Evidence for Electron-transfer Process in Abnormal Grignard Reactions. Enolization and α-Diketone Formation

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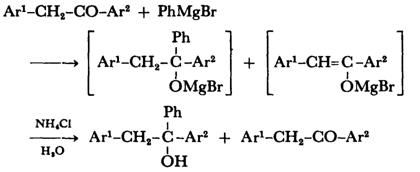
Synopsis. The effect of 2,6-dimethyl groups on enolization *vs.* addition in the reaction of PhMgBr with $PhCH_2COPh$, and also the formation of α-diketone from $2,4,6-Me_3C_6H_2COCl$ by the treatment with MeMgX and *i*-PrMgX in the presence of $CoCl_2$, were studied. The results were discussed on the basis of electron-transfer mechanism.

In Grignard reaction of carbonyl compounds, steric hindrance affects greatly the concentration as well as the spin distribution of initially formed ketyl radicals and consequently the course of reaction.[1,2] Correlation between the spin density and the product distribution was discussed in the studies on aromatic substitution,[1] replacement of anionoid substituents,[2] and conjugate addition.[2] Among representative abnormal Grignard reactions, enolization of ketones[3] and α-diketone formation from hindered aroyl chloride[4] remanined to be studied on the same basis. Some results obtained in these reactions will be reported and discussed in this paper.

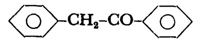
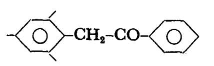
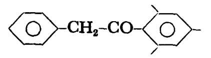
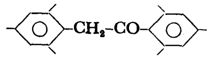


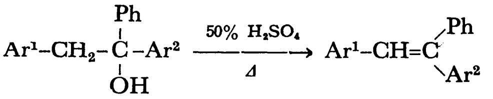
$$Ar^1\text{-}CH_2\text{-}CO\text{-}Ar^2 + PhMgBr \longrightarrow \left[Ar^1\text{-}CH_2\text{-}\overset{Ph}{\underset{OMgBr}{C}}\text{-}Ar^2\right] + \left[Ar^1\text{-}CH{=}\underset{OMgBr}{C}\text{-}Ar^2\right] \xrightarrow[H_2O]{NH_4Cl} Ar^1\text{-}CH_2\text{-}\overset{Ph}{\underset{OH}{C}}\text{-}Ar^2 + Ar^1\text{-}CH_2\text{-}CO\text{-}Ar^2$$

Scheme 1.

Enolizable ketones studied are benzyl phenyl ketone and its *o*-methyl derivatives (Table 1, **1**, **2**, **3**, and **4**), the reaction with PhMgBr being shown in Scheme 1. The reaction was carried out in tetrahydrofuran (THF) under nitrogen atmosphere, the reaction mixture being heated at 50 °C for 30 min. The cooled reaction mixture was quenched with saturated aqueous NH_4Cl. A mixture of products obtained after removal of solvent was heated with 50% H_2SO_4 to convert the alcohols (normal adducts) into the corresponding triarylethylenes (Scheme 2). The product mixtures were finally submitted to GLC analysis. The product distributions thus determined are summarized in Table 1.

TABLE 1. PRODUCT DISTRIBUTION IN THE REACTION OF HINDERED BENZYL PHENYL KETONES

No.	$Ar^1\text{-}CH_2\text{-}CO\text{-}Ar^2$ structure	$\frac{[PhMgBr]}{[Ketone]}$	Product distribution (%) Recovered ketone	Product distribution (%) $Ar^1\text{-}CH{=}C\langle^{Ar^2}_{Ph}$
1		1	36	64
		1.5	27	73
		2	3	97
		3	2	98
2		1	78	22
		5	66	34
		10	54	46
3		10	100	0
4		10	100	0



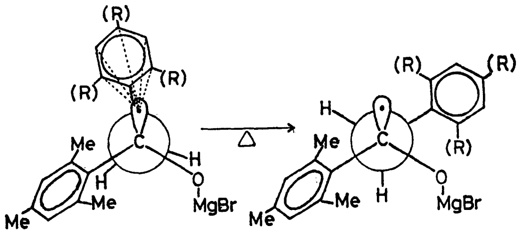
$$Ar^1\text{-}CH_2\text{-}\overset{Ph}{\underset{OH}{C}}\text{-}Ar^2 \xrightarrow[\Delta]{50\%\ H_2SO_4} Ar^1\text{-}CH{=}C\langle^{Ph}_{Ar^2}$$

Scheme 2.

The results show that the presence of 2,6-dimethyl groups affect remarkably the product distribution: the groups on the benzoyl moiety do much more greatly than those on the benzyl moiety, thus inhibiting normal addition completely. In order to estimate the extent of enolization, the reaction mixtures of **3** and **4** were quenched with $D_2O\text{-}D_2SO_4$. Analyses of the NMR spectra show that the recovered **3** has been enolized quantitatively while **4** to *ca.* 60%.

ESR signals were detected in the reactions of **3** and **4** at room temperature. Failure to detect ESR signals in the cases of **1** and **2** is quite reasonable, since it is known that ketones having α-hydrogen atom cannot give stable metal ketyls due to rapid decomposition.[5,6] Existence of the initial electron-transfer step from Grignard reagent to substrates is generally accepted on the basis of recent mechanistic studies.[7,8] The failure to detect ESR signals in the cases of **1** and **2** is thus ascribable to the rapid subsequent processes: enolization and addition.

ESR signal observed in the case of **3** ($a_{\alpha\text{-H}}=2.6$) disappeared completely after heating the reaction mixture at 50 °C for 30 min, whereas that in the case of **4** ($a_{\alpha\text{-H}}=7.5$[9]) did not. In spite of the expected high spin density on the carbonyl carbon atom due to the sterically suppressed spin delocalization on the hindered phenyl group, the fair stability of these ketyls at room temperature could be ascribed to their conformation (Fig. 1): the direction of the $C_\alpha\text{-}H_\alpha$ bond is not in trans to that of the free spin orbital and the free spin may be stabilized by the spatial assistance of the π-electrons of the aryl group on the benzyl moiety (**3a** and **4a**). Predominance of these eclipsed conformations is rationalized since at least two THF molecules affect greatly the bulkiness of the –OMgBr group. By heating the reaction mixture of **3**, however, the conformational rotation to the staggered form (**3b**) occurs, allowing the direction of the $C_\alpha\text{-}H_\alpha$ bond to be in full trans to

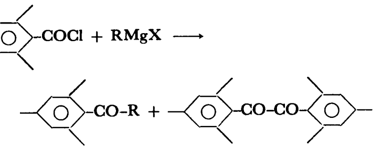


3a (R = H) 4a (R = Me) 3b (R = H) 4b (R = Me)

Fig. 1. Conformation of the ketyl radicals of **3** and **4**.

that of the free spin orbital. This conformation is responsible for the β-scission of the α-hydrogen atom, the original ketone **3** being thus enolized. The great stability of the ketyl of **4** is thus ascribed to the sterically retarded conformational change from **4a** to **4b** (Fig. 1) caused by the hindered aryl group of the benzyl moiety. It should be noted that the electron-transfer process was confirmed for the first time in the reaction of enolizable ketones.

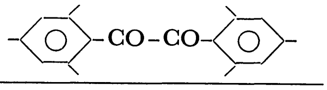
The formation of α-diketone(2,2′,4,4′,6,6′-hexamethylbenzil) from hindered 2,4,6-trimethylbenzoyl chloride by the treatment with Grignard reagents (Scheme 3; R=Me, X=Br and I) in the presence of a catalytic amount of $CoCl_2$ was reported.[4] If isopropylmagnesium halide (Scheme 3; R=*i*-Pr, X=Cl, Br, and I) is used, the bulkier isopropyl group is expected to raise the yield of α-diketone.



Scheme 3.

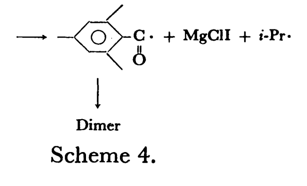
The reaction was carried out in diethyl ether to compare our result with the previous one.[4] A very high yield of the α-diketone was realized by the treatment with *i*-PrMgI (Table 2). This result, however, is explicable in terms of the electron-transfer ability of the reagent instead of ambiguous effect of bulkiness. The thermographic[10] and electrolytic[11] studies of Grignard reagents show that the isopropyl reagent is much more electron-donating than the methyl reagent. Iodide ion has an oxidation potential much lower than that of bromide ion,[12] and is favorable to the α-diketone formation as shown in Table 2. It is thus reasonable to consider that the combination of isopropyl group and iodide ion can transfer single electron to the aroyl chloride most effectively among the five reagents examined.

Table 2. Yields of the α-diketone

Grignard Reagent	Yield of  (%)
Me_2CHMgI	87
$Me_2CHMgBr$	38
$Me_2CHMgCl$	22
MeMgI	63[a]
MeMgBr	31[a]

a) The previous results[4] were reproducible.

Though volatile products[4] could result from *i*-Pr· as well as the equivocal role of $CoCl_2$ remains still to be examined, initial electron-transfer from Grignard reagent to the benzoyl chloride followed by releasing of chloride anion should be emphasized, consequently producing the hindered aroyl radical (Scheme 4) to dimerize to give the α-diketone.



Scheme 4.

Experimental

Materials. Melting points are uncorrected. Friedel-Crafts' method using phenylacetyl chloride was applied to prepare **1** and **3**; **1**: mp 57—59 °C, **3**: mp 101—103 °C. 2,4,6-Trimethylphenylacetyl chloride was used to prepare **2** and **4**; **2**: mp 164.5—165 °C, **4**: mp 181—182 °C. Anthydrous $CoCl_2$ was prepared from commercial hydrated salt.[4] Authentic sample of the α-diketone was prepared according to the reported method[4] using isopropylmagnesium iodide: mp 120.5—122 °C (lit,[4] mp 119—120 °C).

Procedures. PhMgBr (0.0276 mol) in 20 ml THF was prepared in the usual manner. The Grignard solution was cooled to 0 °C and the ketone **1** dissolved in 20 ml THF was added rapidly; the resulting mixture was heated at 50 °C for 30 min. The subsequent procedures were described in the text. The other ketones were treated similarly. The ketones **3** and **4** were recovered quantitatively even by the treatment with 10 molar equivalents of PhMgBr. The apparatus used for ESR measurements was reported previously.[13]

i-PrMgX (0.021 mol) was prepared in diethyl ether (25 ml). $CoCl_2$ (0.0002 mol) was added under N_2, and the resulting black solution was transferred under N_2 into a dropping funnel, the reaction with the aroyl chloride (0.007 mol) in diethyl ether (25 ml) being carried out in the manner of reverse addition.[4] The product mixtures obtained in the reactions of the respective Grignard reagents were submitted to high pressure liquid chromatography on silica gel by use of methyl alcohol–water (65 : 35) as eluent under the pressure of 30 kg/cm². The yield of the α-diketone was estimated by comparison with a straight calibration line obtained by injection of the authentic sample solutions in benzene.

References

1) M. Ōkubo, *Bull. Chem. Soc. Jpn.*, **48**, 1057, 1327, 2057 (1975).

2) M. Ōkubo, *Bull. Chem. Soc. Jpn.*, **50**, 2379 (1977).

3) E. P. Kohler and R. B. Thompson, *J. Am. Chem. Soc.*, **59**, 887 (1939); F. C. Whitmore and L. P. Block, *ibid.*, **64**, 1619 (1942).

4) M. S. Kharasch, R. Morrison, and W. H. Urry, *J. Am. Chem. Soc.*, **66**, 368 (1944).

5) J. E. Bennett, B. Mile, and A. Thomas, *J. Chem. Soc.*, *A*, **1968**, 298.

6) G. A. Russell and G. R. Stevenson, *J. Am. Chem. Soc.*, **93**, 2432 (1971).

7) T. Holm and I. Crossland, *Acta Chem. Scand.*, **25**, 59 (1971).

8) E. C. Ashby, Lecture given at the Conference of Organometallic Chemistry, Dijon, France, Aug. 1979.

9) The $a_{\alpha\text{-H}}$ values were found from poorly resolved ESR spectra. The value of $a_{\alpha\text{-H}}$ of **4** appreciably greater than that of **3** may be due to the twisting of $2,4,6\text{-}Me_3C_6H_2$–group on the benzyl moiety, delocalization of the free spin being thus suppressed.

10) T. Holm, *Acta Chem. Scand.*, **23**, 579 (1969).

11) T. Holm, *Acta Chem. Scand.*, *B*, **28**, 809 (1974).

12) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 2nd ed, John Wiley and Sons, New York (1966), Chap. 22.

13) K. Maruyama, *Bull. Chem. Soc. Jpn.*, **37**, 897 (1964).