Isotope Effect in the Decomposition of Grignard Compounds by Ordinary Phenol and a Sterically Hindered Phenol

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Measurements of the hydrogen isotope effect in the hydrolysis and methanolysis of a number of Grignard compounds in different solvents and under different conditions have been reported in earlier papers¹⁻⁴. Decomposition of Grignard compounds by tritiated phenols has now been carried out. In a series of experiments methylmagnesium iodide and *sec*-butylmagnesium bromide have been decomposed by ordinary phenol, C_6H_5OH , in which tritium has been partially introduced into the hydroxylic position. In another series of experiments the same Grignard compounds have been decomposed by a phenol with steric hindrance, 2,6-di-*tert*-butyl-4-methyl-phenol (called "lonol"), in which tritium has also been partially introduced into the hydroxylic group.

As it seems possible that the reaction mechanism should include a coordination of the hydroxylic compound to the magnesium atom in the Grignard compound (analogous to the coordination of ethers to Grignard compounds), the idea with the present experiments has been to investigate the effect of steric hindrance on this coordination. It is known from v. Braun and Kirschbaum⁵ that steric hindrance can render some Grignard reactions impossible. These investigators state that the Grignard compound of [β -chloroethyl] methyl-aniline does not react with ketones though very well with aldehydes. On the other hand a Grignard compound of [γ -halogenopropyl]-methyl-aniline reacts with ketones as well as with aldehydes.

From its reactions it is obvious that 2,6-di-*tert*-butyl-4-methyl-phenol with its branched alkyl groups in the positions *ortho* to the hydroxylic group will offer strong steric hindrance to reactions concerning the latter. For example the compound is not soluble in aqueous sodium hydroxide or potassium hydroxide and it does not give the colour with ferric chloride solution characteristic of phenols⁶.

Esterification is also retarded⁶. On the other hand it reacts with Zerewitinoff reagent (methylmagnesium iodide) in the usual manner with formation of methane⁶.

The isotope effect in the decompositions by ordinary phenol, given in Table 1, is of the same order of magnitude as those obtained in the hydrolysis and methanolysis.

The isotope effect in the corresponding reactions with lonol, as shown in Table 2, deviates considerably from those obtained with ordinary phenol, methanol and water, but they are not of the same order of magnitude as a "full" hydrogen isotope effect.

The rather large values of k_T/k_H , obtained in the decompositions by phenol, methanol and water, could be explained by a reaction mechanism consisting of a slow coordination of the hydroxylic compound to the Grignard compound followed by a rapid proton transfer with formation of a hydrocarbon (*cf.* Wiberg⁷).

Lonol, on the other hand, could be expected not to be able to be coordinated to the Grignard compounds for steric reasons. If, nevertheless, the coordination takes place, it must be slower than the coordination of ordinary phenol and must consequently give larger ratios k_T/k_H than in the case of ordinary phenol. Actually the experiments give smaller ratios in the case of the phenol with steric hindrance. Therefore the mechanism discussed above can be eliminated, at least for the hindered reaction.

The fact that the reactions with the sterically hindered phenol take place at all (giving about the same ratio k_T/k_H with methylmagnesium iodide and with *sec*-butylmagnesium bromide) indicates, that they are at least partly of dissociative nature. Consequently the phenol must dissociate off its hydroxylic proton, which in some way later reacts with the Grignard compound or with an alkyl carbanion derived from the Grignard compound with formation of the corresponding hydrocarbon. This seems to be in accordance with one of the mechanisms mentioned by Wiberg⁷, who, however, obtained ratios k_D/k_H larger than unity in his methanolysis experiments. If the cleavage of the hydroxylic oxygen-hydrogen bond is supposed to be partly rate determining, it seems natural that the isotope effect should be more pronounced in the case of the hindered phenol than in the ordinary one, since the cleavage is likely to be slower

Table 1. Decomposition of Grignard compounds with phenol-t in *n*-butyl ether at 20°C.

Grignard compound	k_T/k_H	Number of parallel determinations of tritium in combustion water	Mean value (including error in determination of tritium in combustion water from the phenol)
Methyl-Mg iodide	0.757	2	0.78 ± 0.06
	0.814	1	
	0.734	1	
	0.810	2	
<i>Sec</i> -butyl-Mg bromide	0.738	1	0.79 ± 0.06
	0.822	1	
	0.795	1	

and hence more strongly rate-determining in the case of the former.

The Grignard reagents used in the experiments were solutions of the appropriate Grignard compounds in *n*-butyl ether. In the case of *sec*-butylmagnesium bromide part of the solvent plus the "false" butane was distilled off under reduced pressure immediately prior to every decomposition with the phenols⁴. The *n*-butyl ether used as solvent was dried by refluxing over and distillation from metallic sodium. The tritiated phenols were prepared by addition of tritiated water to a solution of the appropriate phenol in an organic solvent. In the case of phenol-t the tritiated water,

ethyl ether and ordinary phenol were mixed after which the tritiated phenol was isolated by distilling under reduced pressure. Lonol-t was prepared in an analogous manner with the difference that a mixture of ethyl ether and ethanol was used as solvent, because the tritiated water used in this case had a smaller specific activity than that used in the phenol-t preparation, for which reason a larger amount of water must be used and consequently also a solvent being able to dissolve more water. The lonol-t was isolated by distilling off the solvent and water in vacuum.

As it is known that an exchange between hydrogen in the hydroxylic group and hydrogen in the benzene ring occurs with phenols,

Table 2. Decomposition of Grignard compounds with lonol-t in *n*-butyl ether at 20°C.

Grignard compound	k_T/k_H	Number of parallel determinations of tritium in combustion water	Mean value (including error in determination of tritium in combustion water from the lonol)
Methyl-Mg iodide	0.307	1	0.29 ± 0.03
	0.299	1	
	0.274	1	
<i>Sec</i> -butyl-Mg bromide	0.306	1	0.33 ± 0.04
	0.322	1	
	0.347	1	

especially at higher temperatures⁸, it was necessary to investigate whether and to what extent such an exchange had taken place in the preparations of phenol-t and lonol-t. The possible transition of tritium from the hydroxylic group to the benzene ring should of course give too small tritium activities in the hydrocarbons evolved with the Grignard compounds.

The check of this exchange proceeded in the same manner as described by Kukhtenko⁹. Tritium in the hydroxylic group of the ordinary phenol was washed off by dissolving the phenol in a large volume of 2 % aqueous sodium hydroxide. The phenolate solution was acidified and the phenol was extracted by benzene. The extract was dried with anhydrous calcium chloride and distilled for isolation of phenol free from tritium in the hydroxylic group. In the case of lonol-t, which is not soluble in sodium hydroxide, the method was modified. The tritiated lonol was dissolved in 96 % ethanol, after which ordinary water was added in portions while shaking the mixture until lonol began to precipitate. The precipitated crystals were carefully washed with much water and dried.

The phenols free from hydroxylic tritium were burned over cupric oxide like the initial tritiated phenols, and the radioactivity of the combustion water after reduction to hydrogen was determined by means of a Geiger-Müller counter. The activities thus obtained indicate that the tritiated phenols are practically free from tritium in the benzene rings.

The technique of the Grignard decompositions was the same as the one used earlier, *i. e.* the Grignard reagent in *n*-butyl ether solution was added by means of an injection syringe to a solution of the phenol in the same solvent. The phenols were present in excess over the Grignard compounds.

The tritiated phenols and the hydrocarbons formed in the decompositions were burned over cupric oxide and the radioactivity of the combustion water was determined (after reduction to hydrogen) in the same manner as in the case of the detritiated phenols.

The ratios k_T/k_H in the tables have not been corrected for the change in the isotopic composition of the phenols taking place during the reaction.

3. Assarsson, L. O. *Acta Chem. Scand.* **11** (1957) 1283.
4. Assarsson, L. O. *Acta Chem. Scand.* **12** (1958) 1547.
5. v. Braun, J. and Kirschbaum, G. *Chem. Ber.* **52** (1919) 1725.
6. Stillson, G. H., Sawyer, D. W. and Hunt, C. K. *J. Am. Chem. Soc.* **67** (1945) 303.
7. Wiberg, K. B. *J. Am. Chem. Soc.* **77** (1955) 5987.
8. Ingold, C. K., Raisin, C. G. and Wilson, C. L. *J. Chem. Soc.* **1936** 1637.
9. Kukhtenko, I. I. *Doklady Akad. Nauk. SSSR* **93** (1953) 487.

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Isotope Effect in the Methanolysis of *n*-Butylmagnesium Bromide.

A Reinvestigation

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In a previous preliminary paper¹ measurements of the hydrogen isotope effect in the methanolysis of *n*-butylmagnesium bromide have been reported. The ratios k_T/k_H obtained in those experiments diverge considerably, the ratio obtained with the freshly prepared Grignard reagent being larger than those obtained with an

Table 1. Results in the decomposition of *n*-butylmagnesium bromide with methanol in *n*-butyl ether at 20°C.

k_T/k_H	Number of parallel determinations of tritium in combustion water	Mean value (including error in determination of tritium in combustion water from the methanol)

1. Assarsson, L. O. *Acta Chem. Scand.* **9** (1955) 1399.
2. Assarsson, L. O. *Acta Chem. Scand.* **10** (1956) 1509.

1.014	1	1.00 ± 0.03
1.002	1	
1.006	2	
0.978	1	