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Impact of reaction products on the Grignard reaction with silanes and ketones

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Abstract

Grignard reactions with alkoxysilanes or carbonyl compounds produce alkoxymagnesium halides as by-products. Kinetic measurements for reactions of silanes and of a ketone were performed with Grignard reagents, enriched in alkoxymagnesium halides and taken in a great excess.

The alkoxide-type reaction products complex tightly with Grignard reagents and enhance in this way their nucleophilicity, thus accelerating the reaction. However, alkoxides branched at α-C atom exert an unfavorable steric hindrance to reaction resulting in a decrease in the reaction rate.

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1. Introduction

Experiments with a great excess of a Grignard reagent preclude the influence of reaction products. Under the preparative conditions, with small or no excess of Grignard reagent, the products accumulated during the reaction can have a certain impact on the results.

Formerly we found that ethoxymagnesium chloride increased the rate of the coupling reaction between ethylmagnesium chloride and ethyltriethoxysilane [1]. In contrast to this, some alkoxymagnesium bromides, e.g., the reaction products, suppressed the rate of the Grignard reaction with ketones [2–4]. In parallel to the kinetic results, it has been signaled in numerous works [2,3,5–9] that with ketones the relative amount of reduction increases readily as the reaction proceeds. By the end of the reaction a higher yield of reduction product was obtained at the expense of the "normal reaction", i.e., of the Grignard addition. Additions of alkoxymagnesium bromides or alkylmagnesium alkoxides imitating the reaction products enhanced largely the relative yield of side reactions, above all that of the reduction reaction. However, it has been noted [3] that the unbranched alkoholates favored the addition reaction while α-branched alkoholates gave rise to reduction of the ketone.

Based on their kinetic investigations Ashby et al. [4,10,11] have shown that the product, alkoxymagnesium halide complexes with the Grignard reagent tightly and the equilibrium lies far toward the complex. The same proved to be valid for alkylmagnesium alkoxides. The branched alkoxide ligands derived from the Grignard addition to ketones caused a considerable decrease in the reaction rate [4,10].

While the impact of alkoxides on the Grignard reaction with silanes has been almost not investigated so far, also a number of inconsistencies remain concerning the reaction with ketones. Among others, relations between the addition and reduction reactions require a further rationalization.

By reason of recent revival of our interest in the Grignard reaction with silanes [12–14], we have addressed also the role of the reaction products in the reaction. We found

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that magnesium chloride from the coupling of organomagnesium chloride with chlorosilanes (Eq. (1)) had no effect on the reaction. This was not the case for alkoxymagnesium chlorides from reactions with alkoxysilanes (Eq. (2)).

$$RMgCl + MeSiCl_3 \rightarrow MeRSiCl_2 + MgCl_2 \qquad (1)$$

$$RMgCl + Si(OEt)_4 \rightarrow RSi(OEt)_3 + EtOMgCl \qquad (2)$$

The experimental method of this work consisted in preparation of Grignard reagents (*n*-butylmagnesium chloride in diethyl ether) with variable content of alkoxymagnesium chlorides and in determination of the rate constants and products ratios for the reactions with silanes and with a ketone. A great excess of modified Grignard reagent over silanes and over the ketone was used to avoid possible contribution of secondary reaction products. The alcohols used for the production of the alkoxymagnesium moieties in Grignard reagents were methanol, ethanol, isopropanol, 2-butanol, and 2-methyl-2-butanol.

2. Experimental

The experiments were carried out under dry argon in a thermostated 100 mL double-necked round-bottom flask equipped with a thermometer and a magnetic stirrer. The *n*-BuMgCl/ROMgCl reagents were prepared adding calculated amounts of dry alcohols to *n*-butylmagnesium chloride solution in diethyl ether. To start the reaction, calculated amount of silane (providing a 10–20-fold excess of the Grignard reagent) was injected into the flask. Samples were taken by a syringe through the rubber septum and quenched with ice-cold water (in case of the ethoxysilane) or with dry ethanol containing pyridine (in case of the chlorosilane thus providing ethoxysilanes). The organic layer was separated, dried, and analyzed for ethoxysilanes by use of GLC.

The fast reactions were investigated in a thermostatic flask equipped with a stirrer and a thermistor. The thermistor was connected through a bridge circuit to a recording potentiometer. To a 15 mL sample of the Grignard reagent was added 0.05 mL of ketone (providing a 20-fold excess of the Grignard reagent), and the temperature change of the reaction solution was recorded as a plot of temperature vs. time. Use of a differential method for calculation of rate constants [14] eliminated the contribution of heat exchange with the reaction vessel.
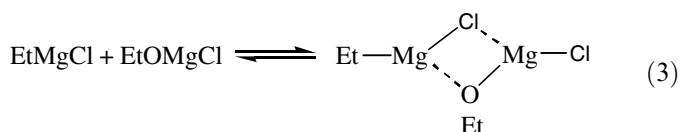
Check experiments using GLC indicated that the consecutive formation of triethylethoxysilane in kinetic measurements of the reaction between ethylmagnesium chloride reagents and ethyltriethoxysilane could be ignored at least during first three half-lives used for calculation of rate constants.

In reactions of tetraethoxysilane formation of dibutyl-diethoxysilane was present, however, the reaction was followed by consumption of the initial reagent tetraethoxysilane with a great excess of the Grignard reagent. Under these conditions kinetics of the reaction obeyed the pseudo-first order law during five half-lives.

The products of the reaction with diisopropyl ketone were identified by their ^{1}H NMR, ^{13}C NMR, and mass spectra. Contribution of the enolization reaction was negligible.

3. Results and discussion

We involved our former kinetic results for the reaction of ethyltriethoxysilane with ethylmagnesium chloride [1] obtained by a thermographic method. As is seen from Table 1, the limit rate constant is $k_\infty = 0.036 \text{ s}^{-1}$, indicating a rate enhancement

$$EtMgCl + EtOMgCl \rightleftharpoons \quad Et\!-\!Mg \overset{Cl}{\underset{O}{\cdots}} Mg\!-\!Cl \qquad (3)$$
$$\hspace{9cm} Et$$

by ethoxymagnesium chloride. Assuming a complete complexation of the reagents according to [4,11], (Eq. (3)) the rate constant can be calculated as

$$k_{\text{calc}} = M_f k_0 + M_C k_\infty,$$

where M_f and M_C are the molar fractions of free and complexed ethylmagnesium chloride, respectively. A good accordance between the observed and calculated rate constants (Table 1) proves the assumption of complete complexation of the reagents. The nucleophilic ethoxy group bound with the magnesium center evidently enhances the nucleophilicity of the Grignard reagent thus accelerating the reaction. This provides a more straightforward explanation of the results than speculations presented in the previous paper [1].

A similar experiment with *n*-butylmagnesium chloride (a GLC method) gave results (Fig. 1) supporting the conclusions above.

Extension of the investigation to alkoxides other than ethoxymagnesium chloride revealed a large contribution of relatively fast replacement reactions at the silicon center resulting in a set of competing and consecutive reactions which made practically impossible to follow the kinetics of the target reaction. However, from the initial periods of the reactions with *i*-PrOMgCl/BuMgCl reagent, rate constants were estimated. It appears that the effect of this ligand is reverse to that of the ethoxy group (Fig. 1).

Table 1
Pseudo-first order rate constants (s^{-1}) for the reaction of ethyltriethoxysilane (initial concentration 0.024 M) with ethylmagnesium chloride (1 M) in the presence of ethoxymagnesium chloride in diethyl ether at 30 °C

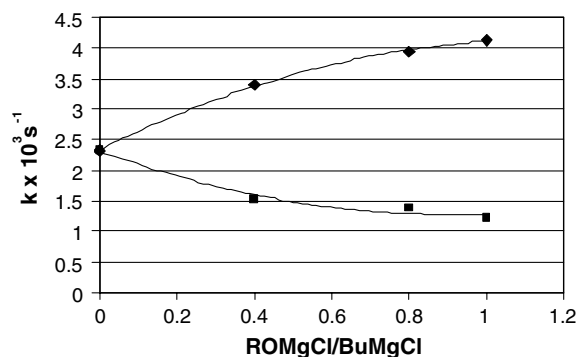| EtOMgCl/EtMgCl	k_{exp}	k_{calc}
0	0.018	–
0.30	0.024	0.023
0.50	0.030	0.027
0.73	0.031	0.031
0.98	0.034	0.035
1.26	0.035	0.036

Fig. 1. Pseudo-first order rate constants ($k \times 10^3$, s^{-1}) for the reaction of *n*-butylmagnesium chloride (0.5 M) with tetraethoxysilane in the presence of ethoxymagnesium chloride (◆) or isopropoxymagnesium chloride at 20 °C (■).

Similar complications were met when chlorosilanes were introduced. Replacement of chlorine atoms by the alkoxy group appeared to be competing with or even dominating over the Grignard reaction under the conditions of our experiment. However, qualitatively, it appeared to us that the additions of methanol to the initial Grignard reagent accelerated the reaction. To rationalize the matter, the reaction with a ketone was subjected to the investigation.

Results of a kinetic investigation of the reaction between *n*-butylmagnesium chloride in a great excess and diisopropyl ketone are presented in Fig. 2. Methoxy- and ethoxymagnesium chlorides showed an accelerating effect while isopropoxy- and other branched alkoxymagnesium chlorides suppressed the reaction rate. These results are qualitatively the same as observed for the reaction with silanes.

The reaction with diisopropyl ketone implicates the competing addition and reduction reactions. After working up the reaction product mixture, the molar ratios of products, 2-methyl-3-isopropylheptane-3-ol (from the addition reaction), and 2,4-dimethylpentane-3-ol (from the reduction reaction), respectively, were determined by GLC measurements. The results are presented in Table 2 together with relevant rate constants. Partial rate constants for competing addition and reduction reactions were calculated from the overall rate constants using the molar ratio of the reaction products (second column in Table 1). It is seen that alkoxy ligands not only affect the rate of the reaction but also the ratio of the products. In the presence of methoxymagnesium chloride both addition and reduction reactions are accelerated while *tert*-pentoxymagnesium chloride suppresses the rates of the reactions. The effect of the ligands upon the addition reaction is considerably stronger than for the reduction reaction. However, the effects are similar with those obtained from the reactions with silanes.

Our experimental results lead to some general conclusions. Grignard reagents, when the halogen is chlorine, are predominantly dimeric in diethyl ether over a wide concentration range, particularly at the 0.5 M concentration [11,15,16]. Therefore, the complexation with an alkoxymagnesium chloride involves a ligand replacement at the magnesium atom (cf. Structures I and II).
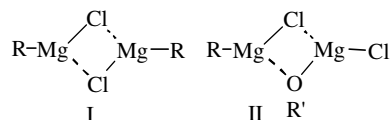
It is obvious that the donating ligand at the magnesium atom, a solvent molecule or other, polarizes the C–Mg bond, increasing the nucleophilicity of the C-atom. It is also obvious that an increase in steric hindrance causes a decrease in donating ability of the ligand regardless of its Broensted basicity. In this context, the alkoxides should arrange in the sequence $RCH_2O^- > R_2CHO^- > R_3CO^-$. However, it should be noted that the branching at the α-C atom actually operates in the β-position relative to the Mg-center, thus reducing the steric requirements of the ligand. As to the basicity/nucleophilicity of the alkoxides, the sequence arising from hydrogen-bond-donating systems cannot be applied and probably the gas-phase basicities should be considered [17] thus resulting in the same sequence as above.
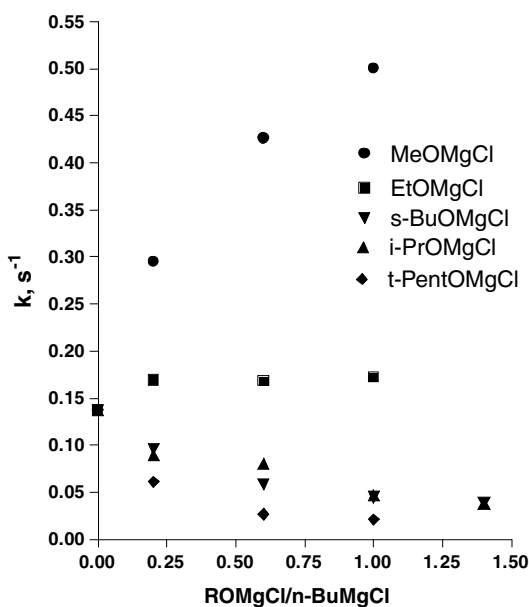

Fig. 2. Rate constants for the reaction of diisopropyl ketone with 0.5 M *n*-BuMgCl in diethyl ether at 20 °C vs. the relative content of alkoxymagnesium chloride in the reagent.

Table 2
Products ratios for the reaction of diisopropyl ketone[a] with Grignard reagents, and relevant rate constants

Reagent	Red/add	k (s^{-1})	k_{Add}	k_{Red}
0.5 M BuMgCl/0.5 M MeOMgCl	0.18	0.50	0.424	0.076
0.5 M BuMgCl	0.30	0.137	0.105	0.032
0.5 M BuMgCl/0.5 M *t*-PentOMgCl	0.73	0.021	0.012	0.009

[a] In product determinations 0.1 equiv. of the ketone relative to the Grignard reagent was used.

At the same time all the alkoxides under consideration, highly branched ones included, appear to complex almost completely with the Grignard reagent thus being better donors than the Cl-atom in the bridge position (cf structures I and II) and consequently should always accelerate the reaction in comparison with the uncomplexed Grignard reagent instead of suppressing the reaction rate. However, in Table 2 the ordinary butylmagnesium chloride takes an intermediate position between the alkoxy complexes as to the reaction rate or to the reduction/addition ratio. It follows inevitably that the course of the reaction cannot be determined exclusively by donating properties of the alkoxide ligands. On the contrary, their steric effects must be largely superimposed upon the reactivity.

Obviously, branched alkyl groups of alkoxy ligands hinder considerably the transition states from gaining favorable conformations, the addition reaction with ketones being more susceptible to the steric effects.

From our experimental data we can conclude that the rate enhancements by methoxy- and ethoxygroups are mainly due to the donating effects while in case of the branched alkyl groups the steric effects are overwhelming and suppress the rates of all Grignard reactions, the coupling reactions of silanes included.

In conclusion, we have revisited an old question of the impact of reaction products on the Grignard reaction. Although addressed in numerous works [1–9], the way how the product magnesiumalkoxydes interfere in the reaction was not entirely clear, not to mention the controversial influence of the products on the reaction rates and addition to reduction ratios.

Application of kinetic measurements to reactions of Grignard-alkoxide complexes taken in a great excess with silanes and with a ketone provided an insight into the problem valid for all Grignard reactions.

We were able to show that alkoxide-type products of Grignard reactions complex tightly with Grignard reagents and enhance in this way the nucleophilicity and the reactivity of the reagent. However, alkoxides branched at α-C atom exert additionally an unfavourable steric hindrance to reactions resulting eventually in a decrease in the reaction rate. As the Grignard addition reaction with ketones is more susceptible to steric effects than the reduction, in case of carbonyl compounds the ratio Red/Add increases with an increase in steric requirements of alkoxides.

Acknowledgements

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