Homolytic Mechanisms in the Reaction of Grignard Reagents with Benzophenone: Electron Transfer Concerted with Magnesium Transfer

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A comparison has been made between the heat of formation, $\Delta H_f[TS]$, of the transition states for the reaction of alkylmagnesium bromides with benzophenone and the sum of the heats of formation of the alkyl radicals and magnesium diphenylketyl, $\Delta H_f[3]$. For tertiary and secondary alkyls $\Delta H_f[TS] \approx \Delta H_f[3]$, while for primary alkyls and especially for methyl $\Delta H_f[TS] < \Delta H_f[3]$. The interpretation is that the rate-determining step is electron transfer concerted with magnesium transfer from carbon to oxygen. With tertiary and secondary reagents the alkyls are free to diffuse out of the cage, but with primary reagents and methyl, weak bonding exists between the radicals ($4-10$ kcal mol^{-1}) preventing diffusion out of the solvent cage.

In the reaction of benzophenone with *tert*-butyl-magnesium chloride and other Grignard reagents a two-step mechanism has been demonstrated, in which the alkyl radical and the ketyl are intermediates.[1] It is assumed that an electron-transfer step is rate limiting, and for a series of Grignard reagents attempts have been made to correlate the rates obtained and the oxidation potentials found for the Grignard reagents according to the Marcus theory for outer-sphere electron transfer.[2,3]

It seems questionable, however, whether the electron transfer is an independent step ($1 \rightarrow 2 \rightarrow 3 \rightarrow 4$; Scheme 1), or whether it is concerted with the transfer of the magnesium atom ($1 \rightarrow 3 \rightarrow 4$). The outer-sphere ET mechanism ($1 \rightarrow 2$) would supposedly require a higher energy of activation than the concerted ET ($1 \rightarrow 3$), since magnesium
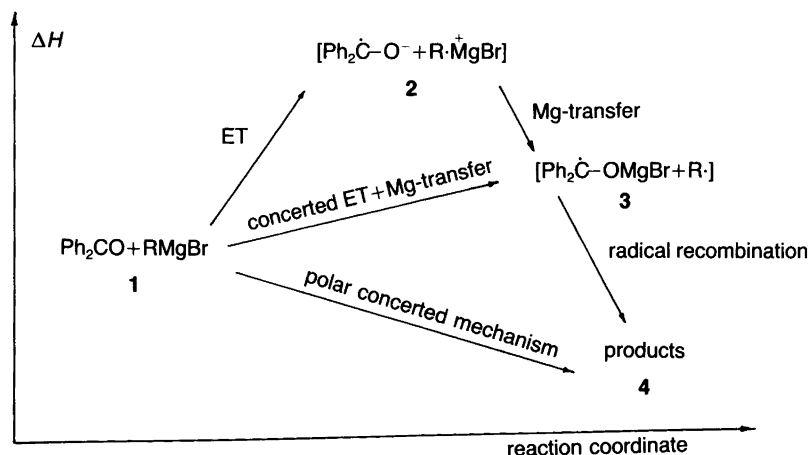
Scheme 1.

forms a very strong bond to oxygen.

In this investigation the enthalpy of formation of the transition state, $\Delta H_f[TS]$, for the reaction between benzophenone and Grignard reagents was found to be the sum of the activation energy for the reaction and the enthalpy of formation of the reactants [eqn. (1)]. $\Delta H_f[TS]$ was then compared with $\Delta H_f[3]$, the sum of the enthalpies of formation of the magnesium diphenylketyl and the alkyl radical [eqn. (2)]. Similarity between the two values, [eqn. (3)], would indicate that the radical pair is not only an intermediate, but should be considered the point of maximum energy on the reaction path, more or less identical with the transition state.

$$\Delta H_f[TS] = \Delta H_f[RMgBr] \text{ (in Et}_2\text{O)}$$
$$+ \Delta H_f[Ph_2CO] \text{ (in Et}_2\text{O)} + \Delta H^{\ddagger} \qquad (1)$$

$$\Delta H_f[3] = \Delta H_f[Ph_2\dot{C}-OMgBr] \text{ (in Et}_2\text{O)}$$
$$+ \Delta H_f[R\cdot] \text{ (in Et}_2\text{O)} \qquad (2)$$

$$\Delta H_f[TS] = \Delta H_f[3] \qquad (3)$$

Results and discussion

The thermochemical data for (1) and (2) were available in the literature except for the heats of solution of benzophenone, benzhydryl alcohol and benzopinacol, and the enthalpy of formation of benzopinacol and of magnesium diphenylketyl. The enthalpy of formation of magnesium diphenylketyl has been related to ΔH_f for ben-
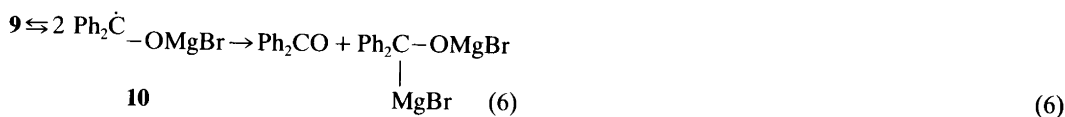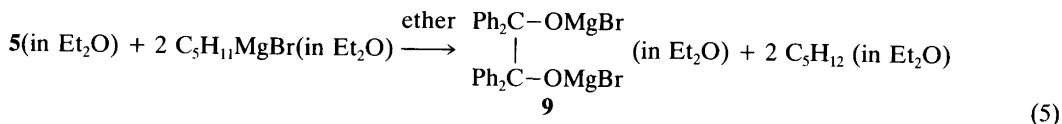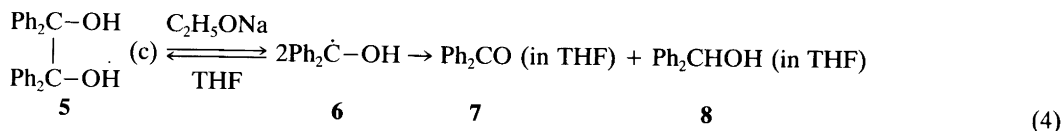
zophenone[4] and for benzhydryl alcohol[4] by the reactions (4) – (6).

Reaction (4) was run in THF with a catalytic amount of sodium ethoxide.[5] The reaction took place quantitatively in 2–3 min as checked by NMR spectroscopy and was exothermic by 6.9 kcal mol^{-1}. The heats of solution of benzophenone and benzhydryl alcohol in THF were determined to be 3.0 and 1.8 kcal mol^{-1}, respectively. The heat of solution of benzopinacol (5) in diethyl ether was 1.0 kcal mol^{-1}. From the known values of the enthalpy of formation of these compounds[4] the ethalpy of formation of benzopinacol in the crystalline state was determined to be -22.0 kcal mol^{-1}. Support for this value was obtained by the determination[6] of the heat of combustion of benzopinacol, which, in 3 experiments, averaged 8678 kcal mol^{-1}, corresponding to ΔH_f° [benzopinacol,c] = -20.7 ± 2 kcal mol^{-1}.

Reaction (5) was run in a flow-stream apparatus as described[7,8] and the results indicated that ΔH_r (5) = -90.0 kcal mol^{-1} and therefore $\Delta H_f[9]$ (in Et$_2$O) = -222 kcal mol^{-1}.

Reaction (6) took place at elevated temperatures. The reaction was run in diethyl ether at $120-140°C$. The concentrations were determined by NMR spectroscopy of the reaction mixtures after work-up and the rates calculated, and the results were compared with those obtained in the thermolysis of benzopinacol itself. Both reactions were found to be approximately 10 times slower at 120 than at 140°C.

Reaction (6) is related to reaction (4) insofar as the initial step in both reactions is the homolytic dissociation of the central carbon–carbon bond in benzopinacol. While this dissociation is fast

$$\begin{array}{l} Ph_2C-OH \\ | \qquad\quad \text{(c)} \\ Ph_2C-OH \end{array} \begin{array}{c} C_2H_5ONa \\ \xrightleftharpoons \\ THF \end{array} 2Ph_2\dot{C}-OH \rightarrow Ph_2CO \text{ (in THF)} + Ph_2CHOH \text{ (in THF)}$$
$$\quad\;\; 5 \qquad\qquad\qquad\qquad 6 \qquad\quad 7 \qquad\qquad\qquad 8 \qquad\qquad\qquad\qquad\qquad (4)$$

$$\begin{array}{l} \text{ether} \quad Ph_2C-OMgBr \\ 5\text{(in Et}_2\text{O)} + 2\ C_5H_{11}MgBr\text{(in Et}_2\text{O)} \longrightarrow \qquad | \qquad\qquad \text{(in Et}_2\text{O)} + 2\ C_5H_{12} \text{ (in Et}_2\text{O)} \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad Ph_2C-OMgBr \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad 9 \end{array}$$
$$(5)$$

$$9 \rightleftharpoons 2\ Ph_2\dot{C}-OMgBr \rightarrow Ph_2CO + Ph_2C-OMgBr$$
$$\qquad\qquad 10 \qquad\qquad\qquad\qquad\qquad\qquad\qquad | \qquad\qquad\qquad MgBr \quad (6)$$
$$(6)$$

when benzopinacol is in the anionic state, the dissociation is very slow using either the dimagnesium salt or benzopinacol itself. This is presumably because the C—C bond in the anion containing negatively charged oxygens is weakened by electrostatic repulsion. In the magnesium salt the O—Mg σ bond is much less polar and there is very little effective charge on oxygen because of back-donation of lone pairs from oxygen to the empty orbitals on magnesium[8] [eqn. (7)]

$$-\overline{\overline{O}} - Mg^{II} \leftrightarrow -\ddot{O}=Mg^{I} \tag{7}$$
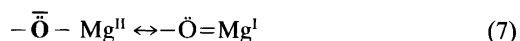
The result is that the O—Mg bond is strong and that the C—C bond is approximately as strong in the dimagnesium salt as in benzopinacol itself. Values for the C—C bond strength in benzopinacol have been obtained from ESR measurements[9] of the dissociation equilibrium at 30 and 141 °C and are estimated to be 33 kcal mol^{-1}. Since, as mentioned above, thermolysis of either **5** or **9** in ether is about 10 times faster at 140 than at 120 °C, it is reasonable to assume that the bond strength of the central C—C bond is about 33 kcal mol^{-1} in both compounds. The conclusion is tentative and is based among other things on the assumption that C—C bond breaking is rate determining in both reactions.

Using the data obtained for reactions (4), (5) and (6) the enthalpy of formation for magnesium diphenylketyl in diethyl ether is estimated to be −94 kcal mol^{-1}.

The activation energies for the reaction of

Table 2. Enthalpies of formation in diethyl ether of the transition state for the reaction of RMgBr + benzophenone, (ΔH_f[TS]) compared with the sum of the enthalpies of formation of magnesium diphenylketyl and free alkyl radical in the condensed phase (ΔH_f[3]; see text).

R	ΔH_f[3]/ kcal mol^{-1}	ΔH_f[TS]/ kcal mol^{-1}	δ/kcal mol^{-1}
CH$_3$	−62.1	−72.0	9.9
C$_2$H$_5$	−71	−75.1	4.0
(CH$_3$)$_2$CH	−79.8	−82.3	2.5
C$_4$H$_9$	−83.7	−87.8	4.1
i-C$_4$H$_9$	−85.4	−91.0	5.6
s-C$_4$H$_9$	−86.4	−87.6	1.2
t-C$_4$H$_9$	−91.4	−90.5	−0.9

Grignard reagents with benzophenone have been obtained[10] from rate measurements at 20 and 40 °C (Table 1) and the enthalpies of formation of Grignard reagents in ether solution have been published.[11] The enthalpies of formation of the transition state in the reaction between benzophenone and Grignard reagents may now be calculated and are given in Table 2. Also given in Table 2 is ΔH_f[3], the sum of the enthalpies of formation of magnesium diphenylketyl and the corresponding free radical. The ΔH_f values for the free radicals are known only in the gaseous state[12] and are approximately corrected to the condensed phase by assuming that $\Delta H_v(R^.) = \Delta H_v(RH)$.

A comparison of the ΔH_f values in the two columns in Table 2 shows that for tert-butyl and sec-butyl they are almost identical and for isopropyl the difference is insignificant. The difference is larger, however, for ethyl, butyl and isobutyl, with a maximum difference of ca. 10 kcal mol^{-1} observed for methyl. That the TS is more stable than should be expected for the completely free radicals may be interpreted by assuming that the spins are not unpaired, and that weak bonding exists between the alkyl and the ketyl groups. The effect is insignificant (< 3 kcal mol^{-1}) for isopropyl and sec-butyl, but increases in the series ethyl, butyl, isobutyl and methyl with respective values of 4, 4, 6 and 10 kcal mol^{-1}.

From these results it may be concluded that the reaction of tert-butylmagnesium halide with benzophenone takes place according to Scheme 1, i.e. **1** → **3** → products, and includes induced
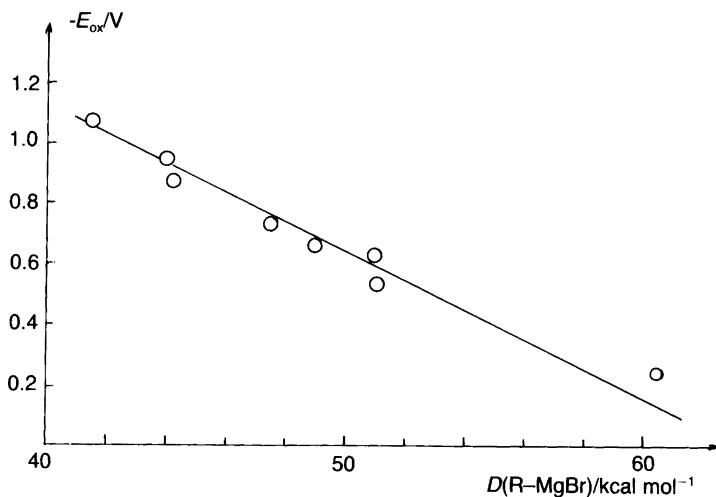
Table 1. Pseudo first-order rate constants at 20 and 40 °C and activation parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ for the reaction between 0.10 M alkylmagnesium bromide and 0.02 M benzophenone in diethyl ether.

R	k_{obs}/s^{-1} at 20 °C	k_{obs}/s^{-1} at 40 °C	$\Delta H^\ddagger$/kcal mol^{-1}	$\Delta S^\ddagger$/cal K^{-1}mol^{-1}
CH$_3$	0.0805	0.386	13.7	−12.2
C$_2$H$_5$	1.97	5.53	8.8	−22.5
i-C$_3$H$_7$	12.0	23.1	5.4	−30.6
n-C$_4$H$_9$	0.85	2.46	9.0	−23.2
i-C$_4$H$_9$	0.38	1.12	9.2	−24.2
s-C$_4$H$_9$	3.6	8.08	6.8	−28.2
t-C$_4$H$_9$	13.1	23	4.5	−33.3

Fig. 1.

homolysis of the carbon−magnesium bond in the rate-determining step to produce magnesium diphenylketyl and a free *tert*-butyl radical.

In the reaction with methylmagnesium halide, concerted electron and magnesium transfer takes place, although free, diffusing radicals are not produced except as a minor by-product. The interaction between the radicals (ca. 10 kcal mol^{-1}) prevents their separation and the product is 99 % 1,2-adduct.[13] With isopropyl and *sec*-butyl the interaction is insignificant, and separation of the radicals may still take place, explaining the formation[13] of radical- type products such as 1,6 adducts. For all Grignard reagents, however, the transition state is related to the pair of free radicals, and it is reasonable that linear free-energy correlations may be obtained between log rate and either D(R−Mg)[11] or E_{ox}(RMgBr)[2] which have a mutual linear correlation, as shown in Fig. 1. A concerted electron and metal transfer has previously been observed using the sodium ketyl of benzophenone.[14]

The heats of formation of the Grignard reagents are considered to be accurate to within 1−2 kcal mol^{-1}, and the activation parameters to within 2−3 kcal mol^{-1}, while the calculated ΔH_f for magnesium diphenylketyl is tentative. In the comparison between the different reagents, however, systematic errors will tend to cancel and there seems a very strong case for concluding that tertiary and secondary Grignard reagents reacting with benzophenone produce free radicals as

intermediates, while primary and methyl reagents produce weakly coupled radical pairs. This coupling is not strong enough to classify the reaction as concerted and methyl and phenyl Grignard reagents are the least reactive towards benzophenone. A truly concerted mechanism is, however, indicated in the reaction of phenylmagnesium bromide with acetone, since the weak electron donor, phenylmagnesium bromide, is extremely reactive toward this substrate.

Experimental

The calorimeter used was a cylindrical magnetically stirred Dewar flask with a rubber seal, in which was mounted a platinum Pt 100 resistance thermometer, a manganin heating coil, a gas inlet and outlet, and a gas-tight lock for the addition of reactants. The temperature was read to 0.0001 °C by means of a Keitley 196 digital multimeter, and a Fluke current calibrator model 382a was used for calibration.

Decomposition of benzopinacol (0.02 mol l^{-1} in diethyl ether) either free or as the bis(bromomagnesium) salt was performed in ampoules placed in a thermostat. Conversion of free benzopinacol after 8 h at 119 °C was 40 % and after 2.5 at 139 °C, 85 %. Conversion of the dimagnesium salt after 2 h at 139 °C was 40 % and after 8 h at 119 °C, 22 %. Reaction mixtures were analysed by NMR spectroscopy using a Bruker HXE 90 instrument.

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