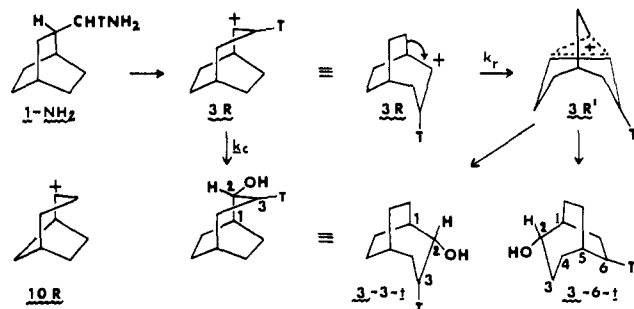
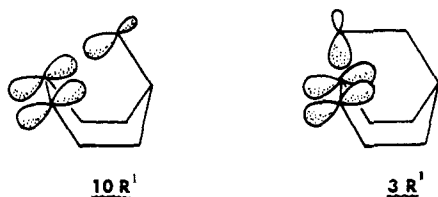


ene group converting **10R** to **3R** thus produces a 30- to 60-fold decrease in the relative rates of rearrangement

Chart III



to solvent capture. This extra ring member causes severe difficulties in achieving proper orbital overlap in a strain-free rearrangement transition state (or intermediate) **3R'**, whereas the lower homolog **10R'** encounters no such problems.



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Stereochemical Behavior of α -Lithio Sulfoxides (α -Sulfinyl Carbanions)¹

Sir:

Recent studies have shown that base-catalyzed hydrogen-deuterium exchange of the diastereotopic protons in sulfoxides of the type $RCH_2S(O)R'$ (R and/or $R' =$ aryl or alkyl) can occur at significantly different rates.² The importance of solvent on the relative rates of exchange of the two diastereotopic protons has also been reported.^{2g,3} Exploitation of the selectivity observed in the H-D exchanges for synthetic purposes,

(1) Presented at the C.I.C. sponsored Heteroatom Symposium, London, Ontario, Sept 1970.

(2) (a) A. Rauk, E. Buncel, R. Y. Moir, and S. Wolfe, *J. Amer. Chem. Soc.*, **87**, 5498 (1965); (b) S. Wolfe and A. Rauk, *Chem. Commun.*, 778 (1966); (c) E. E. Bullock, J. M. W. Scott, and P. D. Golding, *ibid.*, 168 (1967); (d) M. Nishio, *ibid.*, 562 (1968); (e) R. R. Fraser and F. J. Schuber, *ibid.*, 397 (1969); (f) J. E. Baldwin, R. E. Hackler, and R. M. Scott, *ibid.*, 1415 (1969); (g) B. J. Hutchinson, K. K. Andersen, and A. R. Katritzky, *J. Amer. Chem. Soc.*, **91**, 3839 (1969).

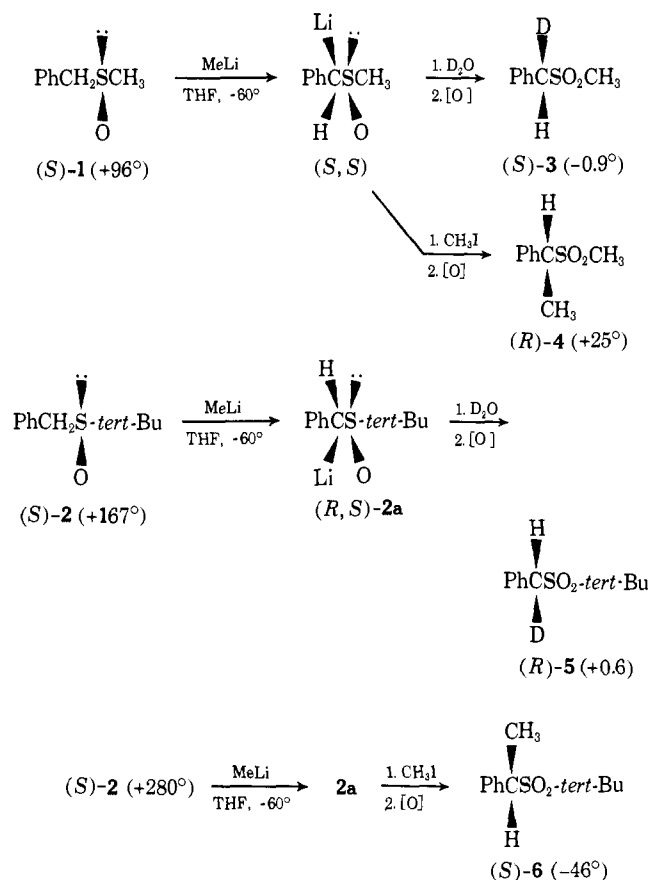
(3) (a) T. Durst, R. R. Fraser, M. R. McClory, R. B. Swingle, R. Viau, and Y. Y. Wigfield, *Can. J. Chem.*, **48**, 2148 (1970); (b) R. R. Fraser and F. J. Schuber, private communications.

especially the use of asymmetric sulfoxides for the synthesis of compounds having optical activity at carbon, has however received much less attention.^{4,5}

In order to evaluate the synthetic possibilities we have studied the reactions of various α -lithio sulfoxides with alkylating agents and carbonyl compounds and compared the diastereomer ratios and stereochemical course in these reactions with those obtained in the H-D exchanges.

Benzyl methyl (**1**) and benzyl *tert*-butyl sulfoxide (**2**) have been studied in greatest detail. Reaction of **1** and **2** with methyllithium in THF at -60° rapidly

Scheme I



generated the corresponding α -lithiobenzyl derivatives. These were quenched after 1 min with excess D_2O and gave mixtures of monodeuterated diastereomeric sulfoxides, the recovery being greater than 85%. The diastereomer ratios were 15:1 and >99:1, respectively. Variable-temperature studies³ indicated that these ratios reflect the ratios of the lithio salts in solution, D_2O serving as a trapping agent. The respective lithio salts were also allowed to react with acetone, cyclohexanone, and methyl iodide (tenfold excess), for 1 min. In each case the resultant diastereomer ratio agreed within experimental error with that obtained on deuteration.⁶ Thus these reagents also

(4) T. Durst, *J. Amer. Chem. Soc.*, **91**, 1034 (1969).

(5) We have succeeded in preparing epoxides from β -hydroxy sulfoxides in a three-step sequence (reduction to sulfide, methylation to sulfonium salt followed by base-catalyzed cyclization). The sequence has been applied successfully to the production of optically pure epoxides; T. Durst and C.-H. Nguyen, unpublished observations.¹

(6) The diastereomer ratios were obtained from integration of the nmr spectra of the total crudes. In the case of the deuteration and hydroxyalkylation reactions the remaining benzylic proton of each diastereomer was used to obtain the ratio;³ for the methylations, com-

Table I. Diastereomer Ratios Obtained from the Reaction of α -Lithio Sulfoxides with Electrophiles in THF at -60°

Lithio sulfoxide	Electrophile	Total diastereomer yield, %	Diastereomer ratio
PhCH(Li)S(O)CH ₃ (1)	D ₂ O	85	15:1
	Acetone	75	15:1
	Cyclohexanone	72	15:1
PhCH(Li)S(O)- <i>tert</i> -Bu (2)	CH ₃ I	76	15:1
	D ₂ O	90	99:1 ^a
	Acetone	77	99:1 ^a
PhCH(Li)S(O)Ph	CH ₃ I	95	99:1 ^a
	D ₂ O	80	1:5:1
	Cyclohexanone	85	1.5:1
PhS(O)CH(Li)CH ₃	CH ₃ I	79	1.5:1
	Acetone	81	13:1
	Benzophenone	73	12:1
<i>tert</i> -BuS(O)CH(Li)CH ₃	Acetone	78	9:1 ^b
	Cyclohexanone	86	9:1 ^b

^a Only one diastereomer could be detected. ^b Not determined accurately.

served as effective traps for the diastereomeric salts. These results, together with the ratios obtained from a number of other sulfoxides, are given in Table I.

In order to determine the stereochemical course of the reaction producing the major diastereomers we prepared the lithio salts from the optically active (*S*)-sulfoxides,⁷ and quenched these with various electrophiles. The crude monodeuterated and monomethylated sulfoxides obtained on quenching with D₂O and CH₃I were oxidized to sulfones whose absolute configurations were determined by comparison with the sulfones prepared from optically active α -deuterio-benzyl alcohol and α -phenethyl alcohol, respectively.⁸

The monodeuterated sulfone obtained from optically pure (*S*)-benzyl methyl sulfoxide, $\alpha_D +96^\circ$ (*c* 0.8, EtOH), lit.⁹ $\alpha_D +96^\circ$, had $\alpha_D -0.9^\circ$ (*c* 1.1, CHCl₃) while that produced from 60% optically pure (*S*)-benzyl *tert*-butyl sulfoxide, $\alpha_D 167^\circ$ (*c* 0.7, EtOH), lit.⁹ $\alpha_D 281^\circ$, had $\alpha_D 0.6^\circ$ (*c* 14, EtOH). Methylation of the above benzyl methyl sulfoxide produced, on oxidation of the total crude product with fivefold excess *m*-chloroperbenzoic acid, the methylated sulfone **4** in about 75% yield, $\alpha_D +25^\circ$ (*c* 0.7, CHCl₃). Similarly optically pure (*S*)-benzyl *tert*-butyl sulfoxide, $\alpha_D 280^\circ$, gave the sulfone **6**, $\alpha_D -46^\circ$ (*c* 1, CHCl₃), in over 90% yield. The optical purities of the sulfones **4** and **6** are 81 and 100%, respectively (assuming max-

imum rotation for the sulfones produced from α -phenethyl alcohol⁸), in good agreement with the 85 and >99% predicted on the basis of the diastereomer ratios as determined by nmr.¹⁰

imum rotation for the sulfones produced from α -phenethyl alcohol⁸), in good agreement with the 85 and >99% predicted on the basis of the diastereomer ratios as determined by nmr.¹⁰

The major isomer produced from deuteration of the lithio salt of (*S*)-benzyl methyl sulfoxide thus had the *S* configuration at carbon⁸ while that obtained on methylation had the *R* configuration. From the (*S*)-*tert*-butyl benzyl sulfoxide, deuteration produced almost exclusively the *R* configuration at carbon while methylation again gave the opposite stereochemical result.¹¹

Evidence has been presented that the H-D exchange proceeds with retention of the carbanion configuration;^{2a,3a,12} thus the methylation reaction must proceed almost exclusively with inversion. The possibility that methylation has proceeded with retention as a result of the less stable lithio sulfoxide reacting more rapidly is made highly unlikely in view of constancy of the methylation and deuteration diastereomer ratios.

Intramolecular alkylations of α -sulfonyl carbanions with inversion of configuration have been noted in the Ramberg-Backlund rearrangement of α -halo sulfones. The bridgehead carbanion from 1-bromo-9-thiabicyclo-[3.3.1]nonene 9,9-dioxide must invert in order to displace bromide ion.¹³ Bordwell and coworkers¹⁴ have concluded that the formation of *cis*- α,α' -dimethylstilbene from *erythro*- α -bromo- α' -methylbenzyl α -methylbenzyl sulfone under Ramberg-Backlund conditions is the result of an inversion process at both benzylic carbons. In this example, alkylation with inversion at the carbanion center is preferred over rotation about the C-S bond followed by alkylation with retention. In the intermolecular methylations of α -sulfinyl carbanions described herein both reaction with retention and inversion could have occurred directly. The inversion process is apparently the preferred pathway. The generality of this preference for α -sulfinyl and α -sulfonyl carbanions remains to be determined.

The stereochemical course of the hydroxyalkylations has not been proved. Based on the α -sulfone carbanion analogy¹⁵ the expected configuration is the one resulting from retention of carbanion configuration. Confirmation of this point and extension of the above stereochemical investigations to a variety of sulfur stabilized carbanions is in progress.

Acknowledgment. Financial support by the National Research Council of Canada is gratefully acknowledged.

(10) The optical purity of the monodeuterated sulfones produced via the lithio salts cannot be determined because of the uncertainty of the optical purity of the α -deuterio-benzyl alcohol from which the comparison sulfones were prepared.

(11) Conclusions regarding preferred α -lithio sulfoxide (α -sulfinyl carbanion) conformations in THF based on these results will be presented in a forthcoming publication.

(12) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, Chapter III.

(13) (a) L. A. Paquette and R. W. Hauser, *J. Amer. Chem. Soc.*, **91**, 2870 (1969); (b) E. J. Corey and E. Block, *J. Org. Chem.*, **34**, 1233 (1969).

(14) F. G. Bordwell, E. Doomes, and P. W. R. Corfield, *J. Amer. Chem. Soc.*, **92**, 2581 (1970); F. G. Bordwell, B. B. Jarvis, and P. W. R. Corfield, *ibid.*, **90**, 5298 (1968).

(15) (a) E. J. Corey and T. H. Lowry, *Tetrahedron Lett.*, 793 (1965); (b) D. J. Cram and A. S. Wingrove, *J. Amer. Chem. Soc.*, **85**, 1100 (1963).

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parison of the benzylic methyl groups gave the required information. In the case of benzyl *tert*-butyl sulfoxide no indication of a second diastereomer was observed in any of the crude reaction products.

(7) No significant loss in the sulfoxide asymmetry occurred under these reaction conditions. (*S*)-Benzyl methyl sulfoxide, $\alpha_D +96^\circ$, yielded monodeuterated sulfoxide having $\alpha_D +92^\circ$; see also J. Jacobus and K. Mislow, *J. Amer. Chem. Soc.*, **89**, 5228 (1967).

(8) The sequence involved conversion of the alcohols to the phenylmethanesulfonates (J. F. King and T. Durst, *ibid.*, **87**, 5684 (1965)), immediate displacement with the respective sodium thiolate in methanol, followed by oxidation with *m*-chloroperbenzoic acid in CH₂Cl₂. Thus (*S*)- α -phenethyl alcohol, $\alpha_D -43.2^\circ$ (neat), greater than 99% optically pure, reported $\alpha_D -43.6^\circ$ (neat) (E. L. Eliel, *ibid.*, **71**, 3970 (1949)), was converted into (*R*)- α -benzylmethyl methyl sulfone, $\alpha_D +31^\circ$ (*c* 7, CHCl₃), and (*R*)- α -benzylmethyl *tert*-butyl sulfone, $\alpha_D +46^\circ$ (*c* 0.2, CHCl₃). (*R*)- α -Deuterio-benzyl *tert*-butyl sulfone, $\alpha_D +0.4^\circ$ (*c* 4, CHCl₃), was obtained from (*S*)- α -deuterio-benzyl alcohol (optical purity $\sim 30\%$) which had been prepared by reduction of benzaldehyde with (-)-pinene ($\alpha_D -48^\circ$) (A. Rauk and S. Wolfe, *Can. J. Chem.*, **44**, 259 (1966), and ref 2f). (*S*)- α -Deuterio-benzyl methyl sulfone, $\alpha_D -0.6^\circ$, has been described.^{2f}

(9) K. Mislow, M. M. Green, and M. Raban, *J. Amer. Chem. Soc.*, **87**, 2761 (1965).