REACTIVITY OF PhMgBr TOWARDS AN ALKYNE IN THF AND NON-DONATING SOLVENTS

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ABSTRACT

Kinetic studies were carried out on the reaction of phenylmagnesium bromide with hex-1-yne in THF, and in the binary mixtures with toluene, chlorobenzene, and dichloromethane. The reaction was accelerated by additions of the non-donating solvents. An analysis in terms of the Kamlet-Taft equation revealed a rate decrease by the polarity of the solvents. The aromatic solvents plausibly enhance the reaction rate stabilizing the transition state via a π-π interaction.

INTRODUCTION

The decisive role of donor solvents in Grignard reactions has been known since long and refereed extensively [1-3]. Non-specific effects caused by solvent polarity and polarizability are usually masked by strong complexing effects. Although Agami[4] predicted an importance of the non-specific solvation in the Grignard chemistry as early as 1967, this issue has been paid relatively little attention. Besides a general interest the effects of nonspecific solvation can be informative concerning the reaction mechanism. In an earlier series of works we were able to show quantitatively that transition states of the Grignard addition reaction to ketones are of lower polarity than the reagents thus probably having a cyclic structure[5-8]. A variation in the medium polarity was achieved by addition of n-heptane or dichloromethane to the Grignard reagent prepared in a donor solvent. Linear plots log k vs. Kirkwood function were obtained for the reactions of pinacolone with ethylmagnesium and n-propylmagnesium bromides[6], dipropylmagnesium[5,7], and diphenylmagnesium[8]. The susceptibility of a reaction to the medium polarity was remarkably dependent on the donating ability of donors (ethers, amines)[8,9].

Recently we made an attempt to apply the same method to the Grignard reaction of alkynes in order to get insight into the solvation phenomena[10]. The reaction of hex-1-yn with phenylmagnesium bromide (cf. Refs. 11,12) was selected as a model process. Kinetic studies were carried out on the reaction of phenylmagnesium bromide with hex-1-yne in diethyl ether, and in the binary mixtures of the ether with toluene, chlorobenzene, and dichloromethane. In this way reaction media of different polarity/polarizability were generated, the specific solvation of the reagents presumably being unchanged. The additions of toluene decreased the polarity and increased the polarizability of the solution, the addition of chlorobenzene and dichloromethane caused an increase in both the polarity and polarizability. However, all the added non-donating solvents caused an increase in the reaction rate regardless of their possible polarity/polarizability contribution. The rate data were analyzed with the Koppel-Palm equation[11,12], the terms for specific solvation being omitted:

$$\log k = \log k_0 + yY + pP.$$ (1)

The polarity, Y, and polarizability, P, were considered as

$$Y = (\varepsilon - 1)/(2\varepsilon + 1)$$ and $$P = (n^2 - 1)/(n^2 + 1).$$

Although the overall correlation was merely satisfactory statistically significant values for the polarity and polarizability terms −1.02 and 9.4 respectively were found. The negative sign of the constant y indicates somewhat lesser polarity of the transition state in comparison with the reactants. This seems to be consistent with the four-centre mechanism for the reaction postulated by Dessy et al[14,15]. On the contrary, the solvent polarizability term was less comprehensible in this context.

To ensure an objective interpretation of the data the density functional theory calculations were addressed (cf. Ref. 16). The principal question was aimed to whether an alkyne molecule can directly attack the organomagnesium compound giving rise to an Sn1 type reaction or a preceding replacement of a solvent molecule is necessary. The main conclusions drawn from the investigation were as follows:

The reaction between an alkyne and Grignard reagent comprises two consecutive steps, the first consisting in the replacement of a coordinated solvent molecule by the alkyne, and followed by a unimolecular reaction of the complex. The complex-formation equilibrium is shifted far towards the initial reagents, therefore in spite of a fast rearrangement of the complex to products the overall reaction is slow. Additions of non-donating solvents enhance the reaction rate presumably by shifting the replacement equilibrium in favour of the
complex formation. Besides that a susceptibility of the reaction rate to changes in the solvent polarity is evident.

In this work we extended our investigation to THF solutions and complexes in order to ascertain the validity of the former conclusions in the case of a considerably stronger complexing agent.

RESULTS AND DISCUSSION

The kinetics of the slow but sufficiently exothermic reaction was followed thermographically by means of the initial rates method similarly to our previous works\textsuperscript{[10,17]}. Phenylmagnesium bromide was prepared in THF and required reagent solutions were obtained by addition of appropriate amounts of toluene, chlorobenzene or dichloromethane to the initial reagent.

The results of the kinetic measurements are presented in Table 1. The rate constants are mean values for several parallel runs the reproducibility of the data being within \( \pm 5\% \) deviations. The reaction rate in THF and in the solvent mixtures is slightly lower than in diethyl ether\textsuperscript{[10]}. The difference is more pronounced in binary mixtures which only exert a moderate effect on the rate of the reaction in the case of THF.

Table 1: Results of the kinetic measurements at 20°C

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Molar fraction of the ether</th>
<th>Concentration mol l(^{-1}) PhMgBr</th>
<th>Concentration mol l(^{-1}) hex-1-yne</th>
<th>( k_\text{II} \times 10^{-3} ) mol l(^{-1}) s(^{-1})</th>
<th>( \varepsilon )</th>
<th>( n )</th>
<th>( \pi^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. THF</td>
<td>1.0</td>
<td>0.364</td>
<td>0.364</td>
<td>4.51</td>
<td>7.390</td>
<td>1.404</td>
<td>0.58</td>
</tr>
<tr>
<td>2. THF-PhMe</td>
<td>0.94</td>
<td>0.342</td>
<td>0.342</td>
<td>5.13</td>
<td>7.046</td>
<td>1.410</td>
<td>...</td>
</tr>
<tr>
<td>3. THF-PhMe</td>
<td>0.32</td>
<td>0.364</td>
<td>0.364</td>
<td>6.42</td>
<td>3.760</td>
<td>1.472</td>
<td>...</td>
</tr>
<tr>
<td>4. THF-PhMe</td>
<td>0</td>
<td>0.362</td>
<td>0.362</td>
<td>7.32</td>
<td>2.601</td>
<td>1.493</td>
<td>0.54</td>
</tr>
<tr>
<td>5. THF-PhCl</td>
<td>0.31</td>
<td>0.364</td>
<td>0.364</td>
<td>5.41</td>
<td>6.088</td>
<td>1.493</td>
<td>...</td>
</tr>
<tr>
<td>6. THF-PhCl</td>
<td>0</td>
<td>0.364</td>
<td>0.364</td>
<td>3.62</td>
<td>5.698</td>
<td>1.519</td>
<td>0.71</td>
</tr>
<tr>
<td>7. THF-CH(_2)_Cl(_2)</td>
<td>0.22</td>
<td>0.364</td>
<td>0.364</td>
<td>5.41</td>
<td>8.522</td>
<td>1.418</td>
<td>...</td>
</tr>
<tr>
<td>8. THF-CH(_2)_Cl(_2)</td>
<td>0</td>
<td>0.364</td>
<td>0.364</td>
<td>4.51</td>
<td>8.862</td>
<td>1.423</td>
<td>0.58</td>
</tr>
</tbody>
</table>

The nature of the phenylmagnesium bromide solution can also be represented by the Schlenk equilibrium.

\[
2 \text{PhMgBr} \rightleftharpoons \text{Ph}_2\text{Mg} + \text{MgBr}_2,
\]

shifted towards \( \text{PhMgBr} \) in diethyl ether ([PhMgBr]/[Ph\(_2\)Mg] \( \approx \) 8\textsuperscript{[20]}). A different position of the Schlenk equilibrium in THF solutions ([PhMgBr]/[Ph\(_2\)Mg] \( \sim \) 2\textsuperscript{[19]}), entangles a straightforward comparison of kinetic data for the ethers; however, it is obvious that a stronger solvation of the species makes the complex formation with the alkynic less favourable.

A treatment of the experimental data analogous to our previous work using the Koppel-Palm equation (1) did not lead to a satisfactory correlation. However, as is seen from Fig.1, the rate constants reveal a tendency to decrease with an increase in the medium polarity.

In order to level off the solvation equilibria shifts, phenylmagnesium bromide – THF complexes were prepared (see Materials and Methods) and dissolved in the non-donating solvents. Corresponding rate constants are presented in Table 1 (entries 4, 6, and 8).

In parallel to the Koppel-Palm equation the Kamlet-Taft equation proved to be useful for describing of solvent effects in many cases\textsuperscript{[1-20]}. While an application of the Kamlet-Taft equation to reactions in binary solvents is complicated the data for THF complexes in the solvents can be considered in terms of a reduced Kamlet-Taft equation (2), i.e. without the terms for specific solvation,

\[
\log k = \log k_0 + d\delta + s\pi^* \tag{2}
\]

In eq. (2) \( \pi^* \) is a solvent dipolarity parameter and \( d\delta \) is a polarizability correction term with \( \delta \) taken as 0.5 for polyhalogenated solvents, 1.0 for aromatic solvents, and zero for all others.

The number of experimental data does not permit any statistical treatment; however, the data afford some speculations upon details of the reaction. When solving eq. (2) for our data the most self-consisting results can be obtained using the unity \( \delta \)-values for the aromatic solvents and a zero-value taken for dichloromethane. Then the susceptibility factor for the medium polarity, \( s = -1.8 \), the sign of which is consistent with the results from the Koppel-Palm equation (see also Fig. 1). We consider plausible that the observed contribution of the medium polarizability in case of both THF and diethyl ether mixtures is specific for phenylmagnesium halides and due to stabilizing \( \pi-\pi \) interactions in the transition state of the reaction as visualized in Scheme 1.
Fig. 1: Dependence of log k for PhMgBr in THF and in binary solvents on the medium polarity (Y) in terms of Koppel-Palm equation (open circles), and for the PhMgBr-THF complex on solvent bipolarity (π*) in terms of Kamlet-Taft equation (full circles).

The transition state can be slightly less polar than the initial complex, as the results above do indicate. However, regardless of the S_N reaction mechanisms among which our case can be classified, except the SET mechanism, a charge delocalization in the benzene ring must occur thus providing a chance for an actually specific interaction with aromatic solvent molecules in the transition state. The hypothesis will probably be verified by the density functional theory (DET) calculations of the reaction mechanism that are in progress.

MATERIALS AND METHODS

Materials. All the operations with the reagents and solutions were carried out under dry argon. The Grignard reagents in THF were prepared in the conventional manner. The reagents in binary solutions were obtained by dilution the Grignard reagent with appropriate amounts of the ether and/or of the nondonating solvent. The PhMgBr and THF complexes in nondonating solvents were prepared by evaporating the ordinary reagent solution at 15 mmHg and 20°C and dissolving the residue of stoichiometry PhMgBr \( \chi (3.38 \pm 0.03) \) THF in the nondonating solvent. A similar treatment of the initial reagent at 90°C leads to a complex PhMgBr \( \chi 1.83 \) THF.

Kinetic measurements. The reaction was carried out in a glass vessel mantled with foam plastic and placed in a thermostated housing. The equipment was sealed with a thermostated lid. The reaction cell was provided with a mechanical stirrer and a thermistor that was connected through a bridge circuit to a recording potentiometer. All parts of the equipment as well as the reagents were thermostated. The reaction vessel was purged thoroughly with pure argon, 15 ml of the Grignard reagent was cannulated into the cell and the stirring was started. After the thermal equilibrium was set 0.92 ml of hex-1-yne was introduced and the temperature change of the reaction solution (usually 0.1-0.2°C) was recorded as a plot of temperature (expressed in mm) versus time. Because the system was nearly adiabatic the heat exchange with the internal part of the calorimeter only caused a little heat loss. The zeroth-order initial rate constants in mol l\(^{-1}\)s\(^{-1}\) were obtained dividing the rate constants in mm s\(^{-1}\) determined as the slope of the tangent to the kinetic curve in its initial point, by the molar temperature rise of the reaction (in mm mol\(^{-1}\)). The latter was determined from the experiments with diethyl ether (see Ref. 10) and corrected for the heat capacity difference. The second-order rate constants were obtained by dividing the initial rate constants by initial concentrations of hex-1-yne and the Grignard reagents.
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REFERENCES

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