REACTIONS OF PARTIALLY SOLVATED GRIGNARD REAGENTS WITH BENZALDEHYDE

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ABSTRACT

Ratios of the yields of addition and reduction products for the reactions of n-butylmagnesium chloride with benzaldehyde in toluene were determined at different THF, diethyl ether and *tert*-butyl methyl ether (MTBE) contents in the Grignard reagent. The results are discussed in terms of the solvation of the species in the reaction mixture.

INTRODUCTION

The most important reactions of Grignard reagents are those with carbonyl compounds. Formation of a tertiary or secondary alcohol is frequently accompanied by the reduction and enolization reactions lowering the yield of the target compound. It has been reported that reactions of ketones with alkylmagnesium bromides solvated with one equivalent of diethyl ether or THF in benzene or toluene solutions afford higher yields of addition products in comparison with those obtained in ethers [1].

Whereas the Grignard reagents in donor solvents are solvated at least by two solvent molecules per atom of magnesium, those obtained in the presence of smaller molar amounts of donors are stoichiometrically only "partially" solvated. Toluene proved to be a particularly suitable solvent for partially solvated Grignard reagents [2-4].

Recently we determined the ratios of the yields of reduction and addition products for the reaction of n-butylmagnesium bromide and chloride with diisopropyl ketone in various toluene-ether mixtures [5,6]. The obtained dependences appeared to be complicated including extreme points, the ratio Add/Red for conventional Grignard reagents being lower than that for partially solvated reagents. The results were discussed in terms of the solvation of the reagents [6]. It became evident that partially solvated Grignard reagents can serve as tools for the investigation of the solvent effects in Grignard reactions. In this work the investigation was extended to aldehydes.

EXPERIMENTAL

Commercial reagents were carefully purified. The reagents and solutions were operated under dry argon, and transferred by the use of syringes. n-Butylmagnesium chloride was prepared in toluene by using iodine–activated magnesium turnings and n-butyl chloride in the presence of a small amount (about 0.01 mol of ether per mole of magnesium) of diethyl ether, THF or MTBE. The obtained heterogeneous systems usually contained about 1.5 moles of the Grignard reagent per litre of toluene.

The basic magnesium content in the reagent was determined by quenching an aliquot with standardized sulphuric acid. The excess acid was back-titrated against aqueous sodium hydroxide. From the vigorously stirred reaction mixture 5 ml aliquots of the suspension were withdrawn and transferred to vials sealed with septums. Calculated amounts of the appropiate ether were added and the reagents were left for few hours or overnight. Then benzaldehyde in the molar ratio 1:2 (aldehyde to Grignard) dissolved in toluene was slowly added at -15 °C to the reagents prepared as described above, and the mixtures were left overnight at room temperature. The solutions also contained n-decane, i.e. the internal standard for GLC analyses.

Reaction mixtures were slowly quenched at -15 °C by the dropwise addition of 10 ml of the 20 % aqueous solution of NH_4Cl. The organic layer was separated and analyzed on a Varian 3700 gas chromatograph with a capillary column SGE BP 10 (0.3 mm x 24 m) and a flame ionization detector. The reaction products were identified according their ^{1}H-NMR spectra (acquired on a Brucker AC 200 P spectrometer in $CDCl_3$ using TMS as internal standard).

RESULTS AND DISCUSSION

The yields of products from the reaction of n-butylmagnesium chloride in toluene with benzaldehyde in the presence of diethyl ether, THF or *tert*-butyl methyl ether (MTBE) were determined.
Grignard reagents with different molar ratios of ethers were prepared as described in the experimental section and further allowed to react with benzaldehyde in a molar ratio 1:2 (aldehyde to Grignard). The reaction products were quantitatively determined by means of GLC. The enolization process recovering the aldehyde

was excluded for benzaldehyde. A precautious quenching of the reaction mixture enabled to avoid the dehydration of the addition product. The use of internal standard in GLC analysis made feasible the calculation of the material balance of the reaction. The sum of yields of addition and reduction was always 96-99%.

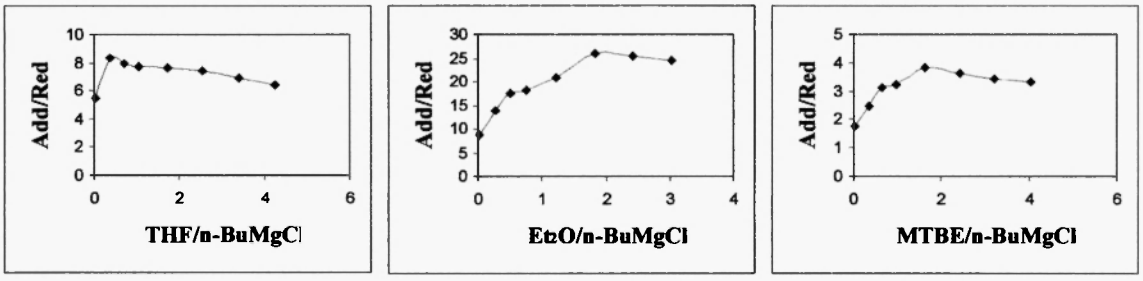


Figure 1. The ratios of yields of addition and reduction products Add/Red vs. the molar ratio of ether to Grignard reagent in toluene.

Results of the experiments are presented in Fig. 1. The addition product of benzaldehyde is 1-phenylpentane-1-ol and the corresponding reduction product is benzyl alcohol. All the experiments including the synthesis of n-butylmagnesium chloride were repeated at least two times. In Fig. 1 the points indicate the mean values obtained from several experiments. The results of parallel experiments agreed within ±5%.

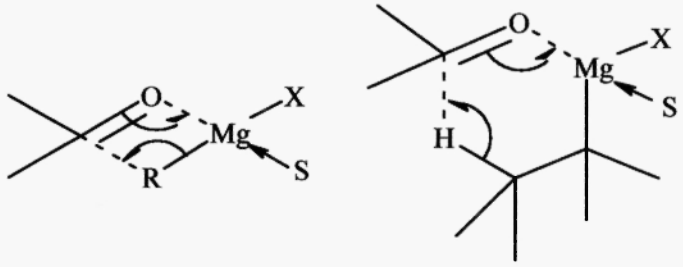
Grignard reagent solutions usually contain an equilibrium mixture of variety of species. Apart from the association equilibria the Schlenk equilibrium is essential (Eq. 1).

$$2\ RMgX \rightleftharpoons R_2Mg + MgX_2 \qquad (1)$$

Both organomagnesium species are highly reactive toward carbonyl compounds but diorganylmagnesiums react faster [7]. The primary reaction products, alkoholates R'OMgX and RMgOR', are able to complex with other species in the solution. Alkylmagnesium alkoxides are capable of alkyl addition to the carbonyl compound, but more by-products of enolization and reduction have been reported [8]. Alkylmagnesium alkoxides do not disproportionate with a recovery of dialkylmagnesiums in hydrocarbon solutions; however, magnesium bromide catalyzes the exchange reaction [9, 10].

General features of the Grignard reaction with ketones and aldehydes are well understood now [11-13]. The coordination of carbonyl compound with magnesium is essential, and occurs by replacement of a donor molecule at the magnesium atom. Thus, one solvent molecule initially coordinated with magnesium is present in the coordination complex influencing its reactivity.

The heterolytic Grignard addition proceeds through a four-centre transition state (I), while a cyclic six-centre transition state (II) is necessary for the reduction reaction [12].

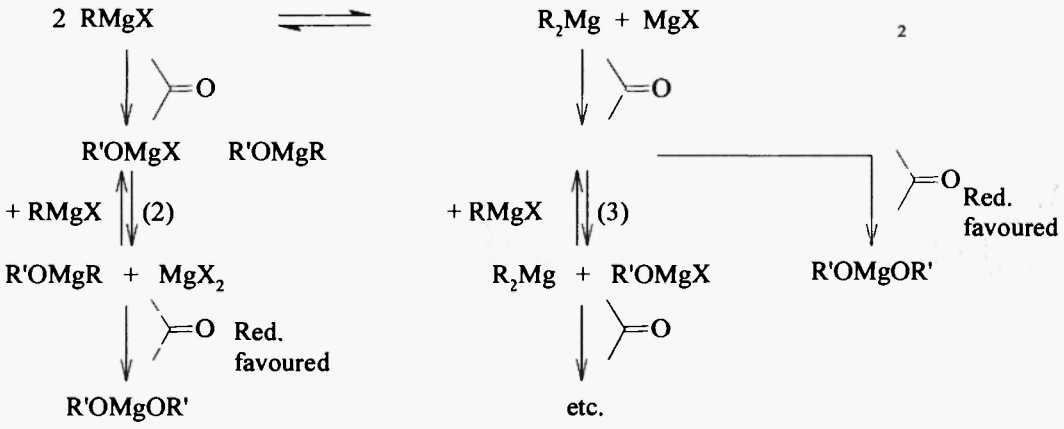


I II

It is obvious that the nucleophilic solvation of the magnesium atom polarizes the carbon-magnesium bond increasing the nucleophilicity of the carbon and thus favouring the addition and enolization reactions. Reduction involves a β-hydrogen transfer, less influenced by the donor at the magnesium centre. Consequently, an increase in the solvating ability of the donor should bring about an increase in the addition reaction yield as well as in the extent of enolization. This conclusion is well supported by the experimental

data (Ref. 14 and references therein). An increase in the addition or enolization to the reduction ratio with an increasing effective basicity of the donors is evident.

It is also obvious that an increase in the steric hindrance causes a decrease in solvating ability of the donor regardless of its Brønsted basicity. Likewise, the increasing bulkiness of the groups bound to the magnesium centre hinders complexing between the donor and the substrate. One can conclude that very bulky alkoxy groups in magnesium alcoholates resulting from Grignard addition reactions considerably hinder complexation with donors, thus supressing the nucleophilicity of the organyl moiety. The consequence of this is the remarkable bias of R'OMgR species towards the reduction mentioned above. For this reason the contribution of the reduction reaction increases during the process, particularly under preparative conditions, when a little or no excess of the Grignard reagent is used [15, 16] (cf. Scheme 1).



Scheme 1

Effectiveness of the solvation of the species is also important for the exchange reactions occuring in the reaction mixture. The primary products from the Grignard species RMgX and R_2Mg, R'OMgX and R'OMgR respectively, enter the dismutation equilibria (2) and (3) in Scheme 1. It is obvious that stronger solvation shifts eq. (2) towards the formation of MgX_2 species similarly with the Schlenk equilibrium [12, 13] and eq. (3) towards RMgX formation. Thus, an increase in the solvating ability of the solvent increasingly produces R'OMgR species prone to reduce the carbonyl compound. It appears that a stronger solvation of the Grignard reagent in parallel to an enhancement of the addition reaction can also favor the reduction reaction.

On the basis of the reasonings above we can interpret the course of the Add/Red ratio with increasing content of the donor in the Grignard reagent (Fig.1). The ratio Add/Red is lower at small additions of the ethers. In this region only a minor proportion of the species are solvated thus favouring the reduction of aldehyde. An increase in nucleophilic solvation of the reagent raises the yield of the addition reaction at the expence of reduction as discussed above. However, increasing solvation involves shifts in all the equilibria, thus favouring again the reduction of the aldehyde. As a result, the ratio Add/Red passes a maximum, expectedly located at greater additions of weaker donors. A further increase in the molar ratio of base to the Grignard reagent leads to the diminishing of the Add/Red ratio to the value for the conventional reagent.

The addition reaction prevails over reduction largely because of lesser steric requirements of the aldehyde and respectively of the groups R'O in reactions products in comparison with ketones (cf. Ref 6).

Variation of the donor reveals the effect of solvation. The ethers employed in this work are of very close Brønsted basicity, however, their effective basicities differ, decreasing in the order THF >> Et_2O > MTBE as it was shown also in our previous paper [4].

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