

Solvation effects in partially solvated Grignard reagents

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Received 7 July 1998; received in revised form 18 September 1998

Abstract

Grignard reagents were prepared from alkyl chlorides (*n*-BuCl, *i*-PrCl, *s*-BuCl and *t*-BuCl) in toluene in the presence of one or less equivalents of various organic bases (ethers, triethylamine). Ultrasound was used to promote the process. Diethyl ether proved to be the most effective donor affording Grignard reagents with a very small content of the base. Some of the reagents are disproportionate to magnesium chloride and the dialkylmagnesium. Stronger solvation of the species is favourable for the dismutation process. Increasing bulkiness of the alkyl group in the Grignard reagent hinders the complexing with the donor and shifts the equilibrium to the formation of unsymmetrical species. The extent and the rate of the reaction are also governed by the solvating power of donors. The importance of specific solvation in the Grignard chemistry and the decisive role of the steric requirements of the reagents over their intrinsic acid–base properties were demonstrated. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Grignard reagents; Grignard reaction; Solvation effects; Ultrasound

1. Introduction

The phenomenon of solvation effects has been one of the challenging problems of organometallic chemistry for a long time [1]. Nevertheless, the nature of the influence of solvent upon the chemical and physical properties of organometallic compounds is not yet fully understood.

A large number of attempts have been made to express the influence of the solvent on the reaction rate or physical properties of organic compounds by means of various correlation equations [1]. In all cases it was assumed that specific and non-specific solvation effects are additive.

Our former investigations of the reactions of organomagnesium compounds with ketones in binary mixtures of donor-unsolvating solvent have revealed that specific and non-specific solvation effects are not additive, and a quantitative separation of them is difficult [2–5].

In one of these works [5], non-linear (non-additive) correlation equations were deduced and successfully applied to rates of the reactions with ketones, solvation equilibria constants, and some physical parameters of organomagnesium compounds. It was shown that the effective basicity (solvating power) of a base in respect to a Lewis acid (to an organomagnesium compound) is greatly determined by the steric requirements of the base and by the effective acidity of the acid, the latter also being strongly dependent on the steric demands of the acid.

For theoretical reasons as well as for several practical purposes, Grignard reagents in hydrocarbon media are of particular interest. Whereas the ordinary Grignard reagents in donor solvents are solvated at least by two donor molecules per atom of magnesium, those obtained in the presence of small amounts of organic bases (one mole per mole of halide or less) are only *partially solvated*. If hydrocarbons of high boiling point are used, the solutions are cheap and present relatively low fire hazards. In addition to this, the partially solvated Grignard reagents exhibit several properties dif-

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ferent from those of both conventional Grignard reagents and unsolvated organomagnesium compounds.

On the other hand, non-specific solvation effects are kept constant for partially solvated Grignard reagents in an indifferent solvent, and thus neat specific effects of donors can be observed separately.

In our previous work [6], toluene solutions of alkylmagnesium chlorides partially solvated by diethyl ether were investigated. It was found that primary and secondary alkyl chlorides can be converted into Grignard reagents in high yields. Tertiary chlorides form only monosolvated on the average organomagnesium compounds. The reagents obtained are heterogeneous, but the solubilities of the partially solvated complexes in toluene are fairly high. Some of the reagents are disproportionate to magnesium chloride and the dialkylmagnesium, the latter being in excess in the supernatant solution. The extent of disproportionation decreases with an increase in the concentration of the reagent or in the steric requirements of the alkyl moiety.

In this work the investigations were extended to a variety of Grignard reagents partially solvated by different organic bases (ethers, triethylamine). Syntheses of several organomagnesium compounds in the presence of small amounts of complexing agents have been reported (see Ref. [6] and references therein), however, we are not aware of comprehensive investigations of solvation effects in such Grignard reagents. Alkylchlorides with different steric requirements of the alkyl group were used in this work. The main purpose of the work was an examination of specific solvation effects of the donors, however, a search for an alternative donor to the highly volatile diethyl ether was also one of our concerns.

2. Experimental

The experiment was mainly carried out as described in the previous paper [6]. The reagents and solutions were operated on under dry argon, and transferred by use of cannulas or syringes. In all preparations ultrasonic promotion was used.

2.1. Preparation of Grignard reagents

A 100 ml stainless steel reactor with a cooling jacket was used. Through the cap of the reactor the horn of the ultrasonication equipment was immersed in the reaction vessel. Ultrasound was generated by use of a probe disrupter UZDN-2T operating at 22 kHz.

The reaction vessel was charged with 3–4 g of magnesium turnings (Fluka, 99.8% Mg), 30 ml of toluene and the appropriate amounts of donor solvents. The magnesium metal was activated prior to use by dry

heating with about 50 mg of iodine. The reaction was initiated with a little of the alkyl halide and by starting ultrasonic irradiation. The rest of the halide was then added dropwise. Ultrasound provided a vigorous agitation of the reaction mixture. The temperature of the reaction mixture was maintained at about 25°C. The extent of the reaction was monitored by the GLC determination of the halide concentration in the reaction mixture. The reaction time was 0.5–6 h depending on the reagents and on the molar ratio of chloride to organic base.

2.2. Analyses of Grignard reagents

Samples for the analysis of dispersions were withdrawn from the vigorously stirred reaction mixture. For the analysis of supernatant solutions the samples were centrifuged. Determinations of active magnesium, basic magnesium and the chloride ion content are described in detail in the previous paper [6]. Yield of the Grignard reagent relative to the initial amount of RCl was estimated on the basis of the amount of unchanged alkyl halide and the extent of side reactions (from the Mg–Cl/R–Mg ratio).

3. Results

The preparation of partially solvated Grignard reagents (one equivalent or less of organic base) was carried out for different donor agents and for various initial amounts of alkyl chlorides. The results of the experiment are given in Table 1. The volume ratios of base to toluene in Table 1 correspond approximately to 1.0–1.5 M concentrations of Grignard reagents monosolvated on the average. Lower concentrations were not used because these are less important for the preparative scale work, and the rate of the reaction decreases considerably with a decrease in the base content.

The systems obtained were heterogeneous, and the amount of the solid phase increased with an increase in the molar ratio of halide to base. However, the solubilities of the partially solvated complexes in toluene are fairly high (seventh column in Table 1).

The compositions of obtained dispersions and centrifuged solutions were determined (see Table 1). The extent of the side reactions can be estimated from the ratio Mg–X/R–Mg for the total reaction mixture (fifth column in Table 1). This ratio indicates the total extent of the various side reactions (mainly the Wurtz reaction), which all lead to a loss of the Grignard reagent and the formation of magnesium halide.

In Table 1 the results are the mean values obtained from several experiments. The results for duplicate experiments agreed within 10% or less. For systems *n*-BuMgCl–Et₂O and *i*-PrMgCl–Et₂O some represen-

Table 1
Partially solvated Grignard reagents prepared from alkyl chlorides in toluene

Reagent	Base	V _{base} /V _{toluene} ^a	[RCl] _O /[base] _O	[MgCl]/[RMg] total ^b	Yield of Grignard reagent (%)	[RMg] in solution (mol l ⁻¹)	[RMg]/[MgCl] in solution
<i>n</i> -BuCl	Et ₂ O ^c	0.17	1	1.03	95	1.05	1.5
		0.17	6	1.06	80	1.12	3.9
		0.33	2	–	–	2.02	2.0
	Bu ₂ O	0.23	1	1.12	90	1.0	–
		0.23	2	1.23	81	1.12	2.0
	THF	0.13	1	1.06	90	1.2	1.65
		0.13	2	1.25	80	1.6	3.0
	MTBE ^d	0.167	1	1.3	–	1.13	1.3
		0.167	2	1.3	75	1.1	1.8
	Et ₃ N	0.177	1	1.08	92	1.01	1.0
0.177		2	1.2	70	1.04	1.0	
<i>i</i> -PrCl	Et ₂ O ^c	0.13	4	1.05	–	0.82	1.1
		0.25	2	1.0	88	1.93	1.0
		0.25	4	1.05	75	1.84	1.0
	THF	0.12	1	1.1	92	1.05	1.4
		0.12	2	1.2	53	1.0	1.5
	MTBE ^d	0.167	1	1.1	83	1.2	1.4
		0.167	2	1.25	40	0.9	1.5
	Et ₃ N	0.137	1	1.0	90	0.85	1.0
		0.137	2	1.0	65	0.8	1.06
	<i>s</i> -BuCl	Et ₂ O	0.17	1	1.04	95	1.1
0.17			2	1.06	93	1.15	1.3
THF		0.13	1	1.15	93	1.15	1.1
		0.13	2	1.25	50	1.25	1.4
MTBE ^d		0.167	1	1.05	95	1.1	1.5
		0.167	2	1.2	45	1.2	1.6
Et ₃ N		0.167	1	1.1	90	0.85	1.0
	0.167	2	1.07	63	0.6	0.9	
<i>t</i> -BuCl	Et ₂ O	0.17	1	1.7	40	0.7	1.0
		0.17	2	2.5	30	0.52	1.0
	THF	0.12	1	2.1	43	0.3	1.0
		0.12	2	3.7	27	0.2	1.0
	MTBE ^d	No reaction					
	Et ₃ N	No reaction					

^a The volume ratio of base to solvent.

^b From the analysis of the dispersion. The ratio indicates the extent of side reactions.

^c From our previous work [6].

^d Methyl *t*-Bu ether.

tative data were taken from our previous paper [6]. Preparations of *t*-BuMgCl–Et₂O complexes were repeated under more strictly controlled temperature conditions in this work, yet, the results do not differ considerably. All the preparations whose results are presented in Table 1 were carried out with the aid of ultrasonic irradiation (see Section 2). Mechanical stirring in the absence of ultrasound led to at least 2-fold longer reaction times and in some cases to a lower extent of the reaction, however, the contribution of the Wurtz reaction was usually the same.

4. Discussion

As is seen in Table 1, Grignard reagents in toluene can be prepared from alkyl chlorides in the presence of various organic bases at least in monosolvated on the

average or in less solvated forms. The investigated halides and donors were chosen with a view to covering the largest possible range of steric hindrance in both reagents.

The obtained reagents were heterogeneous. The concentration of the active Grignard reagent [RMg] in the supernatant solution is sensitively dependent on the amount of the organic base in the system (see e.g. entries *n*-BuCl–Et₂O and *i*-PrCl–Et₂O in Table 1). Therefore, the solubility of a partially solvated Grignard reagent in toluene cannot be unequivocally defined. Some of the reagents undergo extensive disproportionation similarly to the Schlenk equilibrium



In these cases the formation of a precipitate rich in magnesium chloride occurs and the complexes in the

solution contain more dialkylmagnesium than those in the precipitate (see column '[RMg]/[MgX] in solution' in Table 1). The structure of the complexes is not known; even so, they are probably highly associated.

Formerly we found [6,7] that the disproportionation of Grignard reagents partially solvated with diethyl ether is strongly influenced by the steric requirements of the alkyl moiety of the reagent.

It is obvious that increasing steric hindrance causes a decrease in the solvating ability of the donor regardless of its intrinsic basicity. Likewise, increasing bulkiness of the alkyl group in the substrate hinders complexing between the donor and the magnesium center.

It has been suggested that the Schlenk equilibrium in different solvents is determined by the difference in the solvation of species involved in the equilibrium [8,9]. Also, a theoretical relationship between the Schlenk equilibrium constant and solvation effects has been reported [10]. It has been shown that an increase in the bulk of the organic group makes solvation of R_2Mg increasingly less effective than that of $RMgX$, since beginning from $R = Et$ the steric hindrance of symmetrical organomagnesium compounds exceeds that of unsymmetrical ones. In less coordinating solvents the equilibrium should be shifted towards unsymmetrical species. These conclusions are in good accordance with experimental data [9].

In toluene solutions of partially solvated Grignard reagents, equilibria between the solution and the precipitate, association equilibria, donor distribution equilibria etc. may supervene upon the Schlenk equilibrium. Therefore, the Schlenk equilibrium in the highly complex system can be masked to some extent. However, the ratio $[RMg-]/[-MgX]$ for supernatant solutions of 'monosolvated' Grignard reagents satisfactorily manifests the trends observed for ethereal solutions and provides additional information for systems never investigated before. For clarity, relevant data from Table 1 are re-presented in Table 2. It appears that under these conditions the dismutation process is very similar to the Schlenk equilibrium. Stronger solvation shifts the equilibrium to the right, i.e. towards disproportionation.

The reactivity of organic halides in the Grignard reagent formation is also governed by the solvating power of donors. Although no kinetic measurements

Table 2
Disproportionation of Grignard reagents prepared from equimolar amounts of organic halides and bases

Base	[RMg-]/[-MgCl] in the supernatant solution			
	<i>n</i> -Bu	<i>i</i> -Pr	<i>s</i> -Bu	<i>t</i> -Bu
THF	1.65	1.4	1.1	1.0
Et ₂ O	1.5	1.0	1.2	1.0
MTBE	1.3	1.4	1.5	No reaction
Et ₃ N	1.0	1.0	1.0	No reaction

Table 3
Moles of halide per mol of base consumed in the Grignard reaction

Base	<i>n</i> -BuCl	<i>i</i> -PrCl	<i>s</i> -BuCl	<i>t</i> -BuCl
THF	1.9	1.3	1.3	(1.9) low yield
Et ₂ O	~6	4	>2	(~2) low yield
Bu ₂ O	2	–	–	No reaction
MTBE	~2	1	~1	No reaction
Et ₃ N	1.7	1.6	1.5	No reaction

were carried out in this work, the number of moles of halide consumed per mole of base (Table 3) appears to be well representative. Besides, the time of the reaction was usually longer when the final extent of the conversion was reduced.

As is seen from Table 3, an increase in the steric hindrance of the alkyl group diminishes the extent of the reaction. With very bulky *t*-BuCl, the reaction could only be initiated in the presence of diethyl ether and THF, yet the yields were low due to extensive Wurtz coupling.

In Table 3 the organic bases are placed in the order of increasing steric demands. As intrinsic basicities of ethers are very similar, their effective basicities are chiefly determined by the steric requirements. A very strong base triethylamine is usually a weak donor for magnesium compounds because of heavy steric encumbrance [5].

As can be seen from Table 3, stronger solvation of the reaction product generally enhances the extent of the reaction, THF being an exception. This suggests that a solvated organomagnesium complex rather than the free donor substance in a very low concentration is responsible for the promotion of the reaction after the monosolvated Grignard reagent has been formed. As in the presence of THF, the disproportionation equilibrium is shifted far to the right, the strong solvation of magnesium chloride accumulates the donor in the precipitate and deprives the supernatant solution of active species.

The data for triethylamine also seem to be somewhat exceptional, because it is hard to believe that triethylamine could be a better donor than MTBE for isopropyl- and *sec*-butylmagnesium chlorides. A possible explanation is that the very weak donor is not entirely complexed with the Grignard reagent and a fraction of the free base participates in the Grignard reaction as well as the solvated complexes. This is also consistent with relatively low solubilities of Et₃N–Grignards in toluene (Table 1). However, further kinetic investigations can only elucidate the observed phenomena.

Our former quantitative results derived from the kinetic data for organomagnesium reactions [5] could not be fully applied in this work. Nevertheless, we demonstrated qualitatively and once again the importance of specific solvation in the Grignard chemistry

and the decisive role of the steric requirements of the reagents over their intrinsic acid–base properties.

The practical implication of our results is that Grignard reagents can be obtained in toluene in the presence of small amounts of various organic bases. Diethyl ether proved to be the most effective donor affording Grignard reagents with a very little content of the base, however, when monosolvated reagents are suitable, it can be replaced by less expensive and less volatile MTBE. Our preliminary results indicate that MTBE-Grignards are even more favourable for Grignard addition reactions with carbonyl compounds. An investigation of the reactions of the partially solvated Grignard reagents is in progress.

Acknowledgements

The authors thank the Estonian Science Foundation for financial support of this work.

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