

Partially solvated alkylmagnesium chlorides in toluene

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Abstract

Toluene solutions of alkylmagnesium chlorides partially solvated by diethyl ether were investigated. Primary and secondary alkyl chlorides can be converted into Grignard reagents in good yields in the presence of small amounts of ether (less than one mole per mole of halide). Tertiary chlorides form only monosolvated organomagnesium compounds. Ultrasound accelerates the process. The reagents obtained are heterogeneous, but the solubilities of the partially solvated complexes in toluene are fairly high. Some of the reagents disproportionate to magnesium chloride and the dialkylmagnesium. The extent of disproportionation decreases with an increase in the concentration of the reagent or in the steric requirements of the alkyl moiety.

Keywords: Magnesium; Grignard reagents; Sonication

1. Introduction

Although conventional Grignard reagents are usually prepared in diethyl ether or other donor solvents, organomagnesium compounds have for many years also been obtained in hydrocarbon media in the absence of donors, or without use of any solvent [1–3].

Use of ethers in large-scale organomagnesium syntheses in industry is inconvenient and hazardous [4], therefore the replacement of such readily flammable solvents by safer hydrocarbons of high boiling point is desirable. The use of hydrocarbons is economical since they are cheap and non-hygroscopic and present relatively low fire hazards. However, formation of unsolvated organomagnesium halides is limited to primary alkyl and aryl compounds. Branched-chain primary, secondary and tertiary alkyl halides and vinyl, allyl and benzyl halides do not react under these conditions or give Wurtz-type coupling products [2,5]. Methyl-, ethyl-, and propylmagnesium halides are formed only in low yields. Furthermore, the unsolvated organomagnesium compounds are only sparingly soluble in hydrocarbons. In aromatic media, alkylation of the solvent may predominate during the synthesis, particularly in the case of alkyl chlorides [6,7].

Most of the shortcomings of unsolvated organomagnesiums can be overcome by addition of small amounts of solvating species, provided their presence in the reagent is acceptable. In addition, light metal alkoxides [6,8] or tetraethoxysilane in catalytic amounts [9] can be used to promote the formation of organomagnesium halides in non-donor media. Several organomagnesium compounds have been obtained in the presence of small amounts of complexing agents, e.g. ethers and tertiary amines [10–13]. The reagents obtained were soluble, at least in aromatic hydrocarbon solvents. It was thought that at least one molar equivalent of polar solvent had to be present [3], but ethylmagnesium chloride reagents in toluene containing 0.15–0.53 equivalents of diethyl ether have been used for the manufacture of organosilicon monomers [14–16].

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 catalytic amounts of donor substances are only partially solvated. As the solvating agent is firmly bound to the Grignard reagent, such solutions possess almost all the advantages of unsolvated organomagnesium halides in non-solvating media. However, the partially solvated Grignard reagents exhibit several properties different from those of both conventional Grignard reagents and unsolvated organomagnesium compounds.

The reactions of monosolvated alkylmagnesium bromides with ketones in benzene or toluene give higher

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yields of addition products in comparison with those in ethers [17]. The rate of the reaction of the Grignard reagent with ethylethoxysilanes [18] and hydrazones [19] is greatly increased when free ether is replaced by toluene. It has been reported that the molar ratio of diethyl ether to ethyl chloride determines the ratio of the monomers formed in a continuous organomagnesium synthesis of ethylchlorosilanes, thus enabling control of the process [14].

Partially solvated Grignard reagents have also been used in large-scale industrial processes [16], but little information on their chemical and physical properties or on the details of their production are available in the open literature.

We previously studied the kinetics of the formation of organomagnesium halides in the presence of small admixtures of organic bases (less than one mole per mole of halide), and succeeded in establishing the course of the reaction, the influence of the nature of the organic base and of the structure of the organic halide on the rate, and an unexpected catalytic action of the partially solvated Grignard reagent [20–22]. The most important feature is that the formation of the Grignard reagent in toluene in the presence of small amounts of an organic base proceeds in two stages [20]. After the organic base, added in a deficiency, is consumed in formation of the monosolvated Grignard reagent, a relatively slow process proceeds until the organic halide is completely converted into an organomagnesium compound. Under these conditions the reaction of the organic halide with magnesium is catalyzed by the monosolvated Grignard reagent [20]. Alkyl chlorides react more rapidly than bromides [22]. Variation in the nature of the organic base has only a slight influence on the catalytic effect [21], but a more pronounced effect on the yields of the Grignard reagent. In the case of primary alkyl bromides and diethyl ether as catalyst, the Grignard reagents are formed in moderate yields. When diethyl ether is replaced by another base (THF, triethylamine, dibutyl ether), mainly Wurtz reaction products are formed during the slow stage of the reaction and the overall yield of the Grignard reagent is low. This is also the case when secondary or tertiary bromides are used regardless of the catalyst [21]. In contrast, some alkylmagnesium chlorides were obtained in good yields with diethyl ether present in the catalytic complex [22].

The practical implication of our kinetic investigations is that in the procedure involving small additions of bases to toluene, use of diethyl ether and alkyl chlorides gives the highest rate and the best yield of the Grignard reagent. Use of these reagents is also attractive from the economic point of view.

In the present paper we report the results of our investigation of the formation and properties of the Grignard reagents formed in the reaction of alkyl chlorides (the alkyl group being *n*-butyl, isobutyl, isopropyl,

or *tert*-butyl) with magnesium in toluene in the presence of small amounts of diethyl ether (one mole or less per mole of halide).

2. Experimental

Commercial reagents were carefully purified. The reagents and solutions were operated on under dry argon, and transferred by use of cannulas or syringes.

2.1. Preparation of Grignard reagents

The reagents were prepared under dry argon in a 100 ml three-necked flask equipped with a mechanical stirrer. The vessel was charged with magnesium turnings (1.4–8.4 g, 1.5-fold molar excess to alkyl chloride), and the appropriate amounts of diethyl ether (usually 4.0 ml, 38.5 mmol) and toluene (20–30 ml). The magnesium metal was activated prior to use by dry heating with 50–100 mg of iodine. The reaction was initiated with a little of the alkyl halide and the rest was then added dropwise. The reaction mixture was cooled slightly during the formation of the monosolvated Grignard reagent (to prevent loss of diethyl ether), and the temperature was subsequently maintained slightly below the boiling point of the halide. The extent of the reaction was monitored by GLC. The reaction was complete in 2–5 h, depending on the molar ratio of chloride to ether.

In some preparations ultrasonic activation (sonication) was used, ultrasound being known to accelerate the formation of Grignard reagent [23]. In such cases the mechanical stirrer was replaced by a titanium horn immersed in the reaction mixture. The ultrasound was generated by use of a probe disrupter UZDN-2T operating at 22 kHz; its calorimetrically-estimated power output was about 20 W in toluene solutions. During sonication, the reaction flask was cooled in iced water to maintain the temperature of the reaction mixture below 40°C. Ultrasonic irradiation made the induction period practically negligible, and shortened the reaction time by a factor of two or more.

2.2. Analyses of Grignard reagents

For analyses approximately 2 ml samples were withdrawn from the reaction mixture and centrifuged; the basic magnesium content of the supernatant solution was analyzed acidimetrically, and the chloride ion content by the Mohr method.

Because of the high viscosity of solutions, the volumes of the samples were measured in calibrated tubes (about 1 cm³). The tube was filled with Grignard solution up to the mark and then immersed in the appropriate amount of standard sulphuric acid. After the con-

tents of the tube had completely reacted and dissolved, the excess acid was back-titrated against aqueous sodium hydroxide. The chloride ion concentration was determined in the same solution after the acidimetric analysis.

The "active" magnesium was determined by dissolving a similarly measured sample of the Grignard reagent in dry toluene and titrating against a 1 M solution of *n*-butanol in toluene with 1,10-phenanthroline as the indicator [24].

The difference between the concentrations of basic and "active" magnesium was usually 4–6%, and never exceeded 10%. A careful examination of all the operations revealed that some decomposition of the samples by moisture from the air occurred mainly during withdrawal and measurement of the samples. Therefore, we consider our analyses for basic magnesium as a sufficiently reliable measure of the active concentration of the Grignard reagents.

Samples for the analyses of dispersions or precipitates were withdrawn from the vigorously stirred reaction mixture. The dispersion was analyzed as described above without centrifugation. The precipitate obtained from centrifugation was washed with dry toluene and the molar ratio of Grignard reagent moieties was determined by the methods described above.

All the analyses were repeated at least two to three times.

2.3. GLC analyses

The sample was decomposed with a small volume of dilute sulphuric acid and the organic layer was separated and dried over anhydrous sodium sulphate. For quantitative determinations *n*-heptane was used as internal standard.

Gas chromatograms were recorded on a Tsvett-100 gas chromatograph with a flame ionization detector. The column (2.5 m × 3 mm) was packed with 10% Carbowax 20 M on Inerton Super or with PermaBond Cyano DEGS.

The following compounds were detected in the samples: C₄ alkenes (R₍₋₁₁₎, radical disproportionation products from the Wurtz reaction), C₃ and C₄ alkanes (RH, from the decomposition of Grignard reagents and to a minor extent from radical disproportionation, attack on the solvent, etc.), Wurtz-coupling products (R–R), diethyl ether, alkylchlorides (RCl), corresponding alkyl alcohols (ROH, oxidation products of Grignard reagents), and traces of the products of Friedel–Crafts alkylation (a group of close peaks, among which that of 4-*tert*-butyltoluene was identified).

Quantitative determinations were carried out for recovered chlorides, diethyl ether (in some experiments), and alkyl alcohols.

The content of any alcohol was usually less than 0.5% and never exceeded 1% based on the amount of alkyl chloride allowed to react. We consider this to reflect the adequacy of our measures to prevent air oxygen and moisture.

In cases where the content of diethyl ether was to be determined, special steps were taken to prevent loss of this highly volatile compound, i.e. effective cooling and stepwise decomposition of samples.

2.4. Complete analyses of precipitates

Samples of precipitates obtained from centrifugation were washed with dry toluene and then cautiously decomposed (see above) with aliquots of standard sulphuric acid solution. The organic layer was separated and aqueous solution was extracted with toluene. The combined toluene solutions were transferred to a volumetric flask, a calculated amount of *n*-heptane (GLC standard) was added, and the flask filled to the mark with toluene.

The aqueous solution was titrated against the standard base solution and then analyzed for the concentration of chloride ion. The toluene solution was analyzed for diethyl ether content by GLC. The molar ratio R₂Mg : MgCl₂ : Et₂O was calculated.

2.5. Yield of the Grignard reagent

This was estimated on the basis of the amount of unchanged alkyl halide and the extent of side reactions (from the R–Mg/Mg–Cl ratio). In control experiments unreacted magnesium metal was separated, carefully washed with diethyl ether, dried under reduced pressure and weighed. The results agreed satisfactorily (within 10% or better).

3. Results and discussion

The preparation of partially solvated Grignard reagents (one equivalent or less of diethyl ether) was carried out for various amounts of diethyl ether in the reaction mixture. The volume ratios Et₂O:toluene from 0.16 up to 0.50 in Table 1 correspond approximately to concentrations 1.0–2.40 M of the monosolvated Grignard reagent, which acts as a catalyst for further Grignard reagent formation [20]. 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 ether content [20,22]. Further addition of organic halide leads to formation of less-solvated Grignard reagents. The systems obtained were heterogeneous, and the amount of the solid phase increased with an increase in the molar ratio of the

halide to ether. About 20% of the active Grignard reagent formed was usually present in the solution.

The experiments were limited to use of a five- or six-fold molar excess of halide over ether when the agitation of the reaction mixture was hindered by the end of the synthesis. In these cases the rate of the reaction fell dramatically and 10–15% of the added alkyl chloride remained unchanged. Klökov et al. [14] have also reported the formation of only a 72% yield of ethylmagnesium chloride at molar ratio RX/Et_2O equal to 6.7.

The compositions of obtained dispersions and centrifuged solutions were determined, and in some cases also those of the precipitates (see Table 1). The extent of the side reactions can be estimated from the ratio $R-Mg/Mg-X$ for the total reaction mixture (fourth column in Table 1). This ratio indicates the total extent of the various side reactions, i.e. the Wurtz reaction, attack on the solvent by radicals, solvent alkylation (Friedel–Crafts reaction), oxidation of the Grignard reagent, etc., which all lead to a loss of the Grignard reagent and the formation of magnesium halide. The contribution of the Wurtz reaction cannot be correctly estimated from the radical-coupling product determinations, because radical disproportionation products are also formed [1]. The relative extent of side reactions appeared to be similar to that for ordinary Grignard

preparations in ether solutions, except in the case of tert-butylmagnesium chloride. It is noteworthy that solvent alkylation products appeared only in trace amounts. Extensive solvent alkylation has previously been reported for alkyl chlorides [6,7], and it is evident that the alkylation process is suppressed even when only small amounts of diethyl ether are present.

The yields of partially solvated Grignard reagents are also rather good. Lower yields of isopropylmagnesium chloride in some experiments were due to the loss of the highly volatile isopropyl chloride, carried away by the argon stream during the synthesis.

In Table 1 the results are given of some representative experiments and, mainly, the mean values obtained from several experiments. In general, the results for duplicate experiments, including those with sonication, agreed within 10% or less.

n-Butyl chloride forms in toluene a Grignard reagent which disproportionates according to the Schlenk equilibrium



Precipitation of a considerable part of the reagent with a higher content of magnesium chloride also occurs. As can be seen from the data in Table 1, the lower the relative content of ether in the mixture (higher values of the ratio RX/Et_2O), the larger the excess of

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

Reagent	$\frac{V_{Et_2O}}{V_{toluene}}$	$\frac{[RX]_0}{[Et_2O]_0}$	$\frac{[MgX]}{[RMg]}$ total ^a	Yield of Grignard reagent (%)	$[RMg]$ in solution (mol l ⁻¹)	Stoichiometry of the solute ^b	Stoichiometry of the precipitate
ⁿ BuCl	0.13	5	1.05	90	0.92	5.1R ₂ Mg + MgX ₂	R ₂ Mg + 2.3MgX ₂
	0.16	4	1.04	95	1.32	3.1R ₂ Mg + MgX ₂ + 1.7Et ₂ O	R ₂ Mg + 1.5MgX ₂ + 0.39Et ₂ O
	0.17	1	1.03	95	1.05	1.5R ₂ Mg + MgX ₂	
	0.17	6	1.06	80	1.12	3.9R ₂ Mg + MgX ₂	
	0.25	4	1.03	96	1.35	3.7R ₂ Mg + MgX	
	0.25	5	1.06	85	1.24	4.0R ₂ Mg + MgX ₂	
	0.33	1			1.90	1.6R ₂ Mg + MgX ₂ + Et ₂ O	
	0.33	2			2.02	2.0R ₂ Mg + MgX ₂	
	0.33	3			2.12	2.1R ₂ Mg + MgX ₂	
	ⁱ BuCl	0.16	4	1.09	91	1.23	1.7R ₂ Mg + MgX ₂
ⁱ PrCl	0.13	4	1.05	91	0.82	1.1R ₂ Mg + MgX ₂	R ₂ Mg + 1.34MgX ₂
	0.25	2	1.00	88	1.93	RMgX + 0.45Et ₂ O	RMgX + 0.5Et ₂ O
	0.25	3	1.02	88	1.88	RMgX + 0.35Et ₂ O	RMgX + 0.34Et ₂ O
	0.25	4	1.05	75	1.84	RMgX + 0.34Et ₂ O	RMgX + 0.33Et ₂ O
	0.50	1		90	1.96	RMgX + Et ₂ O	
	0.50	2		90	1.94	RMgX + 0.47Et ₂ O	
	0.50	3		90	1.92	RMgX + 0.39Et ₂ O	
	0.50	4		68	1.88	RMgX + 0.37Et ₂ O	
^t BuCl	0.25	1	1.16	80			
		2	6.45		0.24	RMgX	
	0.25 ^c	1	2.06				
		2	2.22 ^d	25	0.93	RMgX	R ₂ Mg + 4.0MgX ₂

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

^b Diethyl ether indicated when its content was determined.

^c Ultrasonication.

^d By the end of the experiment 57% of the initial amount of chloride was consumed.

dibutylmagnesium over magnesium chloride in the solution. Consequently, a deficiency of diethyl ether shifts the disproportionation equilibrium to the right, and since dibutylmagnesium is more soluble, the complexes in the solution contain more dibutylmagnesium than those in the precipitate. The structure of the complexes is not known, but they are probably highly associated [2]. The complexes are very soluble in toluene (see column "[RMg] in solution" in Table 1).

Evidently, the equilibria in the highly complex system are determined by a number of factors, i.e. the concentrations of both the Grignard reagent and the ether, the molar ratio of the Grignard reagent to the ether, etc. In all cases, most of the reagent is present in the precipitate.

iso-Butyl chloride behaves like *n*-butyl chloride except that isobutylmagnesium chloride seems to undergo less disproportionation than *n*-butylmagnesium chloride.

iso-Propyl chloride, although a secondary halide, forms a Grignard reagent under these conditions practically without any side reaction. This is remarkable in view of the fact that secondary alkyl halides, particularly chlorides, have been reported to form almost exclusively Wurtz-type and other by-products in the absence of solvating additives [5,7,8]. It thus seems that the monosolvated Grignard reagent present in the mixture directs the process towards formation of a Grignard reagent. The reagent is very little disproportionated, only at lower concentrations. At higher concentrations, *iso*-propylmagnesium chloride has the stoichiometry RMgX , corresponding to ordinary Grignard reagents. The determination of the ether content in the solution indicates that the complex soluble in toluene has an empirical composition of approximately $3^1\text{PrMgCl} \cdot \text{Et}_2\text{O}$. The solubility in toluene of partially solvated isopropylmagnesium chloride reagents is surprisingly high in view of the slight solubility of unsolvated alkylmagnesium chlorides in hydrocarbons [13].

tert-Butyl chloride gives only the monosolvated Grignard reagent. Under the usual conditions, i.e. without the application of ultrasound, the reaction proceeds smoothly with only slight formation of side products (first entry for $^1\text{BuCl}$ in Table 1). The reagent formed does not disproportionate. Further addition of *tert*-butyl chloride to the reaction mixture does not lead to formation of more Grignard reagent, only magnesium chloride and Wurtz-reaction products being obtained. It can be inferred that monosolvated *tert*-butylmagnesium chloride, unlike the sterically less encumbered primary and secondary alkyl Grignards, is not capable of catalyzing the reaction.

It was previously observed that ultrasonication did not affect the mechanism of the Grignard reagent formation, but only accelerated the process through the microstreaming effect at the metal–solution interface [23]. In the present work, parallel preparations with and

without sonication give identical results within experimental error, except in the case of *tert*-butyl chloride for which sonication did not improve the yield of *tert*-butylmagnesium chloride. For the latter, the monosolvated reagent was obtained in less than 50% yield because of a considerable contribution of side reactions. Further additions of the organic chloride resulted in practically no further reaction. These facts are remarkable in the light of the results of experiments without sonication. It can be supposed that relatively stable *tert*-butyl radicals are transported by powerful microstreaming into the solution, where they give rise to various side reactions, e.g. coupling, solvent attack, etc., resulting in the formation of magnesium chloride. At the same time ultrasound prevents the deposition of the Grignard reagent on the metal surface, restricting its reaction with the intermediates. A detailed investigation of this unusual effect of sonication is in progress.

The general conclusions that can be drawn from this work are as follows. Primary and secondary alkyl chlorides can be converted into Grignard reagents in high yields in toluene in the presence of diethyl ether. Tertiary chlorides form only monosolvated organomagnesium compounds. Application of ultrasound greatly accelerates the reaction. The reagents obtained are heterogeneous, but the solubilities of the partially solvated complexes in toluene are fairly high. Some of the reagents undergo extensive disproportionation, to give magnesium chloride and dialkylmagnesium, the latter being in excess in the supernatant solution. The extent of disproportionation falls with increasing concentration of the reagent and in the steric requirements of the alkyl moiety, so that *isopropyl*- and *tert*-butylmagnesium chloride undergo practically no disproportionation in toluene solution.

The reagents obtained can be used for synthetic purposes in the form of dispersions. An investigation of the reactions of the partially solvated alkylmagnesium chlorides is in progress.

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