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Investigation of Intermediate Radicals in the Grignard Reactions. Rates of Electron Transfer and of Successive R• Transfer to Ketones from Grignard Reagents[†]

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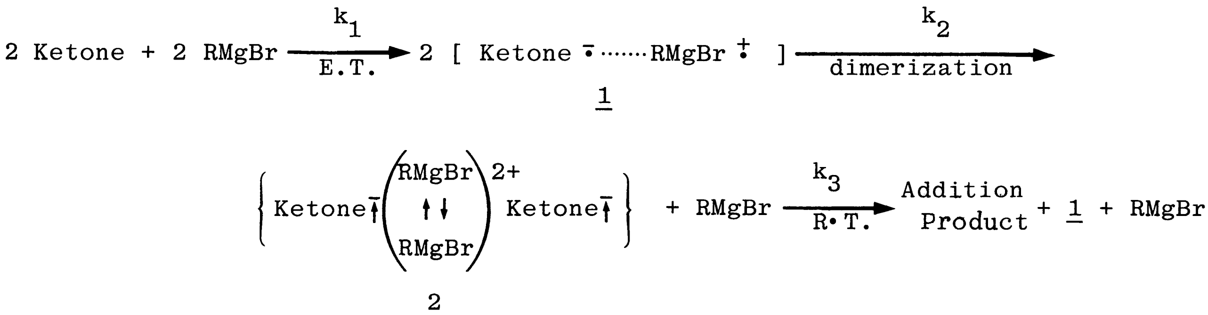
In the Grignard reactions with benzil (diketone) and with benzophenones (monoketone) in THF rates of electron transfer and of successive R• transfer from Grignard reagents were determined by direct observations of intermediate radicals. The electron transfer rates from Grignard reagents to ketones are dependent on both the electrochemical properties of Grignard reagents and ketones.

Recently, it was unambiguously confirmed that Grignard reactions with ketones proceeded by the radical mechanism.[1,2] In the Grignard reaction with benzil in THF we proposed the reaction processes described in Scheme 1.



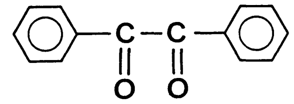
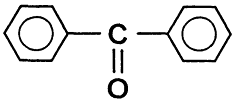
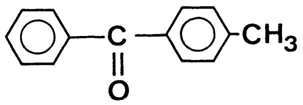
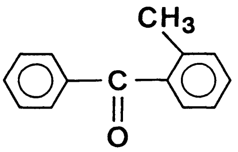
$$2\ \text{Ketone} + 2\ \text{RMgBr} \xrightarrow[\text{E.T.}]{k_1} 2\ \underset{\underline{1}}{[\ \text{Ketone}^{\overline{\cdot}}\cdots\cdots\text{RMgBr}^{\dot{+}}\ ]} \xrightarrow[\text{dimerization}]{k_2}$$

$$\underset{\underline{2}}{\left\{ \text{Ketone}^{\overline{\uparrow}} \begin{pmatrix}\text{RMgBr}\\ \uparrow\downarrow \\ \text{RMgBr}\end{pmatrix}^{2+} \text{Ketone}^{\overline{\uparrow}} \right\}} + \text{RMgBr} \xrightarrow[\text{R}\cdot\text{T.}]{k_3} \begin{matrix}\text{Addition}\\ \text{Product}\end{matrix} + \underline{1} + \text{RMgBr}$$

Scheme 1.

[†] This paper is dedicated to the late Professor Ryozo Goto, Kyoto University.

Table 1. Electron Transfer (k_1) and R• Transfer (k_3) Rate Constants in the Grignard Reactions at 25 °C in THF

Ketone	RMgBr (R-)	k_1 a)/ $M^{-1}s^{-1}$	k_3 a)/ $M^{-1}s^{-1}$
	Ph b)	3×10^2	8×10
	Me b)	2×10^4	4×10^2
	n-Bu b)	$>> 1 \times 10^5$	8×10^3
	Et b)	$>> 1 \times 10^5$	1×10^4
	Ph c)	6	5×10^{-2}
	Me c)	1.1×10	1×10^{-1}
	n-Bu d)	2.3×10^2	$\sim$ 3
	Et d)	7×10^2	$\sim$ 3
	Ph e)	– f)	– f)
	Me e)	– f)	– f)
	n-Bu c)	1.5×10	8×10^{-1} g)
	Et c)	1.1×10	1.2
	Ph e)	– f)	– f)
	Me e)	– f)	– f)
	n-Bu e)	3×10^{-1}	6×10^{-2} g)
	Et e)	3×10^{-1}	1×10^{-1}

a) 1 M = 1 mol dm^{-3}. Ten times excess amounts of Grignard reagents over ketones were used. Since all the pseudo-first order rate constants were proportional to the initial concentrations of the Grignard reagent in each case, the rate constants were expressed as the second order rate constants derived from pseudo-first order rate constants divided by initial concentrations of the Grignard reagent. The standard deviations of these constants are 25% of them at most. b) Observed at 610 nm by stopped-flow method under N_2. c) Accumulation of the radical was observed at 540 nm by stopped-flow method under N_2. Decay of the radical was observed at 540 nm by visible spectrometer under deaerated conditions. d) Accumulation of the radical was observed at 600 nm by stopped-flow method under N_2. Decay of the radical was observed at 540 nm by visible spectrometer under deaerated conditions. e) Observed at 540 nm by visible spectrometer under deaerated conditions. f) The amount of radical species was too small to do enough kinetic treatments. g) Besides of this major process, there exists the other slower decay process which is independent of the initial concentrations of the Grignard reagent, see Ref.5.

The initial electron transfer from a Grignard reagent to a ketone results in the formation of monomeric ion radical pair (1) which instantly forms a stable dimer (2). Since, in general, with exception of some cases[3)] the relation $k_2 >> k_1 >> k_3$ can be kept, we are able to determine k_1 and k_3 by direct observation of 2. The stable dimer (2) showed well-resolved ESR signals. Then, alkyl or aryl radical transfer induced by participation of another neutral molecule of Grignard reagent results in the completion of addition reaction.

Keeping this reaction scheme in mind, we determined k_1 and k_3 by stopped-flow technique measuring directly the rate of accumulation and decay of these radical species. The rate constants were summarized in Table 1.[4)] To simplify the situation, we used ten times excess amount of Grignard reagents over ketones. Accumulation curve of the radical species fitted well with pseudo-first order kinetics, and was analyzed by Guggenheim plottings. The pseudo-first order rate constants were proportional to the initial concentrations of the Grignard reagent in each case. In addition, decay of the radical species obeyed the pseudo-first order kinetics.[5)] Thus, in Table 1, the reaction rate constants are expressed as the second-order rate constants derived from pseudo-first order rate constants divided by initial concentrations of the Grignard reagent.

From Table 1, in the reactions of different kinds of Grignard reagents, we can realize that accumulating rate constants of radical species are related to both the reduction potentials of ketones (benzil: -0.58 V,[6)] benzophenone: -1.776 V,[7)] 4-methylbenzophenone: -1.835 V,[7)]

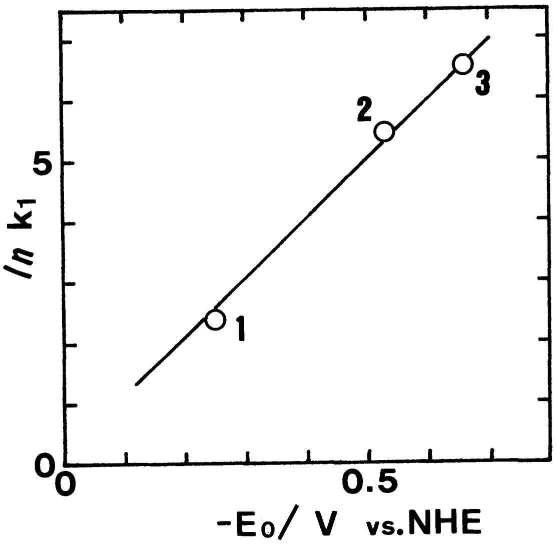


Fig.1. Relation between electron transfer rate constants (k_1) and reported standard oxidation potentials of Grignard reagents relative to NHE (see Ref.8) in the reaction of Grignard reagents with benzophenone in THF.
1: MeMgBr, 2:n-BuMgBr, and 3:EtMgBr.

2-methylbenzophenone: -1.851 V vs. SCE[7]), and the oxidation potentials of Grignard reagents (MeMgBr: -0.25 V, n-BuMgBr: -0.53 V, EtMgBr: -0.66 V vs. NHE[8,9]). In the reactions of PhMgBr and MeMgBr (higher oxidation potential) with 4-methylbenzophenone and 2-methylbenzophenone (lower reduction potential), we could detect radical species by ESR. However, the amount of radical species was too small to do enough kinetic treatments under this conditions. In the reaction of Grignard reagents with benzophenone, we found a good linear correlation between logarithm of k_1 and oxidation potentials of the Grignard reagents (Fig.1, correlation coefficient r = 0.998).

References

1) K.Maruyama and T.Katagiri, J.Am.Chem.Soc., 108, 6263 (1986) and references cited therein.

2) K.Maruyama, J.Hayami, and T.Katagiri, Chem.Lett., 1986, 601.

3) In the reactions of n-BuMgBr or EtMgBr with benzophenone the condition of $10 > k_1[\mathrm{RMgBr}]/k_2[\underline{1}] > 1$ was attained. Both k_1 and k_2, therfore, were determined; in the case of n-BuMgBr, $k_1 = 2.3 \times 10^2$ ($M^{-1}s^{-1}$), $k_2 = 1.1 \times 10^7$ ($M^{-1}s^{-1}$), and in the case of EtMgBr, $k_1 = 7 \times 10^2$ ($M^{-1}s^{-1}$), $k_2 = 1.1 \times 10^7$ ($M^{-1}s^{-1}$).

4) We observed appearance of 2 at 540 nm in the reactions of benzophenones and at 610 nm in the reaction of benzil at 25 °C in THF.

5) Besides of the major process (addition reaction), in the reactions of 4-methylbenzophenone or 2-methylbenzophenone with n-BuMgBr the other slower decay process (first order) of 2, which might be attributed to the formation of reduced products, was also observed, because fairly large amounts of 4- or 2-methylbenzhydrol were detected in the products.

6) R.H.Phlip, R.L.Flurry, and R.A.Day,Jr., J.Electrochem.Soc., 111, 339 (1980).

7) J.Grimshaw and R.Hamilton, J.Electroanal.Chem.Interfacial Electrochem., 106, 339 (1980).

8) T.Holm, Acta Chem.Scand.,Ser.B, 37, 567 (1983).

9) The oxidation potential of PhMgBr has not been reported.

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