COMPLEXATION AND SELF-ASSOCIATION OF METHYL ARYL ETHERS

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Abstract—Previous evidence for complexation between 1-methoxynaphthalene and n-butyllithium involving changes in the chemical shift of the ether protons has been shown to be the result of solvent effects on a self-association of the ether. The characteristics of this association have been determined. Evidence for a complex and its stoichiometry has been obtained by observation of the n-butyllithium protons.

It is generally recognized that N and O atoms coordinate with Li atoms and that this results both in reducing the size of lithium alkyl aggregates[1] and in increasing the chemical reactivity of the lithium alkyl.[2] Thus toluene, which is essentially unreactive to lithium alkyls, could be metalated in at least 75% yield by treatment with a lithium alkyl in the presence of tertiary amines.[2c] Similarly, 1,2-dimethoxyethane increased the rate of triphenylmethane metalation by a factor of five relative to ethyl ether.[2a] Several studies by Brown,[1b] Waack[1c] and Eastham[1d] and their respective co-workers have shown that n-alkyllithium most likely exists as tetramer and/or dimer in ether solvents.

Methyl aryl ethers have been studied in this context particularly because of their greatly increased reactivity toward metalation relative to unsubstituted benzene. While some researchers invoke substituent electronegativity as a dominant factor,[3] others prefer to put forward coordination of the lithium alkyl and the heteroatom as the primary influence[4] and there is ample circumstantial evidence to support this.[5] NMR spectroscopy has been used in several instances as evidence for coordination of ethers to lithium alkyls. Thus interaction of ethyl ether and n-butyllithium in hexane resulted in a 14·5 Hz displacement downfield in the chemical shift of the methylene protons α to oxygen and a 9·0 Hz upfield shift for the methylene protons α to lithium.[1d] In a study of the metalation of 1-methoxynapthalene (1) Graybill and Shirley observed a similar shift for the Me singlet upon treatment with n-butyllithium[6] and offered this as evidence for a reactive complex. Upon repeating

this work we found that this effect could be attributed to solvent effects and present other evidence for the existence of a complex.

NMR spectra were taken of 1-methoxynaphthalene and anisole (2) in hexane both with and without one equivalent of n-butyllithium. In both cases the concentration of aryl ether in hexane was held constant, thus obviating this variable. The results are shown in the Table. In the case of 1-methoxynapthalene no more than 1·0 Hz change in the chemical shift of the Me protons could be attributed to the presence of n-butyllithium. In the case

Table 1. Effect of n-butyllithium on methoxy proton resonance

Sample composition	Ether	Ether molarity	MeO— Chem. shift (Hz)[a]
Hexane, aryl ether	1-methoxy-naphthalene	0·65	227
	1-methoxy-naphthalene	1·20	221
	anisole	0·77	219
	anisole	1·41	217
Hexane, n-butyllithium: aryl ether = 1:1	1-methoxy-naphthalene	0·65	227·5
	1-methoxy-naphthalene	1·20	222
	anisole	0·77	223[b]
	anisole	1·41	220·5

[a]Downfield from TMS in hexane at 31°.
[b]Anisole: n-butyllithium = 1:2.

of anisole a 4·0 Hz shift was observed. While these shifts may be real, they do not compare with the much larger values obtained for ethyl ether.

When the effect of ether concentration on the Me chemical shift was studied, it became clear that the 14·0 Hz shifts observed by Graybill and Shirley

1   **2**   **3**
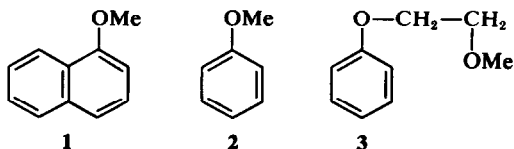
were due to sample dilution.* The magnitude of the concentration effect is seen in the Fig. An approximately 8-fold dilution of anisole or 1-methoxynapthalene resulted in a downfield shift for the Me protons of 7·5 and 22 Hz respectively. Shifts of similar magnitude were observed for both compounds in carbon tetrachloride and chloroform while a negligible shift was seen in benzene. These results are consistent with self-association of the aryl ethers in solution. An example of this phenomenon in aryl aldehydes has been reported by Gurudata, et al.[7]
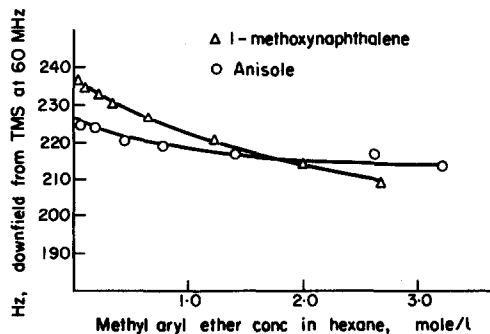

Fig 1.   Effect of concentration on methoxy proton.

To examine this more carefully, we characterized this association for dilute (0·5–5·0 mole %) hexane solutions of 1-methoxynapthalene. The mole fraction equilibrium constant (K_N) was calculated at several temperatures using Eq. (1)[7] and from this values for ΔH (− 1·43 kcal mole^{-1}) and ΔS (− 2·13 cal deg mole^{-1}) were derived from a typical plot of log K_N

$$K_N = \frac{\gamma\gamma_C}{2N_{A_0}(\gamma_C - \gamma)^2} \qquad (1)\dagger$$

$$p = \frac{n_C}{n_{A_0}} = \frac{1}{2}\frac{(\gamma_A - \gamma)}{(\gamma_A - \gamma_C)} \qquad (2)\ddagger$$

$$K_C = \frac{p[A_0]}{[(1 - 2p)[A_0]]^2} \qquad (3)\S$$

vs $1/T$. From a plot of $n\gamma$ vs N_{A_0}[7] the degree of

association of the complex was shown to be 2·03 from − 50 to 31°. Alternatively, using Eq. (2),[8] the concentration equilibrium constant could be derived via Eq. (3). Practically speaking, 1-methoxynapthalene was complexed to the extent of 5·3% and 12·4% at 31° and − 70° respectively.

We therefore sought other evidence for an ether-lithium alkyl complex. Addition of increasing amounts of either 1-methoxynapthalene or anisole to a hexane solution of n-butyllithium resulted in an upfield shift of the protons α to lithium. Starting at − 49·5 Hz (upfield from TMS), the chemical shift of the methylene triplet became constant at − 53·5 Hz at a mole ratio of 1 : 1. Addition of more ether caused no further shift. While these differences are not large, they compare more favorably with those observed for the same protons in the ethyl ether complex than the corresponding values for the ether protons. These less dramatic shifts for the lithium alkyl coupled with the lower degree of association may be due to the weaker basicity of the aryl O atom as well as steric hindrance from the aryl ring. From other work[9] we have evidence for a 1 : 2 complex involving 1-methoxy-2-phenoxy-ethane (3) and n-butyllithium in which the lithium alkyl proton shift is 9·0 Hz. While this undoubtedly involves participation of the methoxy oxygen, observation of the ether spectrum was precluded by rapid decomposition of the ether yielding a complex spectrum.

Thus, at least in hydrocarbons, metalation of methyl aryl ethers results in the disruption of both the highly aggregated lithium alkyl and the partially dimerized ether to yield a reactive complex. The stoichiometry of this complex appears to vary with the structure of the ether.

EXPERIMENTAL

Materials. Anisole and 1-methoxynapthalene were obtained from Aldrich Chemical Company and were purified by distillation. n-Butyllithium in hexane (15·03%) was obtained from Matheson, Coleman and Bell and the concentration determined by a previously described method.[10]

Spectra. NMR spectra were obtained on a Varian A-60-A instrument equipped with a V-6057 variable temp accessory. Temps were calibrated (±2·0°) using a standard plot of methanol OH proton chemical shift vs temp. Chemical shifts were measured in Hz (±0·5 Hz) relative to internal TMS.

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*Professor Shirley has recently reinvestigated this work and came to the same conclusion (private communication).

†γ = observed OMe proton chemical shift, γ_C = OMe proton chemical shift in the complex (obtained by extrapolation of a plot of γ vs T to 0°K), N_A = initial ether mole fraction.

‡p = fraction of complex formed, n_C = moles of complex formed, n_{A_0} = initial moles of ether, γ_A = OMe proton chemical shift in uncomplexed ether (obtained by extrapolation to infinite dilution).

§[A_0] = initial molar concentration of ether.

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