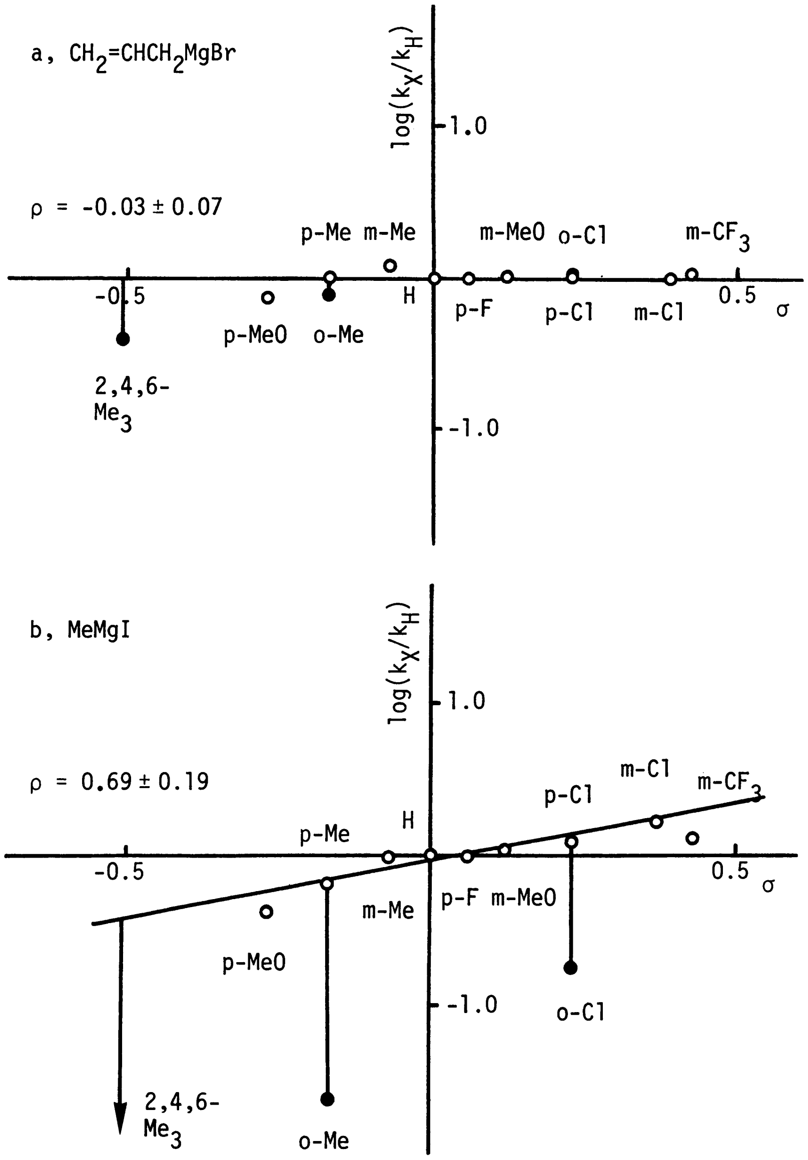


Fig. 1. Variation of reactivity with σ values for the reactions of substituted benzophenones with Grignard reagents.

kinetic nature, we carried out the following experiments. To **5** or **6** MeMgBr was added to produce the magnesium bromoalkoxides. Then ^{14}C-labeled benzophenone was added and allowed to react at 0 °C for 30 min. After appropriate workup, the radioactivity of the recovered benzophenone was measured. The results that the molar radioactivity of the recovered ketone was the same within the experimental error as that of the added ketone confirmed that the reversion does not occur under the reaction conditions.

The difference in the reaction mechanism between allylic Grignard reagents and MeMgI is noteworthy. The conclusion that the R transfer step is slowest in the MeMgI reaction while the SET step is slowest in the reactions of **3** and **4** may look strange if one takes into consideration that **3** is a better electron donor than MeMgI.[1b] A possible explanation for this is that although the SET step is faster for **3** and **4** than for MeMgI, the R transfer step becomes even faster for **3** and **4** because a sterically favored six-membered TS is possible in the C-C bond formation step for **3** and **4**. A reported much faster overall rate for **3** compared with that for MeMgI is consistent with this explanation.[1b] The difference of the rate-determining step is also compatible with the fact that MeMgI when treated with cis-2,2,6,6-tetramethylhept-4-en-3-one induces isomerization of the unreacted enone while **3** results in practically no isomerization.[11] Thus, no back ET from the initially formed anion radical of the enone occurs in case of **3**.

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8) Since the σ constants of the ortho substituents are not available, the $\log(k_X/k_H)$ values for the ortho derivatives were plotted against corresponding σ_p and are indicated by closed circles. The deviations observed for the MeO derivatives may be attributed to the inadequacy of applying the standard σ constants of the hydrogen-bond accepting substituents for the reaction carried out in the nonpolar solvent. Other substituents gave reasonably good straight lines in these reactions, from which the ρ values were calculated.
9) The reason why the rate-determining SET gives a Hammett ρ value of near zero is given in Ref. 7.
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