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THE OPTICAL ACTIVITY OF ETHERS SOLVATING GRIGNARD COMPOUNDS.

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It is generally known that reactions of Grignard compounds are influenced by the solvent. This can be ascribed to the strong interaction between the reagent and the solvent,which makes the latter "an integral part of the molecules of the organomagnesium compounds" (1). One way to make use of these solvent effects is asymmetric synthesis with Grignard compounds in optically active ethers (2). Our interest (3) in the structure of the Grignard reagent has lead us to investigate the role of the solvent in the Grignard complex with the aid of optically active ethers. Related investigations were reported in the field of organo-aluminium (4) and organolithium compounds (5). We wish to report some of our preliminary results,showing the diversity of applications of this method in the Grignard field.

A In the first place we determined the influence of complex formation on the optical activity of ethers in the presence of one molar equivalent of ethylmagnesium bromide with benzene as solvent. The results,listed in TABLE I,indicate that the influence of complex formation on the optical activity of the ethers varies with the structure of the ether.

TABLE I

Run	Optically active ether	$[\alpha]_D$ of the free ether	$[\alpha]_D$ of the complexed ether
a	(+)(S)-1-ethoxy-2-methylbutane[x]	+ 0.95°	+ 16.0°
b	(+)(S)-1-n-octyloxy-2-methylbutane[x]	+ 1.25°	+ 12.5°
c	(-)(R)-2-ethoxybutane[xx]	- 1.60°	- 1.60°

[x] optical purity 95% ; contaminated with 5% 1-alkoxy-3-methylbutane.
[xx] optical purity approximately 4% (see ref. 4).

It is remarkable that the optical activity of (-)(R)-2-ethoxybutane is unaffected by ethylmagnesium bromide. In this connection it is interesting to mention the unsuccessful attempts of Tarbell and Paulson (6) to obtain asymmetric synthesis with Grignard compounds solvated by this ether, contrary to successful asymmetric synthesis with the other two ethers (2). This suggests a correlation between the degree of asymmetric synthesis and the change in optical activity of the ether[xxx].

B When another solvating agent is added to a Grignard solution containing an ether, a competitive solvation will occur. This assumption forms e.g. the basis of the Meisenheimer theory of the reaction of Grignard reagents with carbonyl compounds. The enhancement of the optical activity of certain complexed ethers (TABLE I) makes it

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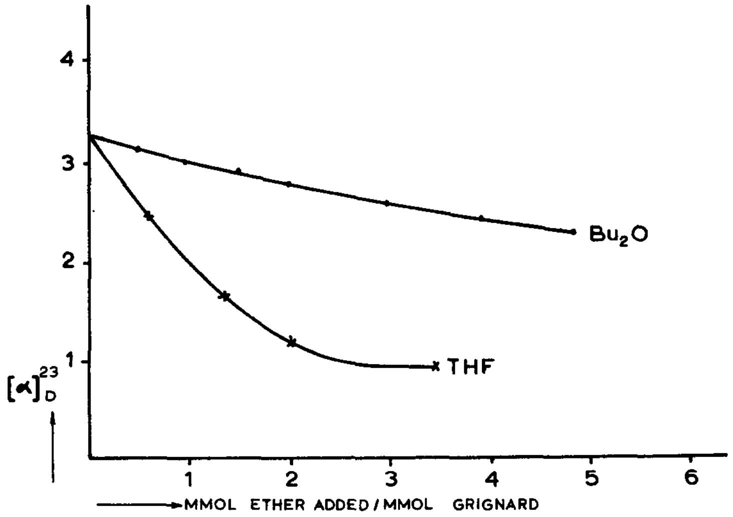
[xxx] It has to be considered however that one molar equivalent (-)(R)-2-ethoxybutane does interact with ethylmagnesium bromide in benzene solution, since ethylmagnesium bromide itself is insoluble in benzene.

possible to investigate this competitive solvation:

To a solution of ethylmagnesium bromide and seven molar equivalents of (+)(S)-1-ethoxy-2-methylbutane in benzene several small portions of either tetrahydrofuran (THF) or of di-n-butyl ether were added up to a total amount of approximately 4 molar equivalents per mole ethylmagnesium bromide. After the addition of each portion the specific optical activity of (+)(S)-1-ethoxy-2-methylbutane could be calculated from the rotation of the solution.The results,plotted in FIG.I,indicate clearly the strong basicity of THF compared with di-n-butyl ether:the addition of 3.5 molar equivalents of THF is sufficient to reduce the specific activity of (+)(S)-1-ethoxy-2-methylbutane to its neat value of + 0.95°. Thus this method opens an elegant way of measuring the scarcely known relative basicities of ethers towards organomagnesium compounds. A quantitative evaluation of the results requires measurements of association numbers, work which is in progress.

FIG.I



A further example of the versatility of optical rotation measurements on Grignard solutions is the reaction between the 1:1 complex of ethylmagnesium bromide and (+)(S)-1-n-octyloxy-2-methylbutane in benzene and one molar equivalent of 2-ethyl-1,3-dioxolane. The enhanced optical activity of the ether was reduced to about one half of its original value within three minutes after the addition of the dioxolane (the time necessary for homogenizing the solution). Thereafter the reaction (7) between the Grignard compound and the dioxolane could be followed by measuring the change of the rotation of the solution versus time. The results are listed in TABLE II:

TABLE II

Run	T (°K)	$k_1 \times 10^5$ (sec^{-1})	
1	298.1	1.12 ± 0.016	$E = 21.7$ kcal
2	299.6	1.54 ± 0.025	$\log A = 11.01$ sec^{-1}
3	303.9	2.57 ± 0.017	$\Delta H^{\ddagger} = 21.1$ kcal
4	309.3	4.97 ± 0.072	$\Delta S^{\ddagger} = -10.2$ e.u.
5	315.95	9.11 ± 0.12	

This reaction followed first order kinetics. The activation energy E and the frequency factor log A were calculated by means of the method of the least squares from the Arrhenius equation, the activation enthalpy and the activation entropy from the Eyring equation. The activation entropy is more negative than was found for the acid-catalyzed hydrolytic cleavage of 2-alkyl substituted-1,3-dioxolanes (8,9). Work on the possible implication of this result on the precise nature of the transition state is in progress.

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