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THE REACTION OF GRIGNARD REAGENTS WITH 1,3-DIOXOLANES

II *. FURTHER ELABORATION OF THE MECHANISM

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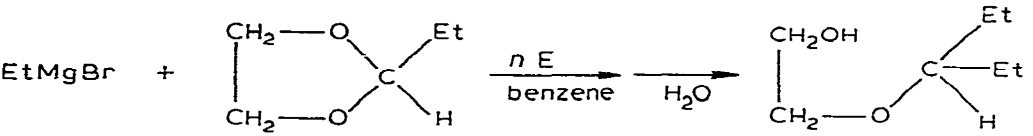
Summary

A kinetic study has been made of the reaction of $(EtMgBr \cdot Et_3N)_2$ with 2-ethyl-1,3-dioxolane. The results, considered along with new information on the degree of association of Grignard reagents in benzene, lead to reinterpretation and refinement of the mechanism.

Introduction

In the previous paper of this series [1] we reported on the investigation of the reaction of 2-ethyl-1,3-dioxolane (D) with ethylmagnesium bromide in benzene in the presence of small amounts of a basic solvent E (E = $i\text{-}Pr_2O$, Et_2O, THF-d_8; eq. 1).



(1)

It was shown that the reaction proceeds in part via a first order and in part via a second order mechanism, and that the rate of the reaction increases with decreasing basicity of E. Rate constants were derived for the different processes involved, based on plausible assumptions about the degree of association of ethylmagnesium bromide in benzene, namely that this compound, which is dimeric in benzene in the presence of one molar equivalent of E, reacts with additional E or D to form monomeric species (eq. 2), and that a large excess of D shifts the equilibrium completely in favour of $EtMgBr \cdot 2D$ (eq. 3). Whereas

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* For Part I: see ref. 1.

$$(\mathrm{EtMgBr}\cdot\mathrm{E})_2 + 2\mathrm{E}\ (\text{or D}) \rightleftharpoons 2\ \mathrm{EtMgBr}\cdot 2\mathrm{E} \qquad (2)$$

$$(\text{or } 2\ \mathrm{EtMgBr}\cdot\mathrm{E}\cdot\mathrm{D})$$

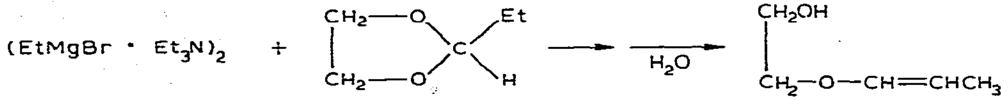
$$\mathrm{EtMgBr}\cdot\mathrm{E}\cdot\mathrm{D} + n\mathrm{D} \rightleftharpoons \mathrm{EtMgBr}\cdot 2\mathrm{D} + (n-1)\mathrm{D} + \mathrm{E} \qquad (3)$$

the latter of these assumptions is obviously still valid, experimental determination [2] of the degree of association of ethylmagnesium bromide in benzene in the presence of varying numbers of equivalents of a basic solvent has revealed that the dimer—monomer equilibria of eq. 2 are such that only on addition of considerable amounts of base does the monomeric species predominate in solution; this is certainly not the case for the ratio ErMgBr/E/D = 1/1/1. Although the main conclusions [1] about the mechanism are not affected by this new result it is necessary to reinterpret some of the quantitative aspects to take account of the presence of both dimeric and monomeric species in solution.

We have also measured the rates of the reaction of ethylmagnesium bromide with dioxolanes in benzene in the presence of triethylamine as the basic solvent E, and this has furneshed additional confirmation of the mechanism of ring cleavage of dioxolanes by Grignard reagents.

Results and discussion

The reaction of ethylmagnesium bromide with D in benzene in the presence of triethylamine showed first order kinetics, as observed for ethers as basic additives. However, the situation was more complex in that alongside the normal ring-cleavage/addition reaction represented by eq. 1, a side reaction occurred to a degree which depended on the conditions. This side reaction consisted of a ring-cleavage/elimination sequence, leading to the formation of a β-hydroxyethyl enol ether (eq. 4).



(4)

The scope and mechanism of this reaction will be discussed in detail in the next paper [3]; it has been shown that the rate-determining step is presumably the same for both reaction pathways, and that the two products are subsequently formed from a common intermediate [3]. For this reason, the kinetic results are directly comparable with those obtained with the three ethers as basic solvent E [1]. They were obtained as previously described [1] by measuring the disappearance of characteristic peaks in the ^{1}H NMR spectrum; the experimental overall first order rate constants $k_{1\text{exp}}$ were determined by plotting ln c vs. time, c being the concentration of the reactant which was not in excess. The dependence of $k_{1\text{exp}}$ on different ratios $[\mathrm{D}]/[\mathrm{EtMgBr}]_0$ is shown in Table 1, and is compared with the previously determined [1] values of $k_{1\text{exp}}$ for E in Fig. 1.

As mentioned in the introduction, the recent determination of the degrees of association of ethylmagnesium bromide in benzene with different bases E requires reinterpretation of the results on the basis of a system of dimeric and monomeric species depicted in Scheme 1.

Each of the four components of Scheme 1 containing D can give rise to

TABLE 1

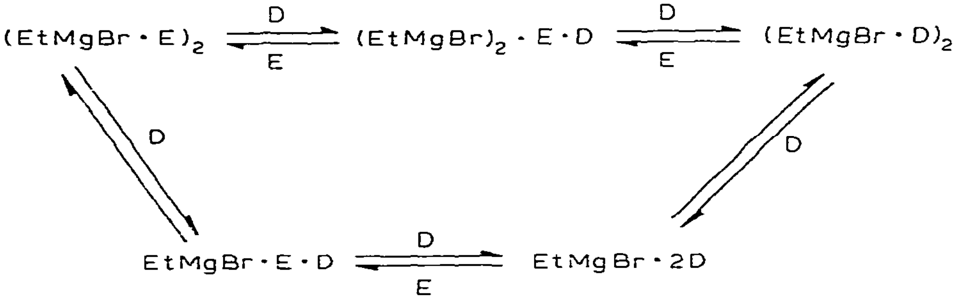
EXPERIMENTAL FIRST ORDER RATE CONSTANTS FOR THE REACTION OF $(EtMgBr \cdot Et_3N)_2$ [a] WITH D IN BENZENE AT 40.5°C AT VARYING RATIOS $[D]_0/[EtMgBr]_0$ [b]

$[EtMgBr]_0$	$[D]_0$	$[D]_0/[EtMgBr]_0$	$(k_{1exp} \pm \sigma) \times 10^5$ [c]
0.310	2.078	6.7	2.41 ± 0.19
0.195	0.530	2.7	3.20 ± 0.66
0.349	0.702	2.0	4.14 ± 0.24
0.278	0.288	1.04	4.61 ± 0.33
0.315	0.182	0.58	8.68 ± 0.42
0.238	0.0559	0.23	12.6 ± 0.99
0.242	0.0545	0.15	14.8 ± 4.56
0.239	0.0272	0.11	14.5 ± 1.84

[a] The ratio $[EtMgBr]_0/[Et_3N]_0$ was 1/1.26. The solution contained excess $MgBr_2$; the ratio $[EtMgBr]_0/[MgBr_2]_0$ was 8.1/1.0. [b] The index 0 stands for starting concentration at zero time. [c] σ is standard deviation of the mean.

product formation, so that the situation becomes too complicated for a simple straightforward analysis as previously [1] applied. In particular, it is not justified to equate k_{1exp} at $[D]/[EtMgBr] = 1$ with the rate of reaction $EtMgBr \cdot E \cdot D$, as the assumption that this complex is essentially the only one present in solution at this point no longer holds. Consequently, it is not possible to determine rate constants for the individual species. However, in qualitative terms, the previously proposed mechanism [1] still holds, and indeed is supported by the results with triethylamine.

SCHEME 1 *



At relatively low concentrations of D (at a ratio of $[D]_0/[EtMgBr]_0$ of about 2 or lower), D will be incorporated mainly into the complex $(EtMgBr)_2 \cdot E \cdot D$; this, of course, depends also on the basicity of E, a more basic E shifting the limit to lower ratios [2]. This complex (r) will react either via a first order pathway (A) or a second order pathway (B) (Scheme 2). In the first order reaction pathway A, complex r passes through the transition state s to the oxocarbonium ion u (see also Fig. 2). In addition to the evidence presented previously [1] the existence of a discrete intermediate u must be postulated for two reasons. First, it is obvious that the movement of the electrons required for a concerted process,

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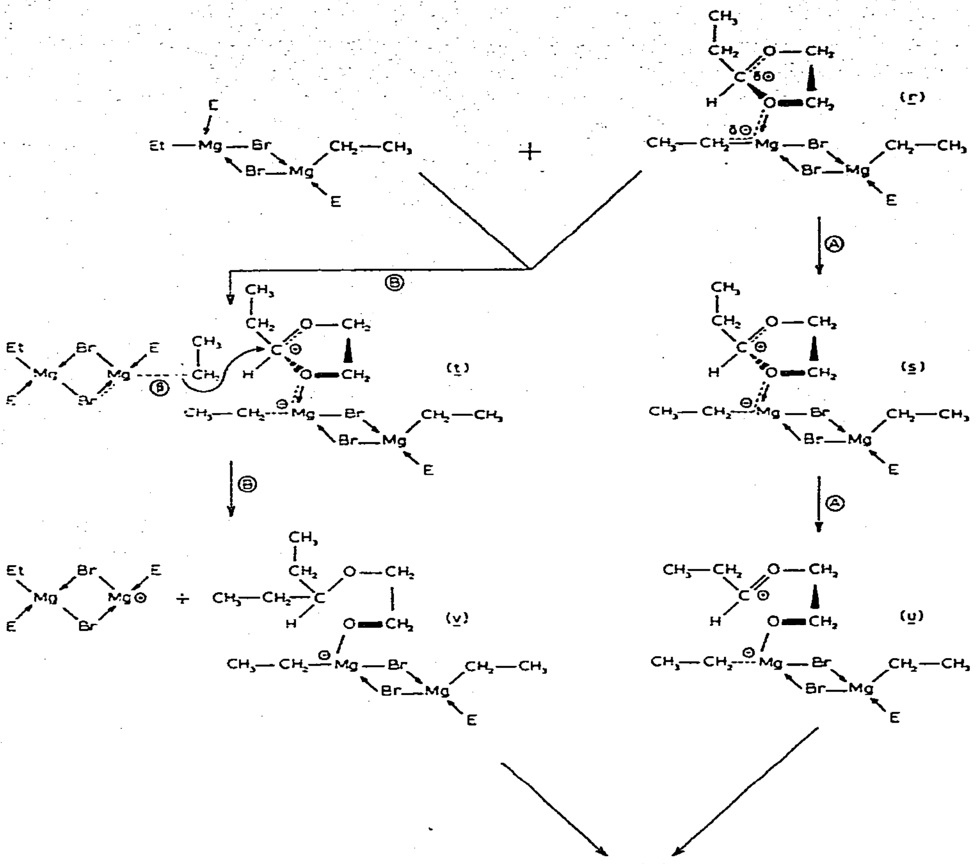
* No dimers containing three molecules of a base (such as $(EtMgBr \cdot E)_2 \cdot E$) have been considered in this scheme, which is probably justified except possibly for E = THF [2].



SCHEME 2

i.e. simultaneous shift from O(1) via C(2) and O(3) to Mg combined with a transfer of the ethyl anions from Mg to C(2), is unlikely to be concerted for stereoelectronic reasons. Secondly, the formation of two products in the case of the reaction in the presence of excess triethylamine (addition as well as elimination) at the same rate would be very unlikely if they did not come from the common intermediate u. On the other hand, it should be noticed that u cannot be a very stable intermediate, since the reaction of $(EtMgBr \cdot E)_2$ ($E = Et_2O$ or Et_3N) with *cis*- and *trans*-2-ethyl-4-methyl-1,3-dioxolane no *cis*—*trans* isomerization was observed in the unchanged starting material [3]. From u, the reaction may be envisaged to proceed very rapidly to the addition products via a four-center transition state, as postulated for the addition of Grignard reagents to ketones [4]. Therefore, the solid line in Fig. 2 seems to be a reasonable representation of pathway A.

The second order pathway B becomes prominent when a high concentration of dimeric species such as $(EtMgBr \cdot E)_2$ is present (very low ratio of $[D]_0/[EtMgBr]_0$). As has been pointed out previously, this pathway also gives rise to first order kinetics, because the excess of Grignard reagent is not consumed in the reaction. Essentially, the sequence of steps involved in ring opening of the dioxolane (Scheme 2) is similar to that of pathway A.

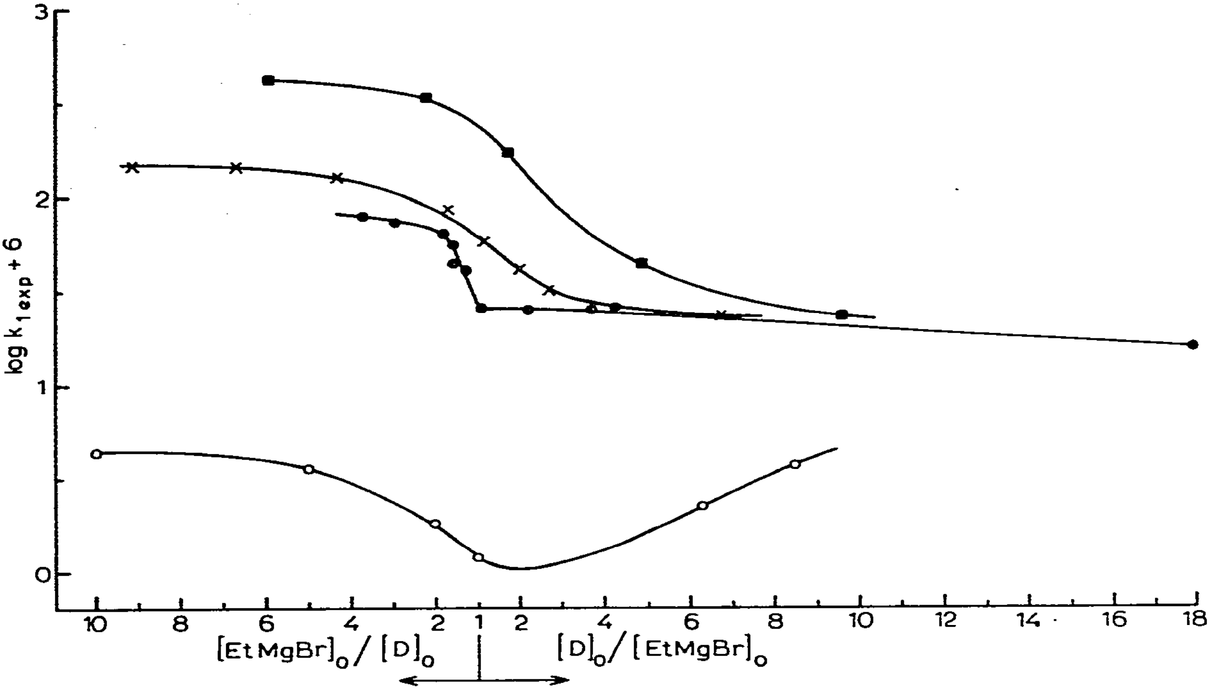


Fig. 1. Experimental first order rate constant for the reaction of (EtMgBr · E)$_2$ with D vs. [EtMgBr]$_0$/[D]$_0$ or [D]$_0$/[EtMgBr]$_0$, respectively, E = i-Pr$_2$O (■) [1], Et$_3$N (x), Et$_2$O (●) [1] and d8-THF (○) [1].

A number of factors may be responsible for the rate enhancement of pathway B over pathway A. The main one is probably that the formation of the energetic intermediate u is more or less circumvented by (nearly) simultaneous cleavage of the C(2)—O(3) bond and attack of the ethyl group from the second, uncoordinated dimer on C(2). In contrast to the situation in r, stereoelectronic requirements for this process are geometrically feasible in t. This process is further facilitated with dimeric species, because the charges generated in its course can be better accommodated than in monomeric species, the excess of electron density (and electron deficiency) being distributed over more bonds (cf. v). Moreover, a comparison of the crystal structures of monomeric (e.g. EtMgBr · 2Et$_2$O [5]) and dimeric species (e.g. [EtMgBr · i-Pr$_2$O]$_2$ [6]) reveals that in

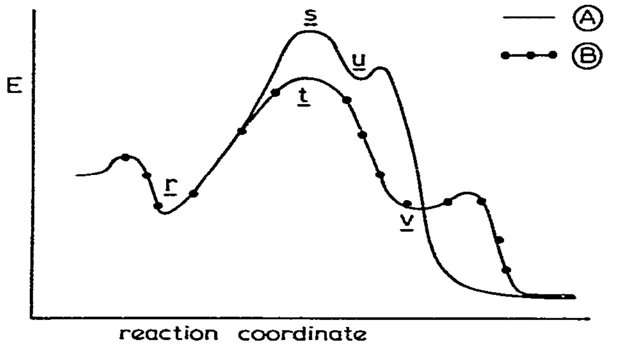


Fig. 2. Energy diagram for the reaction of ethylmagnesium bromide with 1,3-dioxolanes.

the latter the valence angle C—Mg—O (≈120°) is larger than in the former (≈110°). Therefore, the ethyl group in the complexed dimer (pathway A or B) is farther removed from C(2) of the dioxolane and in a less favourable position for transfer; on the other hand, the larger angle makes the ethyl group in the second dimer of pathway B more exposed and more available for attack on C(2).

At higher ratio's $[D]_0/[EtMgBr]_0$, EtMgBr · E · D and especially EtMgBr · 2D will be the predominating species, and the reaction will take a course which, mutatis mutandis, will be essentially that of pathway A (Scheme 2).

Experimental

The experimental procedures were as previously described [1].

Acknowledgement

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