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EFFECT OF SALTS ON THE STEREOSELECTIVITY OF REACTIONS OF α-LITHIO SULFOXIDES

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In the course of re-investigating a controversy regarding the kinetic preference in the abstraction of the diastereotopic hydrogens of benzyl methyl sulfoxide in THF by alkyllithiums*,(1-4) we have observed a large effect on the diastereomer ratio produced upon quenching of the α-lithiobenzyl methyl sulfoxide with some electrophiles due to the presence of other THF-soluble lithium salts. Variations in the diastereomer product ratios were also observed with some, but not all, the other sulfoxides investigated. Since LiBr and LiI are both quite soluble in THF, whereas LiCl is not, methyllithium in ether prepared from CH_3Cl may give different results than if prepared from CH_3Br or CH_3I. The results reported below are thus of both synthetic and mechanistic importance and great care should be exercised in comparing results obtained from different laboratories.

Thus, for example, when benzyl methyl sulfoxide, (**1**), 0.03 - 0.05 M in THF at -60° was reacted with 1.1 equiv. of F-CH_3Li (prepared from CH_3Cl by Foote Mineral Co., 1.6 M ether) and quenched after 1 min. with excess D_2O, the product consisted of a 15:1 mixture of the SS/RR and RS/SR monodeuterated isomers **3** and **4** respectively.[5] When the same sequence was carried out using V-CH_3Li (prepared from CH_3Br by Ventron Corporation, 2 M in ether) the ratio of **3**:**4** was found to be about 3:1. The same ratio was obtained when 1 equiv. of LiBr was added to the THF solution

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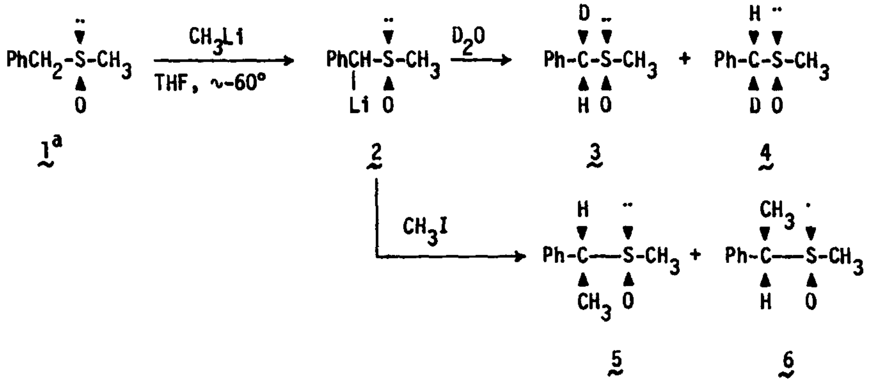
* Both we and Prof. Brauman's group (J.I. Brauman, W.E. Farneth, and W.N. Olmstead, private communication) have repeated and reconfirmed the earlier reported observations.[3,4] Since the results reported in this communication show that small changes in the conditions can have a dramatic effect in the benzyl methyl sulfoxide system, the differences in the results could possibly be due to different reaction conditions used by the two groups, e.g., CH_3Li vs nBuLi. Space limitations do not allow a more complete discussion of this unresolved problem.

prior to the addition of the F-CH_3Li. A further decrease in the ratio of 3:4 was observed upon increasing the LiBr concentration until at a LiBr to sulfoxide mole ratio of about 60 (THF saturated with LiBr) the ratio of 3:4 had dropped to 0.45:1.



[a] Although we were working with racemic mixtures, all formulae are presented with the sulfur chirality as S.

When 1 equivalent of LiI was added instead of LiBr prior to the use of F-CH_3Li, the ratio dropped to 1.2:1 and no further change in the ratio was observed when the solution was saturated with LiI (less than 2 equivalents). Additions of $LiClO_4$, from 1.0 equivalent to saturation (less than 2 equiv.) gave a ratio of 2.2:1, but tetra-n-butylammonium perchlorate produced no change in the 15:1 ratio either at 1 or 5 equivalents. The results are summarized in the Table.

A noticeable difference in the diastereomeric product ratio was also observed in the D_2O quenching of α-lithiobenzyl ethyl sulfoxide generated with the two sources of CH_3Li; F-CH_3Li gave a 10:1 while V-CH_3Li afforded a 5:1 ratio. No measurable effects were noted for benzyl iso-propyl and benzyl tert-butyl sulfoxides. In each case, only one diastereomeric product was detectable by n.m.r.

When acetone was used to quench α-lithiobenzyl methyl sulfoxide, (2), the diastereomer product ratio changed from 15:1 using F-CH_3Li to 4:1 using V-CH_3Li. This ratio change parallels, but does not completely match that observed in the D_2O quench. Reaction of 2 with CH_3I produced a 15:1 diastereomer ratio independent of the type of CH_3Li employed in the generation of 2.

TABLE

Effect of Added Lithium Salts on the Diastereomer Ratio

Obtained by D_2O Quench of α-Lithiobenzyl Methyl Sulfoxide in THF at -60°

Type of CH_3Li	Added Lithium Salt (equiv.)		Diastereomer Ratio[a] 3:4 (number of runs)	
F	-		15:1	(10)
V	-		3.1:1	(5)
F	LiBr	(1.0)	3.2:1	(2)
V	LiBr	(1.0)	2.2:1	(1)
F	LiBr	(2.0)	2.2:1	(1)
V	LiBr	(5.0)	1.3:1	(1)
V	LiBr	(10)	1.1:1	(1)
V	LiBr	(60)	0.45:1	(1)
F	LiI	(1.0)	1.2:1	(4)
F	LiI	(2.0)[b]	1.1:1	(1)
F	$LiClO_4$	(1.0)	2.2:1	(2)
F	$LiClO_4$	(2.0)[b]	2.2:1	(1)

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[a] Measured on an HA-100 NMR Spectrometer in DMSO-d_6 by integration of the areas due to the remaining benzylic hydrogen of 3 and 4 during deuterium decoupling.

[b] The salt did not completely dissolve.

The results reported above show that the stereochemical features of the reaction of α-lithio sulfoxides with electrophiles are more complex than our preliminary results had indicated them to be.[2] Obviously the conclusion that D_2O, acetone or CH_3I are all able to trap the equilibrium between the diastereomeric α-lithio sulfoxides (diastereomeric carbanions) generated under a variety of conditions is too simplistic and should be discarded. This conclusion was reached earlier by Bory and Marquet[6] based on the comparison of the stereochemistry of the methylation and deuteration products of the lithio derivatives of a number of 4-*t*-butylthiane-S-oxides, and more recently by Biellman and Vicens[7] who showed that the deuteration and methylation ratios obtained from 2 differed significantly when the reactions were carried out in HMPA in the presence of the macrocyclic polyether-(2,2,2). Solutions of 2 in THF, DME, HMPA or triglyme were found to be non-conducting, indicating that 2 existed as intimate or solvated ion-pairs and/or aggregates. The addition of the polyether produced a conducting solution interpreted as indicating the presence of cryptate separated ion pairs and some free carbanions.

Thus, a number of forms of 2, ranging from a covalently bound species to a free carbanion are possible, each of which may have a different reactivity and stereoselectivity toward various electrophiles.[6-9] The manner in which the various soluble lithium salts affects the relative amounts of each possible species is difficult to rationalize. The lithium salt effects are not due to changes in the ionic strength of the medium, since the presence of *tetra-n*-butylammonium perchlorate changed neither the deuteration nor the methylation ratios.

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