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THE FORMATION OF GRIGNARD COMPOUNDS—III[1]

THE INFLUENCE OF THE SOLVENT

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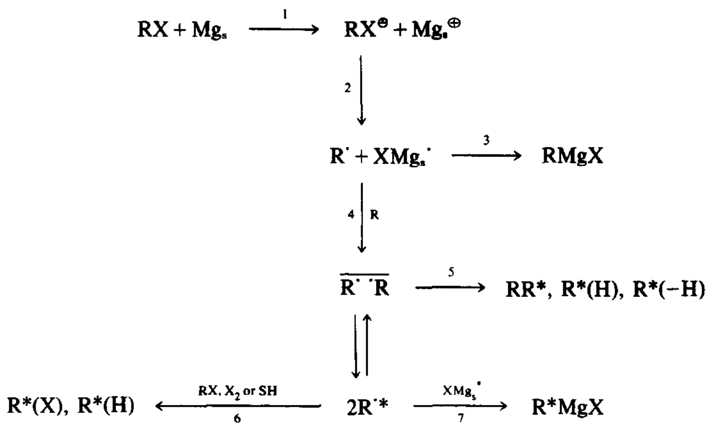
Abstract—The reaction of 6-bromo-1-hexene with Mg was studied in order to obtain information on the role of the solvent during the formation of Grignard reagents. The 5-hexenyl radical ($R_{nc}^{\cdot}$) is known to cyclize rapidly and irreversibly to the cyclopentylmethyl radical ($R_c^{\cdot}$). Changes in yields of the cyclized and non-cyclized Grignard compounds have been found on varying the solvent. Information on the radical pairs involved is obtained from the yields of the three possible coupling products ($R_{nc}R_{nc}$, $R_{nc}R_c$ and R_cR_c). Results are correlated to the intensity of the CIDNP spectra of the Grignard compounds. It is found that basicity and viscosity of the solvents influence the reactions at the site of single electron transfer. Formation of Grignard compounds via radical pairs increases: (a) with decreasing basicity of the solvent, (b) with decreasing viscosity of the solvent, and (c) on dilution of THF with benzene. It is proposed that interaction between the radical and the π-electron rich solvent benzene plays a role in reactions run in Bz/THF mixtures.

INTRODUCTION

The radical nature of the formation reaction of Grignard compounds has recently become evident in stereochemical studies by Walborsky[2] and—in a direct way—by our study[1] of the Chemically Induced Dynamic Nuclear Polarization phenomena (CIDNP).

It is well known that the solvent plays an important role in the formation reaction of Grignard compounds, but its exact role has not been investigated in detail. Such a detailed investigation was expected to lead to a better understanding of the processes occurring on the Mg surface, the influence of the solvent on these processes and on the solvation of the species present during and after the reaction.



Scheme 1†

In a previous publication[1] we stated that the reaction of $R^{\cdot}$ with $XMg_s^{\cdot}$ (Eqn (3), Scheme 1), formed at the site of single electron transfer (SET) from the metal to the alkyl halide (Eqn 1), is the major reaction leading to the Grignard compound.

From the intensities of the CIDNP spectra of the Grignard compounds it is impossible to draw quantitative conclusions with regard to the amount of RMgX formed via radical pairs (Eqn 7). However CIDNP spectra indicated[1] that solvent plays an important role in the reactions depicted in Scheme 1.

More information on these reactions by other means than CIDNP can be obtained by a system in which the radical $R^{\cdot}$ can rearrange to $R'^{\cdot}$ in such a way that the total amount of RMgX does not change due to differences in reactivity of the two radicals.

Such a system is provided by the 5-hexenyl radical ($R_{nc}^{\cdot}$)

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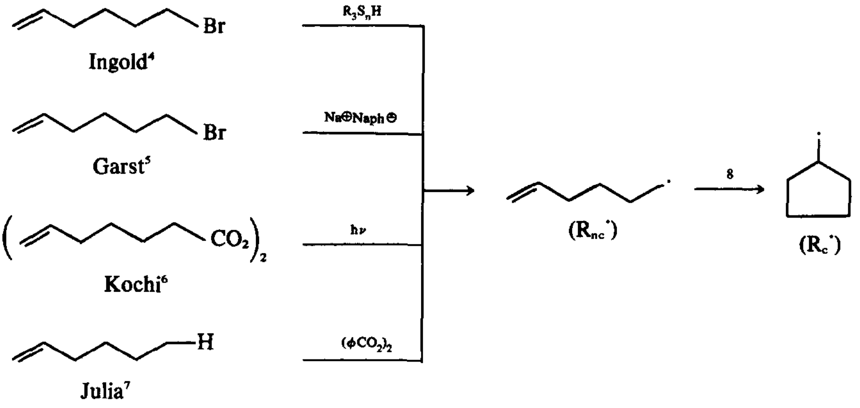
†R* denotes polarization in the product; the subscript "s" used for magnesium denotes surface bound species.

which is known to cyclize rapidly and irreversibly[3] to the cyclopentylmethyl radical ($R_c^{\bullet}$), with $k = 10^5$/sec.[4] This system has been well investigated by several groups (Scheme 2).



Scheme 2

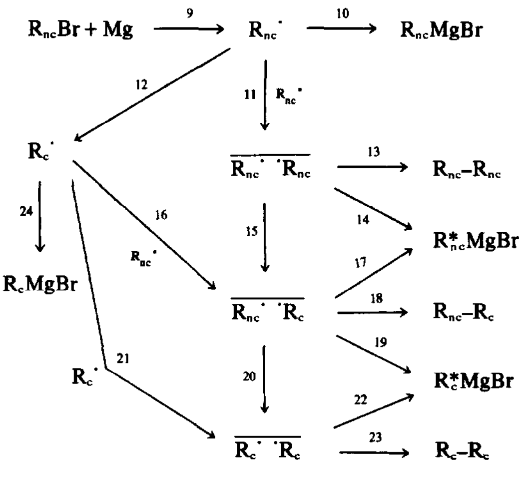
In the reaction of 6-bromo-1-hexene with Mg one might expect the formation of 5-hexenylmagnesium bromide ($R_{nc}MgBr$) and cyclopentylmethylmagnesium bromide (R_cMgBr), both being primary Grignard compounds. Garst[8] reported the formation of R_cMgBr in 5–7% yield in diethyl ether in vacuum-manifold experiments and in 3–4% yield in experiments under nitrogen. Walling[9] reported the formation of 6·5% R_cMgBr during preparation of a 1·11 M Grignard solution in diethyl ether. Richey[10] reported that varying amounts of the cyclized Grignard compound are formed in THF.

From the CIDNP spectra one can obtain information on the degree of polarization both in $R_{nc}MgBr$ and in R_cMgBr in different solvents. This information, combined with the absolute yield of each of the two Grignard compounds, gives insight into the fate of the radical $R_{nc}^{\bullet}$ initially created in the reaction of 6-bromo-1-hexene with magnesium (Scheme 3). Furthermore the ratio of the absolute and relative yields of the three coupling products $R_{nc}R_{nc}$, $R_{nc}R_c$ and R_cR_c gives insight into the ratio of the amounts of the three possible radical pairs from which polarization might originate.

From Scheme 3 it can be seen that $R_{nc}^{\bullet}$, created at the site of SET (Eqn 9), can react in three different ways, i.e. formation of $R_{nc}MgBr$ (Eqn 10), cyclization to $R_c^{\bullet}$ (Eqn 12) and formation of a radical pair in the sense of CIDNP theory (Eqn 11) by diffusive encounters with another radical. $\overline{R_{nc}^{\bullet}\,{}^{\bullet}R_{nc}}$ may be transformed to the two other possible radical pairs by cyclization of each of the radicals (Eqns 15 and 20). These radical pairs may also be formed by diffusive encounters of radicals $R_c^{\bullet}$ formed outside the radical pair (Eqns 16 and 21).

Unambiguous information can only be obtained in the present investigations if the following two reactions are of minor importance under the experimental conditions applied. Firstly Wurtz type coupling reactions (Eqn 25) should not occur.

$$RMgBr + RBr \longrightarrow R{-}R + MgBr_2. \qquad (25)$$



Scheme 3

From the lit.[11] evidence is obtained that appreciable amounts of Wurtz coupling products are formed from primary alkyl bromides and their corresponding Grignard compounds only when their solutions in strongly basic solvents are heated during relatively long periods (65° and 4 hr). Secondly, formation of R_cMgBr by cyclization of $R_{nc}MgBr$, which occurs at high temperatures (100°) as reported by Richey,[10] should not occur under the experimental conditions applied. Information discussed below shows that both reactions do not play a role of any importance in our studies.

Determination of the amounts of other products formed during the reaction, such as R(H) and R(–H) (Scheme 1), is less informative for the following reasons. Firstly because disproportionation to combination ratios (k_d/k_c) are smaller than 0·1 for the 5-hexenyl and cyclopentylmethyl radicals.[6] Secondly, R(H) is formed not only in disproportionation reactions, but also in hydrogen abstraction reactions.

We expected that the role of the solvent in the Grignard formation reaction can be studied in more detail by means of the 5-hexenyl system, because cyclization will compete with other radical reactions at the site of SET, which are expected to be solvent dependent, and because solvent may influence the diffusional behaviour of the radicals during the encounter processes in the radical pair.

RESULTS AND DISCUSSION

When a reaction of 6-bromo-1-hexene with Mg in ethereal solvent is performed in a NMR tube in high magnetic field (Experimental) a five line CIDNP spectrum[12] is observed, which changes to its thermal equilibrium spectrum after 2–3 min (see stick diagrams in Fig. 1). The spectra were identified as belonging to the α-protons of the Grignard compounds by their high field shift from δ (TMS) = 0 ppm depending on the composition of the solvent. As was previously reported[1] only multiplet effects with phase E/A were found in the NMR spectra of the Grignard compounds. The features of the CIDNP spectra of both Grignard compounds can be seen separately, as can be concluded from the coupling constants J = 7 Hz in 5-hexenylmagnesium bromide and J = 8 Hz in cyclopentyl-methylmagnesium bromide as well as from the phase E/A of the polarization in both Grignard compounds. Sometimes in the CIDNP and usually in the final NMR spectrum the high field peak of R_cMgBr and the low field peak of $R_{nc}MgBr$ coincide.

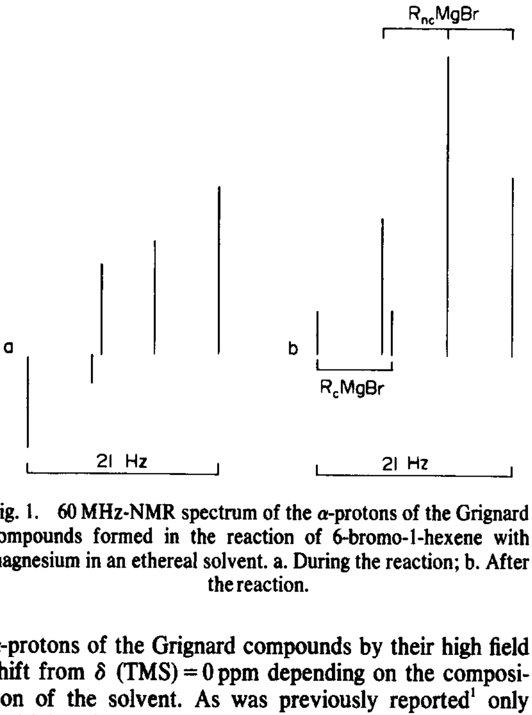


Fig. 1. 60 MHz-NMR spectrum of the α-protons of the Grignard compounds formed in the reaction of 6-bromo-1-hexene with magnesium in an ethereal solvent. a. During the reaction; b. After the reaction.

Concerning side reactions that may occur the following remarks have to be made. Cyclization of $R_{nc}MgBr$ has not been observed in THF at 40° during 2·5 hr. At 70° cyclization takes place with a half-life time of more than 8 days in THF and of 4·5 and 3 days in diethylether (DEE) and di-n-butylether (DBE) respectively, corresponding to k values of approx. $10^{-6}\,sec^{-1}$. When the Grignard formation reaction was performed in DBE at 100° the yield of R_cMgBr was 45% (18% at 40°), whereas the yield of RR_{tot} did not increase appreciably as compared to the results of the reaction at 40°. Thus it may be concluded that the amount of R_cMgBr encountered throughout the present paper originates only from the formation reaction.

With regard to the Wurtz reactions (Eqn 25)—in all our experiments a twofold excess of $R_{nc}Br$ over Mg was used—experiments at temperatures up to 60° and reaction times as long as 1 hr showed that no change in the yields and the ratios of the three coupling products could be detected.

Reactions in DEE, THF, DBE *and* DPE. In THF the polarization in $R_{nc}MgBr$ as well as in R_cMgBr is weak but clearly discernable and a low yield of R_cMgBr (2·5%) is obtained. In DBE, which is much less basic and more viscous than THF, polarization in $R_{nc}MgBr$ is still weak but polarization in R_cMgBr is moderate, whereas the yield of R_cMgBr is high (18%) as compared to the yield in THF. In DEE, which is less basic than THF and much less viscous than THF and DBE, the yield of R_cMgBr is low (2·5%). Unfortunately we were unable to obtain CIDNP spectra during reactions in DEE because of its low boiling point.

As can be seen from Table 1 the absolute yield of RR_{tot} depends on the ether used. In THF, being by far the most basic ether, the yield is the lowest (4%) which indicates that most of the radicals have reacted to form Grignard compounds. From the low yield of R_cMgBr and from the occurence of polarization in R_cMgBr it may be concluded that the direct reaction to $R_{nc}MgBr$ (Eqn 10) is by far the major pathway. The remaining radicals seem to get involved in radical pair formation (Eqn 11) and most likely do not cyclize to $R_c^{\cdot}$ (Eqn 12), otherwise a larger amount of R_cMgBr (Eqn 24) and more polarization in R_cMgBr would have been found (via Eqns 16 and 21).

The higher yields of RR_{tot} and consequently the lower yields of $RMgBr_{tot}$ in DEE and DBE, as compared to the yields obtained in THF, are due to the lower basicity of both ethers and not to the differences in viscosity, for the changes in the yields of the products do not follow the changes in viscosity.

Regarding the ratio of the yields of the three coupling products a remarkable difference is observed between the results obtained in DEE and DBE. Whereas in DEE most of the entities R are non-cyclized, in DBE the fraction of cyclized entities has increased considerably. Combining this with the large yield of R_cMgBr in DBE and with the moderate polarization observed in R_cMgBr one comes to the conclusion that there is extensive cyclization at the site of SET (Eqn 12) with subsequent formation of unpolarized cyclized Grignard compound at that site (Eqn 24). In DEE on the other hand radicals escaping from the site of SET will mainly be $R_{nc}^{\cdot}$.

This difference in behaviour of the radicals in the two ethers has probably to be attributed to the large difference in viscosity. In the much more viscous DBE, $R_{nc}^{\cdot}$ radicals will stay longer at the site of SET; although one would expect a large amount of RR_{tot} to be formed in DEE due to its lower viscosity, this is balanced by the somewhat

Table 1. Yields of Grignard compounds and side products in the reaction of 6-bromo-1-hexene with magnesium in different ethers at 40°

Exp.	Number of runs	Solvent*	Viscosity[13] η_{40} (in cP)	Absolute yields (%) $R_{nc}MgBr$[a]	R_cMgBr[a]	RR_{tot}[b]	Relative yields[c] (%) $R_{nc}R_{nc}$	$R_{nc}R_c$	R_cR_c
1.	5	DEE	0·194	85·5 ± 2·0	2·5 ± 0·5	9·0 ± 3·0	64·5 ± 5·0	28·0 ± 2·5	7·5 ± 2·0
2.	4	THF	0·389	86·0 ± 5·0	2·5 ± 0·5	4·0 ± 1·0	54·5 ± 6·5	29·0 ± 4·0	17·0 ± 3·5
3.	8	DBE	0·506	73·5 ± 5·0	18·0 ± 1·5	7·0 ± 1·5	39·0 ± 4·5	40·0 ± 2·5	21·0 ± 3·0
4.	4	DPE	0·80	65·5 ± 2·0	27·0 ± 1·5	4·0 ± 0·5	35·0 ± 0·5	38·5 ± 0·5	26·5 ± 0·5

*DEE = diethyl ether; THF = tetrahydrofuran; DBE = di-n-butyl ether; DPE = di-n-pentyl ether.

[a] Calculated from the peak areas in the NMR spectra and based on the total amount of magnesium used.

[b] $RR_{tot} = R_{nc}R_{nc} + R_{nc}R_c + R_cR_c$, calculated from GLC and based on the total amount of magnesium used.

[c] Calculated from GLC and based on total yield of RR.

higher basicity of this ether, leading to a higher rate of the Grignard formation reaction (Eqn 10).

The conclusions obtained from the experiments in DEE and DBE are confirmed by the results of the experiments in di-n-pentyl ether (DPE). In this very viscous ether, as compared to DEE and DBE, the yield of R_cMgBr increases considerably, whereas the CIDNP spectrum is comparable to the one obtained in DBE. The yield of RR_{tot} drops to 4% because the viscosity increases whereas the basicity of the ether remains practically unchanged as compared to DBE. The rise in cyclization is also found in the ratio of the three coupling products.

The recovery of groups R, related to the amount of magnesium used in the reaction, is 97·0% in DEE, 98·5% in DBE and 92·5% in THF, indicating that in THF other side reactions, most likely hydrogen abstraction,† are more important than in DEE and DBE.

Reactions in mixtures of DBE *and* DEE. Dilution of DEE with DBE leads to a relatively small decrease in basicity of the solvent mixture, but to a rather large increase in viscosity.

Using solvent mixtures with increasing molar fractions of DBE, the yields of the two Grignard compounds and of the three coupling products were determined. As could be expected from the results obtained from the reactions in the two ethers (Table 1), the yields of RR_{tot} did not change in the various solvent mixtures (Table 2), contrary to the ratio of the coupling products. As is shown in Fig. 2, there is a linear decrease of the relative yield of $R_{nc}R_{nc}$ and a linear increase of the relative yields of $R_{nc}R_c$ and R_cR_c with increasing viscosity of the solvent.

Also the yield of R_cMgBr increases linearly with viscosity. The ratio R_cMgBr/R_c entities in RR_{tot} (calculated from absolute yields based on magnesium used) increases with increasing molar fraction of DBE (Table 2). Obviously cyclization at the site of SET (Eqn 12) with subsequent formation of cyclized Grignard compounds (Eqn 24) becomes more important as the solvent mixtures contain relatively more DBE, as compared to formation of R_cMgBr via radical pairs (Eqns 19 and 22); the increase in viscosity and the slight decrease in basicity of the solvent mixture leads to a longer life time for the radical created at the site of SET.

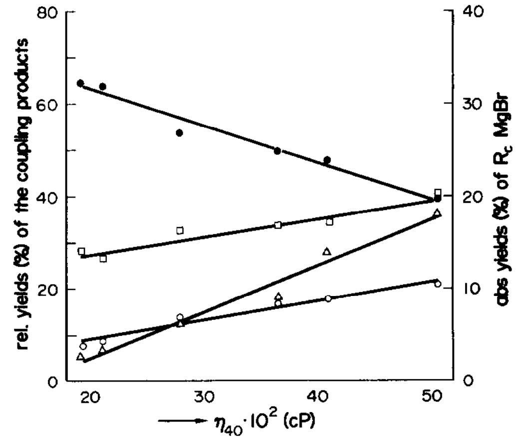


Fig. 2. Absolute yields of R_cMgBr (△) and relative yields of $R_{nc}R_{nc}$ (·), $R_{nc}R_c$ (□) and R_cR_c (○) vs the viscosity of the DEE/DBE solvent mixtures.

A comparable relation between the ratios of the coupling products and viscosity is obtained for DEE/DPE mixtures, although the values do not exactly fit the curves for DEE/DBE mixtures, as could be expected from experiments of Szwarc on the influence of viscosity on cage recombination in different solvents.[14]

Plots of the ratios of the coupling products and the yield of R_cMgBr versus the molar ethereal oxygen content of the solvent mixtures led to poor correlations with no obvious trends.

Reactions in mixtures of THF *and other ethers.* The results of the reaction of 6-bromo-1-hexene with magnesium in a mixture of THF and DEE (Exp 9, Table 3) show in every aspect the same picture as those in THF, indicating that a decrease in viscosity of the solvent (0·389 cP for THF compared to 0·289 cP for THF/DEE) has no influence; due to its higher basicity THF predominates in determining the course of the different processes at the site of SET.

Diluting THF with DBE in the volume ratio 0·09 ml/0·33 ml (Exp 10, Table 3) gives an absolute yield of RR_{tot} of 4%. Thus the amount of radicals diffusing away from the site of SET equals the amount in THF. The ratio of the three coupling products lies somewhere in between the ratios obtained in THF and DBE. The ratio

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†It has been shown that both the solvent and alkyl groups derived from the starting halide can act as hydrogen sources.[2,15]

Table 2. Yields of Grignard compounds and side products from the reaction of 6-bromo-1-hexene with magnesium in mixtures of DEE and DBE at 40°

Exp.	Number of runs	Solvent	Molar ratio	Viscosity[13] η_{40} (cP)	Absolute yields (%)			Relative yields[c] (%)			$\frac{R_cMgBr}{R_c \text{ in } RR_{tot}}$
					$R_{nc}MgBr^a$	R_cMgBr^a	RR_{tot}^b	$R_{nc}R_{nc}$	$R_{nc}R_c$	R_cR_c	
1	5	DEE	—	0·194	85·5 ± 2·0	2·5 ± 0·5	9·0 ± 3·0	64·5 ± 5·0	28·0 ± 2·5	7·5 ± 2·0	1·2
5	6	DEE/DBE	9·75/1	0·212[d]	85·0 ± 2·0	3·0 ± 0·5	9·5 ± 2·5	64·0 ± 5·5	27·0 ± 3·5	9·0 ± 3·0	1·5
6	6	DEE/DBE	1·62/1	0·279[d]	85·0 ± 0·5	6·5 ± 1·0	6·5 ± 0·5	54·0 ± 6·5	32·5 ± 4·5	13·5 ± 1·0	3·2
7	8	DEE/DBE	1/2	0·369[d]	82·0 ± 4·0	9·0 ± 1·0	7·0 ± 0·5	49·5 ± 5·5	34·0 ± 4·0	16·5 ± 2·5	3·9
8	6	DEE/DBE	1/3·7	0·412[d]	78·5 ± 4·0	14·0 ± 1·5	6·0 ± 0·5	47·5 ± 4·0	34·5 ± 3·5	18·0 ± 2·0	6·7
3	8	DBE	—	0·506	73·5 ± 5·0	18·0 ± 1·5	7·0 ± 1·5	39·5 ± 4·5	39·5 ± 2·5	21·0 ± 3·0	6·3

[a,b,c] See Table 1.

[d] Calculated from the equation according to Arrhenius: $\log \eta = x \log \eta_1 + (1 - x) \log \eta_2$, where x is the molar fraction of compound 1 in solution and η_1 and η_2 are the viscosities of compounds 1 and 2.

Table 3. Yields of Grignard compounds and side products in the reaction of 6-bromo-1-hexene with magnesium in THF and mixtures of THF/DEE and THF/DBE at 40°

Exp.	Number of runs	Solvent	Molar ratio	Viscosity[13] η_{40} (cP)	Absolute yields (%)			Relative yields[c] (%)			$\frac{R_cMgBr}{R_c \text{ in } RR_{tot}}$
					$R_{nc}MgBr^a$	R_cMgBr^a	RR_{tot}^b	$R_{nc}R_{nc}$	$R_{nc}R_c$	R_cR_c	
2	4	THF	—	0·389	86·0 ± 5·0	2·5 ± 0·5	4·0 ± 1·0	54·5 ± 6·5	29·0 ± 4·0	17·0 ± 3·5	2·0
9	5	THF/DEE	1·28/1	0·286[d]	88·0 ± 2·0	3·0 ± 1·0	4·0 ± 0·5	56·0 ± 3·0	30·0 ± 2·0	14·0 ± 1·0	2·6
10	5	THF/DBE	1/1·77	0·461[d]	84·5 ± 2·5	9·0 ± 1·0	4·0 ± 0·5	45·5 ± 8·5	31·5 ± 5·0	23·0 ± 3·5	5·8
3	8	DBE		0·506	73·5 ± 5·0	18·0 ± 1·5	7·0 ± 1·5	39·5 ± 4·5	39·5 ± 2·5	21·0 ± 3·0	6·3

[a,b,c,d] See Tables 1 and 2.

R_cMgBr/R_c in RR_{tot} is almost the same as in DBE indicating comparable diffusional behaviour of the radicals in both solvents. CIDNP spectra strongly resemble those in DBE, i.e. moderate polarization in R_cMgBr and weak polarization in $R_{nc}MgBr$ (Fig. 3a).

Fig. 3. CIDNP spectra of the α-protons of the Grignard compounds formed during the reaction of 6-bromo-1-hexene with magnesium in: a. THF/DBE (vol. ratio 0·09 ml/0·33 ml) and b. THF/allyl phenyl ether (vol. ratio 0·09 ml/0·33 ml).

Our interpretation of these results is as follows. As the electron transfer from magnesium to the hexenyl bromide, leading eventually to the formation of the radical $R^{\cdot}_{nc}$, may be assumed not to be strongly solvent dependent (Discussion), the radicals may be generated with molecules of DBE or of THF as nearest neighbours. DBE as nearest neighbour will decrease the diffusion rate, which leads to increased cyclization (R_cMgBr) at the site of SET. Apparently, rapid exchange of solvent molecules (as compared to diffusion of the radicals) takes place, so that THF with its strong solvating power towards $BrMg_s^{\cdot}$ determines the rate of Grignard formation as evidenced by the low yield of RR_{tot}.

Diluting THF with anisol or with di-isopropyl ether reveals the same CIDNP characteristics as on equivalent dilution of THF with DBE. The relative yields of R_cMgBr, based on $RMgBr_{tot}$, are also high for these solvent mixtures (14% for THF/anisol and 9% for THF/di-isopropyl ether; no absolute yields have been determined).

On dilution of THF with allyl phenyl ether moderate polarization in $R_{nc}MgBr$ is found, besides strong polarization in R_cMgBr (Fig. 3b), while the relative yield of R_cMgBr is high (18·5%).

Diluting THF with 1,2-dimethoxyethane (DME, vol. ratio THF/DME 0·12 ml/0·30 ml; $\eta_{40} = 0{\cdot}383$ cP) the CIDNP spectrum shows weak polarization in R_cMgBr and $R_{nc}MgBr$, almost similar to the results in THF. Unfortunately, during this reaction $MgBr_2$ precipitated so that the reaction could not be followed till the end. The results indicate that the basicity of DME towards $XMg_s^{\cdot}$ is comparable with or lower than the basicity of THF.

Reactions in mixtures of THF *and benzene.* On dilution of THF with a nonethereal solvent, like benzene (Bz), the probability that the radical $R^{\cdot}_{nc}$ formed at the site of SET has a base as nearest neighbour decreases. Therefore direct Grignard formation is expected to diminish with the amount of benzene added, whereas Grignard formation via radical pairs will increase. Indeed the CIDNP spectra show an increase in the intensity of the polarization in both $R_{nc}MgBr$ and in R_cMgBr roughly parallel with the increase in the Bz/THF ratio.

As can be seen from Fig. 4 the amount of $R_{nc}MgBr$ formed diminishes roughly linearly with increasing molar ratio Bz/THF (for Bz/THF > 1), whereas the amount of R_cMgBr formed increases. For molar ratios Bz/THF < 1 the solvent mixture behaves like pure THF. From the same figure it can be concluded that the total yield of RMgBr diminishes also linearly with the increase of the Bz/THF molar ratio. From Fig. 5 it can be seen that there is an increase in the yield of RR_{tot} corresponding with the change in the yields of $R_{nc}MgBr$ and R_cMgBr. Therefore, for reactions at the site of SET the picture is quite clear. THF is required for solvation of $XMg_s^{\cdot}$, leading to the formation of Grignard compound, and thus an increase in the Bz/THF molar ratio enhances the amount of radicals $R^{\cdot}_{nc}$ diffusing away on the magnesium surface to get involved in radical pair formation.

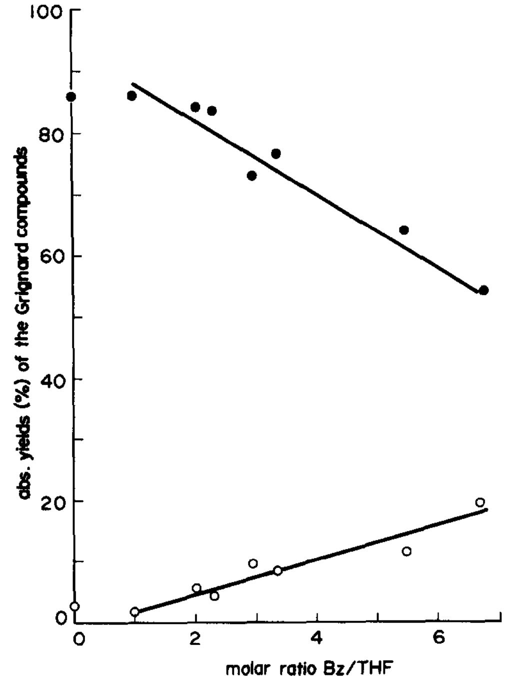


Fig. 4. Absolute yields of $R_{nc}MgBr$ (·) and R_cMgBr (O) vs the molar ratio Bz/THF.

The ratio of the three coupling products, depicted in Fig. 5, remains constant. This, combined with increasing polarization in the Grignard compounds, indicates that for all solvent mixtures with molar ratio Bz/THF > 1 there is a common distribution mechanism of the radicals over the radical pairs (Scheme 2). The constant ratio of R_c entities

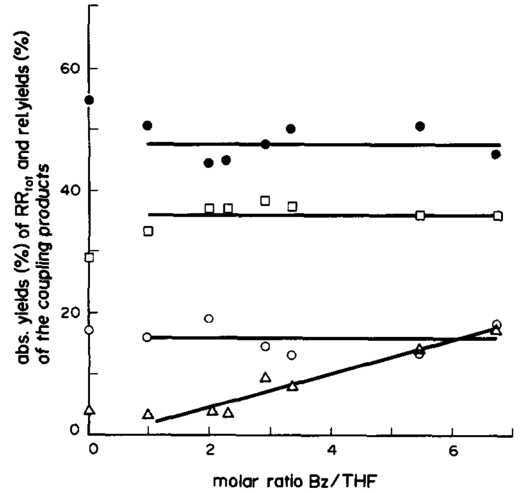


Fig. 5. Absolute yield of RR_{tot} (△) and relative yields of $R_{nc}R_{nc}$ (·), $R_{nc}R_c$ (□) and R_cR_c (○) vs the molar ratio of Bz/THF.

in R_cMgBr to R_c entities in RR_{tot} for molar ratio Bz/THF > 1 confirms this conclusion (see Table 4). Therefore it can be concluded that formation of the cyclized Grignard compound via Eqn (24) does not play an important role in these solvent mixtures.

DISCUSSION AND MECHANISM

It should be noted that all experiments reported are performed under completely identical conditions (Experimental). In view of the reaction conditions which are different from those used in the usual preparative reactions the reproducibility of the results is remarkably good; only the initiation of the reaction is difficult to control.

These results show that the solvent plays a role at two different stages during the formation reaction: in the processes at the site of SET and in the diffusion of the radicals at the metal surface.

At the site of SET the solvent could play a role in the following three processes, (a) the one electron transfer from magnesium to the lowest anti-bonding orbital of the carbon–halogen bond,[1] (b) the complexation of $XMg_s^{\cdot}$ and (c) the solvation of the RMgX species formed. Terms like basicity, polarity, solvating power, etc. describing the ability of the solvent to promote these processes, should be related to each of these specific processes and do not necessarily have to be equal to those used in connection with RMgX in solution.

Walborsky[2] has suggested that THF is much more effective than diethyl ether in promoting the single electron transfer to RX due to the greater solvating ability towards the radical anion $RX^{\ominus}$ and towards the magnesium (I) halide $XMg^{\cdot}$. However arguments cited from the lit.[16] in favour of this view deal with the greater cation solvation ability of THF, while little or no specific interaction with anions is to be expected.[17] So it seems unlikely that stabilization of the radical anion $RX^{\ominus}$ by any solvent plays an important role in the Grignard reaction. Furthermore, as is shown by Symons[18] by ESR spectroscopy, $RX^{\ominus}$ is a very unstable intermediate so that addition of one electron to the carbon–halogen bond in bromomethane with subsequent formation of the $CH_3^{\cdot}$ radical and the $Br^{\ominus}$ anion is a continuously adjusting process with no energy minimum at 77 K. Therefore it has been suggested[18] that one deals with the formation of a radical-anion adduct rather than with a radical anion. At this time we do not further discuss the relative rates of the first steps in the Grignard reaction (Eqns 1–3); this has recently been done by Whitesides.[19]

The complexation of $XMg_s^{\cdot}$ by an ethereal solvent will be influenced by the electron donating ability and the steric requirements of the ethers. Because we are dealing with a surface reaction, steric factors are expected to be more important in complexation of $XMg_s^{\cdot}$ than in solvation of preformed RMgX. The solvation of the RMgX species formed is essential during the reaction because the metal surface is cleaned from the products formed and thereby becomes better accessible to RX for further reaction.

That THF is a good base for the Grignard reaction is due to its relatively strongly polar character and to its geometry as a five membered ring compound, which makes it most suitable to act as a complexing agent for $XMg_s^{\cdot}$ at the metal surface. For di-n-alkyl ethers, being all of comparable low basicity relative to THF, basicity diminishes with increasing chain length; however, at the same time the viscosity of these ethers increases. Therefore, for DEE and DBE the total effect of these two properties on the Grignard reaction is roughly compensating, as can be concluded from the equal yields of RR_{tot} and $RMgBr_{tot}$ (Exp 1 and 3). Only the much higher yields of R_cMgBr in DBE and DPE discloses that in these solvents the life time of the radicals is longer than in DEE.

In view of the vital role which the basic solvent plays in the mechanism presented here, it should be pointed out that organomagnesium compounds can also be prepared from alkyl halides and magnesium in hydrocarbon solvents at higher temperatures. Initiation of these reactions does not require special conditions but progress of the reaction requires forceful stirring at temperatures between 80 and 120°. Unfortunately at such high temperatures cyclization of $R_{nc}MgBr$ and possibly formation of Wurtz coupling products take place, which prevented us to use pure benzene as a solvent for studies with our system. Moreover it should be noted that possibly not RMgX, but some other organomagnesium compound is the initial product of this reaction, since the endproduct consists mainly of R_2Mg;[20] the large differences in reaction conditions indicate that most likely different mechanisms are operative in the two types of formation reactions. On the other hand our results clearly demonstrate that at 40° the yield of $RMgBr_{tot}$ diminishes linearly with increasing molar ratio Bz/THF, demonstrating the great influence of base on RMgX formation.

Information on the diffusion processes of the radicals at the metal surface are obtained from the experiments in ethers as well as in mixtures of THF and benzene. The results in each of the ethers and in mixtures of DEE/DBE

Table 4. Yields of Grignard compounds and side products in the reaction of 6-bromo-1-hexene with magnesium in mixtures of THF/Bz at 40°

Exp.	Number of runs	Solvent	Molar ratio	Viscosity[13] η_{40} (cP)	Absolute yields			Relative yields^{c}			$\frac{R_cMgBr}{R_c \text{ in } RR_{tot}}$
					$R_{nc}MgBr^{a}$	R_cMgBr^{a}	RR_{tot}^{b}	$R_{nc}R_{nc}$	$R_{nc}R_c$	R_cR_c	
2	4	THF	—	0·389	86·0 ± 5·0	2·5 ± 0·5	4·0 ± 1·0	54·5 ± 6·5	29·0 ± 4·0	17·0 ± 3·5	2·0
11	2	THF/Bz	1/1	0·439^{d}	86·0	2·0	3·0	50·5	33·5	16·0	1·8
12	2	THF/Bz	1/2·03	0·457^{d}	84·0	5·5	4·0	44·5	36·5	19·0	4·0
13	6	THF/Bz	1/2·28	0·460^{d}	83·0 ± 5·5	4·5 ± 0·5	3·5 ± 1·0	45·0 ± 5·0	36·5 ± 1·0	18·5 ± 4·0	3·3
14	2	THF/Bz	1/2·92	0·466^{d}	73·0	9·5	9·0	47·5	38·0	14·5	3·1
15	9	THF/Bz	1/3·34	0·468^{d}	76·5 ± 6·0	8·5 ± 2·0	8·0 ± 2·0	50·0 ± 3·0	37·0 ± 1·5	13·0 ± 1·5	3·4
16	2	THF/Bz	1/5·46	0·477^{d}	64·0	11·5	14·0	50·5	36·0	13·5	2·6
17	2	THF/Bz	1/6·7	0·480	54·0	19·5	17·5	46·0	36·0	18·0	3·1

^{a,b,c,d}See Tables 1 and 2.

clearly demonstrate that the diffusion processes are determined by the viscosity of the solvent. In the more viscous solvents the life time of the radicals increases leading to more cyclization (Eqn 12) before encounters with other radicals. So there is an increase of R_c entities in RR_{tot} with increasing viscosity (Fig. 2). It should be noted, however, that still a high percentage of RR_{tot} consists of $R_{nc}R_{nc}$ in all ethers used, indicating that diffusion leading to encounter processes competes with cyclization or that cyclization is prevented because the radical is attached to the metal surface as was tentatively proposed earlier.[1] The viscosity dependence observed is more in accordance with the first explanation. Furthermore, it is reasonable to suppose that all radicals are created at the metal surface at very short distance from each other; due to a high local concentration of the radicals, diffusion to encounters indeed has a chance to compete with the rapid cyclization.

For all experiments in Bz/THF the ratio THF/Mg exceeds two, which implies that two THF molecules, necessary to obtain the usual tetra-coordination of magnesium in RMgX, are available. The fact that organomagnesium compounds can be prepared in hydrocarbons (see above) suggests that the single electron transfer is not strongly solvent dependent. In line with this reasoning, the yields of Grignard compounds do diminish with increasing Bz/THF ratio, as one would expect if radicals keep being produced, at more or less constant rate, whereas their combination with $XMg_s^{\cdot}$ becomes increasingly difficult.

With regard to the diffusion processes in Bz/THF mixtures, with almost constant viscosity (0·44–0·48 cP), it should be noted that, although the yields of RR_{tot} change considerably (4–17%), the ratio of the three coupling products is almost constant. Thus although the complexation of $XMg_s^{\cdot}$ by THF becomes more and more retarded with increasing molar ratio Bz/THF, the partition of radicals diffusing away from the site of SET, between radicals that cyclize outside (Eqns 12, 16 and 21) and radicals that cyclize inside the radical pair (Eqns 11, 15 and 20), is constant and might be determined by the viscosity.

However there is another possible explanation for the constant ratio of the three coupling products. From lit[21] there is rather pertinent indication that a small but distinct interaction exists between radicals and π-electron rich solvents such as benzene. Such an interaction between the hexenyl radical and benzene could retard cyclization. Thus all radicals diffusing from the site of SET will be uncyclized and will therefore form radical pairs $\overline{R_{nc}^{\cdot}\,R_{nc}^{\cdot}}$, from which a constant distribution over the different pathways (Scheme 3) will take place leading to a constant ratio of the three coupling products. Cyclization of the radicals will take place during the collisions in the encounters of the radical aggregates, which have been proposed by Burkhart.[21a]

Further indication that this type of radical solvent interaction does play a role can be obtained by comparing equal dilution of THF with benzene (Exp 15) and with DBE (Exp 10). At this dilution (0·09 ml/0·33 ml) the molar ratio THF/DBE (1/1·77) is almost twice as large as for THF/Bz (1/3·34). The viscosities of both solvent mixtures are almost equal. The yield of RR_{tot} is twice as large in THF/Bz as in THF/DBE, but the yields of R_cMgBr are comparable (8·5% and 9·0%). These results indicate that the life time of the radicals at the site of SET is large in both cases relative to the rate of Grignard formation, but that in Bz/THF this leads to a more extensive diffusion from that site as compared to THF/DBE. The same indication is obtained from the CIDNP spectra in both solvent mixtures (Fig. 6).

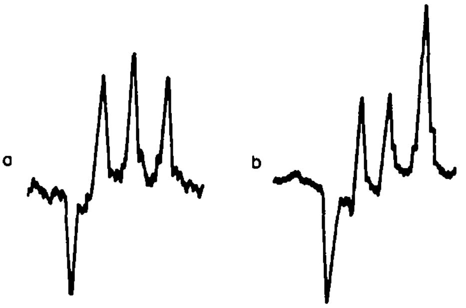
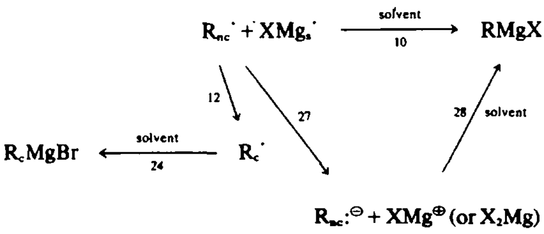


Fig. 6. CIDNP spectra of the α-protons of the Grignard compounds, formed during the reaction of 6-bromo-1-hexene with magnesium in: a. THF/DBE and b. THF/Bz (vol. ratios 0·09 ml/0·33 ml).

Although the yield of R_cMgBr is comparable, polarization is stronger in Bz/THF. The most striking difference in polarization is found in the spectra of $R_{nc}MgBr$. The same type of results is obtained on diluting THF with allyl phenyl ether, which is also π-electron rich (Fig. 3b). The striking difference in diffusion abilities from the site of SET may be considered as a support for the working hypothesis that stabilization of radicals occurs by π-electron rich solvents. Unfortunately the most obvious experiment to support this hypothesis, i.e. dilution of THF with inert solvents lacking this possibility of π-complexation, e.g. cyclohexane or n-heptane, results in the formation of two layer systems and of precipitates which made the results rather unreliable. Nevertheless in these cases there was indication that less RR_{tot} is formed while the amount of R_cMgBr remained unchanged. Also the CIDNP spectra did not show the intense polarization obtained in Bz/THF.

As stated previously[1] the formation of RMgX from the radical $R^{\cdot}$ and $XMg_s^{\cdot}$ can be depicted (Scheme 4) as a radical combination reaction (Eqns 10 and 24) or as an ionic reaction (Eqns 27 and 28). The latter can be considered to represent a second SET to form a carbanion



Scheme 4

and a $XMg^{\oplus}$ cation which will combine to RMgX. In this study we found a reduction of the yield of $RMgBr_{tot}$ formed at the site of SET when working in less basic solvents as compared to THF. If it is accepted that electron transfer is not solvent dependent (see above), a solvent effect on the ionic pathway could only occur during the second step (Eqn 28). However, the reduction of the yield of $RMgBr_{tot}$ has been accompanied by an increase in R_cMgBr and RR_{tot} formation, both typical radical reactions.

This result can easily be explained on the basis of the radical pathway, but it is difficult to reconcile with the intermediacy of the carbanion $R_{nc}:^{\ominus}$, especially as far as the cyclization is concerned. Although the issue cannot be considered being definitely settled by the present evidence we feel that there are no convincing arguments in support of the ionic pathway, whereas the occurrence of radicals is amply demonstrated.

CONCLUSION

Based on variations in ratios of the two Grignard compounds formed from 6-bromo-1-hexene and on changes in RR_{tot} and CIDNP polarization with solvent variations, this study has added further qualitative evidence to the conclusion that direct coupling of a radical $R^{\cdot}$ with magnesium subhalide $XMg^{\cdot}$ (Eqn 3) is the major pathway in the formation of the Grignard reagent.

A quantitative evaluation of the different rates of reaction is impossible at the present time. However, if one considers the high yield of Grignard reagents ($RMgX_{tot}$) in relation to the very rapid cyclization (R_cMgX) and diffusion steps (RR_{tot}, CIDNP), it is evident, that the formation is an extremely fast process. Radical pair formation becomes more important (a) in less basic solvents, (b) in less viscous solvents and (c) by dilution with non-ethereal (especially π-electron donating) solvents.

EXPERIMENTAL

Chemicals. In all experiments use was made of Mg crystals Specpure®, Johnson and Matthey Chemicals Ltd., London (spectral analysis: Mg contained 5–7 ppm of impurities). All chemicals were used as commercially available and distilled before use. All solvents were distilled from sodium under vacuum or nitrogen atmosphere and stored on mol. sieves.

6-Bromo-1-hexene. To 120 g (0·37 mole) 1,2,6-tribromohexane[22] in 300 ml diethyl ether and 1 ml AcOH, 32·5 g (0·5 gat) Zn powder was added in 5 portions. Reaction took place under reflux of the ether and reflux was maintained by a steambath for 1 hr.

After completion of the reaction the solution was filtered and washed with sat $NaHCO_3$ aq and water. The organic layer was dried on $MgSO_4$. The ether was evaporated on a rotary evaporator and the residue was distilled under vacuum. This yielded 80% of the crude product, which was purified twice by distillation on a spinning band column. The final product had b.p. 64° (60 mm) and $n_D^{22} = 1{\cdot}4667$. The product was shown to be more than 99% pure by GLC (15% SE 30, 2m, 150°; Apiezon L 60/80, 2m, 150° and 50–220° progr. temp.). ^1H NMR: $-CH_2Br$: δ 3·35 ppm (t); $-CH_2-$: δ 1·30–2·25 ppm (m); $=CH-$: δ 5·45 – 6·10 ppm (m); $CH_2=$: δ 4·85 – 5·15 ppm (m). All values are relative to δ (TMS) = 0 ppm.

Coupling products. The two symmetric coupling products were prepared by reaction of the corresponding bromides with sodium in n-pentane, whereas the mixed one was obtained as a side product in the reaction of $R_{nc}Br$. The products were purified by preparative GLC. Structures were assigned by means of ^1H NMR spectra and mass spectra.

General procedure for the experiments

CIDNP spectra. About 12 mg (0·5 mgat) Mg crystals in a NMR tube were carefully flushed with a dry N_2 flow under warming. 0·42 ml solvent was added and N_2 was led through the soln. Then about 0·13 ml (1·15 mole) 6-bromo-1-hexene was added and the tube, closed with a cotton wool plug, was placed in a Varian A-60 NMR spectrometer. Spectra were run during and after the reaction. The percentages of the cyclic and open chain Grignard compounds were calculated from the peak areas in the final spectrum.

Analysis. The soln was poured into water and the NMR tube was carefully rinsed. The amount of Grignard compound was determined by acid-base and Complexon III (Merck) titration. After the acid-base titration but before the Complexon titration the solution was carefully extracted with n-pentane to collect all hydrocarbon products. The pentane extract was dried on $MgSO_4$ and the pentane was removed on a rotary evaporator at aspirator pressure and finally at a vacuum pump. To the residue 3 ml n-pentane was added. The yields of the coupling products were obtained from the GLC data of the pentane solution by reference to authentic samples of the three coupling products and to n-pentadecane as an internal standard (Apiezon L 60/80, 2m, 50–250° progr. temp.).

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