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Abstract

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INTERACTION OF ORGANOMAGNESIUM COMPOUNDS WITH ALKYL HALIDES IN DIMETHOXYETHANE SOLUTION

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The first systematic study of the interaction of Grignard reagents with alkyl halides was undertaken by Späth in 1913 ([1]). In contrast to Abegg ([2]), who considered the principal reactions of organomagnesium compounds to be ionic, Späth, on the basis of his experiments, came to the conclusion that the interaction of Grignard reagents with alkyl halides proceeds through the formation of free radicals:

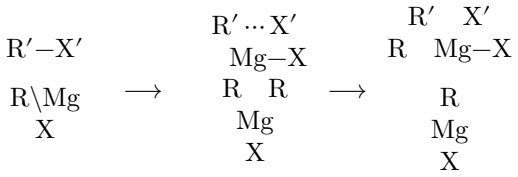
$$\mathrm{RMgX} + \mathrm{R'X'} \rightarrow \mathrm{MgXX'} + \mathrm{R}\cdot + \mathrm{R'}\cdot$$

It is characteristic in this connection that, with primary saturated R and R', the products of the "normal" Wurtz reaction were practically absent among the reaction products (except for the case $R = R' = \mathrm{CH_3}$):

$$\mathrm{RMgX} + \mathrm{R'X'} \rightarrow \mathrm{MgXX'} + \mathrm{RR'}$$

The products formed were mainly those of disproportionation of the free radicals $R\cdot$ and $R'\cdot$ ($\mathrm{RH} + \mathrm{R}_{-H}$). In the case of secondary and tertiary R', partial formation of the hydrocarbons RR or $R'R'$ was also observed. Subsequently, the work of many authors showed that the formation of appreciable quantities of RR' hydrocarbons takes place only in the case of allylic-type radicals and highly branched (tertiary) radicals ([3]).

The absence of RR' hydrocarbons in amounts even approximately close to statistical, and the high reactivity of free aliphatic radicals, which inevitably react with the solvent, make, in Kharasch' s opinion ([3]), a free-radical course of the reaction highly improbable. In those cases where formation of RR' nevertheless does occur (for example, with $R' = \mathrm{C_6H_5CH_2}$), an alternative scheme is the "push-pull" scheme with intermediate formation of a quasi-six-membered ring ([3]):



However, Letsinger ([4]) showed that, in the reaction of benzylmagnesium chloride with *l*-2-bromobutane (yield of 1-phenyl-2-methylbutane 17%), racemization occurs to the extent of 91% and inversion only to the extent of 9%, which argues against the scheme given above.*

In addition, in the reactions of methylmagnesium halides with certain secondary alkyl halides, significant amounts of methane are nevertheless formed ([1]).

Thus, when the principal studies carried out in this field are considered, the question of the mechanism of the interaction of organomagnesium compounds with alkyl halides remains unclear. The totality of the data available in the literature leaves open both schemes for the decomposition of alkylmagnesium halides in the presence of alkyl halides.

It could be supposed that, if in the interaction of reagents

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* In the case of sodium-organic compounds, the Wurtz reaction proceeds with retention of optical activity (inversion) ([5,6]).

of Grignard reagents with alkyl halides the "normal" Wurtz reaction proceeds as a reaction of heterolytic exchange, then the use of strongly solvating solvents, which facilitate nucleophilic substitution reactions, will promote this reaction:

$$\mathrm{R{:}MgX} + \mathrm{R'{:}X} \rightarrow \mathrm{RR'} + \mathrm{MgXX}.$$

For this purpose, in the present work we studied the interaction of *n*-alkylmagnesium halides with alkyl halides in a solution of ethylene glycol dimethyl ether (dimethoxyethane, DME), which is a strongly solvating solvent. We found that, in this solvent, methyl iodide and ethyl iodide and bromide readily react with organomagnesium compounds with the formation of considerable amounts of products of the "normal" Wurtz reaction; moreover, in the case of lower RMgX and CH_3J this reaction pathway proves to be the principal one, and the main reaction products are hydrocarbons RCH_3:

$$\mathrm{RMgX} + \mathrm{CH_3J} \xrightarrow{\mathrm{DME}} \mathrm{RCH_3} + \mathrm{MgXJ}.$$

When this reaction is carried out in a dimethoxyethane solution, not only the main direction of the process is characteristic, but also the ease with which it pro-

ceeds. If the interaction of Grignard reagents with alkyl halides in ether occurs only upon prolonged heating of their mixture ([1],[7]), then in dimethoxyethane the reaction proceeds with the evolution of heat. Methyl iodide reacts so readily with methylmagnesium iodide that, under ordinary conditions, the latter cannot be obtained at all in dimethoxyethane, since the reaction immediately proceeds further:

$$Mg + 2CH_3J \xrightarrow{DME} MgJ_2 + C_2H_6.$$

Similarly, ethylmagnesium iodide could not be obtained in dimethoxyethane from ethyl iodide.

In the interaction of organomagnesium compounds with alkyl halides in a dimethoxyethane solution, along with hydrocarbons RR′, a mixture of hydrocarbons RR, R′R′, RH, R_{-H}, R′H, and R'_{-H} is formed.

The results of the experiments are summarized in Table 1.

On the basis of these data (Table 1), the general scheme of the interaction of alkylmagnesium halides with alkyl halides in dimethoxyethane can be represented as follows:

$$RMgX + R'X' \rightarrow RR' + RR + R'R' + R_H + R_{-H} + R'_H + R'_{-H}.$$

In considering the data of Table 1, it should be borne in mind that in experiment 2 the hydrocarbon RH and R′R′ is ethane, and in experiments 6 and 7 R—R, R—R′, and R′R′ are butane; therefore it was not possible to determine their origin.

Comparison of the data obtained in the study of this reaction in diethyl ether solution with our data shows that the transition to a more solvating solvent led to a substantial increase in the amount of products of the "normal" Wurtz reaction.

The formation of considerable amounts of products of the "normal" Wurtz reaction in a strongly solvating solvent medium (dimethoxyethane) appears, in our opinion, to be convincing evidence in favor of the heterolytic character of this reaction.

The formation of "dimeric" products RR and R′R′ can be explained in two ways. Kharasch ([3]) assumes that dimeric products are formed through free radicals R· and R′·.

It seemed to us that their formation could be explained by an exchange reaction:

$$RMgX + R'X \rightleftharpoons RX + R'MgX$$

with the subsequent "normal" Wurtz reaction:

$$RMgX + RX \rightarrow RR + MgX_2, \qquad RMgX + R'X \rightarrow R'R' + MgX_2.$$

Indeed, we found that, when amylmagnesium bromide and methyl iodide were mixed in dimethoxyethane even at a temperature of 0-5°, there rapidly pro-

redistribution of radicals occurs, and upon hydrolysis of the reaction mixture 31.7% methane is evolved:

$$n\text{-}C_5H_{11}MgBr + CH_3J \overset{DME}{\rightleftharpoons} CH_3MgBr + n\text{-}C_5H_{11}J.$$

An analogous exchange takes place under the same conditions in the system n-$C_8H_{17}MgBr + CH_3J$ (20.7% methane upon hydrolysis).

The reaction of radical redistribution in the system $RMgX + R'X'$ is therefore a side process in the "normal" Wurtz reaction and, if the exchange rate is sufficiently high, can suppress it. This explains the lower yield of pentane and hexane from n-C_4H_9MgBr and n-$C_5H_{11}MgBr$ and CH_3J: the CH_3MgJ formed reacts more readily with CH_3J than with C_4H_9X and $C_5H_{11}X$, and methyl groups are removed from the reaction sphere in the form of ethane (Table 1).

Table 1

Interaction of alkylmagnesium halides with alkyl halides in dimethoxyethane at 70°

No.	RMgX	R′X′	R–R′	RH	R–H	R′H	R′–H	R–R	R′–R′
1	$[CH_3MgJ]^*$	CH_3J	91	–	–	1.3	–	–	–
2	C_2H_5MgBr	CH_3J	54.8	12.9	7.0	0.7	–	5.3	–
3	C_3H_7MgBr	CH_3J	68.5	13.7	9.0	0.5	–	10.3	8.1
4	C_4H_9MgBr	CH_3J	40.6	9.5	3.4	2.5	–	–	17.5
5	$C_5H_{11}MgBr$	CH_3J	26.5	18.7	11.3	1.6	–	–	14.2
6	$[C_2H_5MgJ]^*$	C_2H_5J	30.8	26.7	24.9	–	–	–	–
7	C_2H_5MgBr	C_2H_5Br	50.5	6.5	7.5	–	–	–	–
8	C_3H_7MgBr	C_2H_5J	49.3	0.2	0.2	16.5	9.9	–	1.2

* In the interaction of alkyl iodides with magnesium, the alkylmagnesium iodide formed immediately enters into reaction with the alkyl iodide.

The formation of free methyl radicals in the interaction of alkylmagnesium halides with methyl iodide should also be excluded because, in our experiments, it was shown that methyl radicals formed during the photolysis of dimethylmercury in dimethoxyethane readily react with the solvent, giving

mainly methane. Free ethyl radicals formed during the photolysis of diethylmercury in dimethoxyethane likewise recombine only to an insignificant extent (Table 2). In our experiments on the interaction of methyl iodide with organomagnesium compounds, however, the amount of methane was only 1-2%. The mechanism of formation of hydrocarbons R and R—H requires further study. To explain their occurrence, the assumption of the formation of free radicals is also not necessary [6].

Table 2

Photolysis of dialkylmercury in dimethoxyethane

HgR_2	CH_4	C_2H_6	C_2H_4	C_4H_{10}
$Hg(CH_3)_2$	66	34	–	–
$Hg(C_2H_5)_2$	–	76.5	14.7	9.8

Although, as is evident from the data presented above, in the presence of strongly solvating solvents the "normal" Wurtz reaction proceeds as a heterolytic substitution, in an inert solvent homolytic cleavage of the C–Mg bond may occur. As Kharash and Urry [8] showed, the thermal reaction between alkylmagnesium halides and alkyl halides in isopropylbenzene (100°) proceeds with the formation of considerable amounts of dicumyl, which indicates the free-radical character of the process.

A hydrocarbon solvent and dimethoxyethane, which has a high solvating power, are two, to a certain extent, limiting cases–

partly. In solvents occupying an intermediate position, the predominant character of cleavage of the C–Mg bond depends on the nucleophilic mobility of the halogen in the alkyl halide R′X. In the presence of a sufficiently mobile halogen atom (for example, in tertiary alkyl halides, allyl halides, and benzyl halides), favorable conditions are created for a heterolytic reaction leading to the formation of products of the "normal" Wurtz reaction, which apparently is what occurs in the formation of the hydrocarbons RR′ in ether (in those cases where they are formed).

In this connection, the assertion of Kharasch (6) seems unfounded that Fuson (9), who studied the interaction of benzyl chloride with methylmagnesium iodide, could not have obtained ethane, since the methyl radicals, at whose expense it might have been formed, should react with the solvent. There is every reason to suppose that Fuson, along with ethylbenzene (23-27%), which was formed in the heterolytic "normal" reaction, did indeed have ethane, and not methane, as Kharasch asserts. Ethane could also be formed without the participation of free methyl radicals, according to a scheme analogous to that given above:

$$C_6H_5C_2H_5 + MgClJ \leftarrow C_6H_5CH_2Cl + CH_3MgJ \rightleftarrows C_6H_5CH_2MgCl + CH_3J,$$

$$CH_3MgJ + CH_3J \rightarrow MgJ_2 + C_2H_6,$$

$$C_6H_5CH_2MgCl + C_6H_5CH_2Cl \rightarrow C_6H_5CH_2CH_2C_6H_5.$$

Thus, the data we have obtained on the interaction of organomagnesium compounds with alkyl halides in dimethoxyethane solution allow us to consider that the "normal" Wurtz reaction

$$RMgX + R'X' \rightarrow RR' + MgXX'$$

proceeds (at least in solvating solvents) not by a radical, but by a heterolytic mechanism, and that the formation in this reaction of dimeric compounds RR and R′R′ as by-products is due not to the intermediate formation of free radicals $R\cdot$ and $R'\cdot$, but to the parallel exchange reaction

$$RMgX + R'X' \rightleftarrows RX' + R'MgX$$

and subsequent "normal" Wurtz reactions

$$RMgX + RX' \rightarrow RR$$

and

$$R'MgX + R'X' \rightarrow R'R'.$$

Experimental Part

Interaction of alkylmagnesium halides with alkyl halides in dimethoxyethane. a) To a solution of a Grignard reagent (from 0.1 mole of alkyl halide) in 35 ml of dimethoxyethane, 0.1 mole of alkyl halide in 20 ml of dimethoxyethane is added at 70° over 1.5 hours; the mixture is stirred at the same temperature for another 2.5 hours, and the product mixture is distilled off. Analysis of the mixture is carried out on a capillary chromatograph with a flame-ionization detector. The results obtained are presented in Table 1.

b) To a solution of amylmagnesium bromide (from 0.1 mole of amyl bromide) in 35 ml of dimethoxyethane, 14.2 g (0.1 mole) of methyl iodide in 20 ml of dimethoxyethane is added at 0–5°; the mixture is stirred at the same temperature for 20 min and hydrolyzed. 747 ml of methane is evolved (31.7%).

When the reaction is carried out with octylmagnesium bromide under analogous conditions, after hydrolysis 20.7% of methane is evolved.

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Note: Figure translations are in progress. See original paper for figures.