Experimental Section

Tris(2,4,6-trimethylphenyl)phosphine was prepared according to a modification of the procedure previously developed by Worrall[26] for the synthesis of triarylphosphines. Phosphorus trichloride (8.22 g, 0.06 mole) was added to a solution of powdered sodium (13.8 g, 0.6 g-atom) and freshly distilled bromomesitylene (38.8 g, 0.18 mole) in 300 ml of dry benzene. The solution turned greyish green on heating; it was allowed to reflux for 12–14 hr. The still warm, green solution was filtered by gravity to yield a clear yellow filtrate from which, after removal of solvent, 6.8 g (30%) of yellow solid was obtained. Crude yields in various runs ranged from 22 to 31%. The yellow solid was purified by chromatography on a silica gel column prepared with petroleum ether (30–60°) and eluted with 10% benzene–petroleum ether. After several recrystallizations from absolute ethanol, about 1 g of product was obtained, white needles, mp 191.6–192.8° (lit.[27] mp 206°); dipole moment[28] in benzene at 25°, 1.37 ± 0.04 D.; $\lambda_{max}^{ethanol}$ 312 mμ (log ε 4.20).

Anal.[29] Calcd for $C_{27}H_{33}P$: C, 83.46; H, 8.56; P, 7.97; mol wt, 389. Found: C, 83.10; H, 8.63; P, 8.35; mol wt, 356.

(26) D. E. Worrall, *J. Am. Chem. Soc.*, **62**, 2514 (1940).

(27) A. Michaelis, *Ann. Chem.*, **315**, 43 (1901).

(28) We thank Professor N. L. Allinger for this determination.

(29) Analyses by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. The molecular weight was determined by osmometry in benzene.

Racemization and Cleavage of Sulfoxides by Methyllithium[1,2]

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Contribution from the Department of Chemistry, Princeton University, Princeton, New Jersey 08540. *Received May 1, 1967*

Abstract: Reaction of optically active aryl methyl sulfoxides with methyllithium in dimethoxyethane followed by hydrolysis affords arene and partially racemized starting sulfoxide. A mechanism is suggested to account for these transformations in which the initially formed arenesulfinylmethide ion suffers reversible elimination to methylene sulfine (CH_2SO) and aryl carbanion. Alternative mechanisms are also discussed.

The racemization of sulfoxides may be induced by heating,[4] by photochemical means,[5] and by treatment with hydrogen chloride,[6] sulfuric acid,[7] polyphosphoric acid,[8] nitrogen tetroxide,[9] and acetic anhydride.[10] However, no report has thus far appeared in which the *base-catalyzed* racemization of sulfoxides has been claimed. Quite to the contrary, it has been emphasized by several investigators that the sulfoxide pyramid retains its configurational integrity even under conditions where base-catalyzed α-hydrogen isotope exchange takes place. Thus Cram and Pine[11] observed that stereomutation of 2-octyl phenyl sulfoxide by reaction with potassium *t*-butoxide in *t*-butyl alcohol or dimethyl sulfoxide at 60° proceeds exclusively by epimerization at carbon, not at sulfur, and they noted[12] their failure to racemize optically active benzyl *o*-carboxyphenyl sulfoxide with strong base. Similarly, Oae and coworkers observed no racemization in the reaction of (+)-methyl *p*-tolyl sulfoxide with potassium *t*-butoxide in *t*-butyl alcohol or dimethyl sulfoxide at 105–135°, conditions under which base-catalyzed hydrogen isotope exchange on both methyl groups is appreciable.[13]

We have found that reaction of optically active aryl methyl sulfoxides with methyllithium in dimethoxyethane (DME) under homogeneous conditions at room temperature, followed by hydrolysis, leads to recovery of partially racemized sulfoxide; salient results are collected in Table I.[14] The rate of racemization of methyl phenyl sulfoxide in DME ($[CH_3Li]/[C_7H_8SO] = 1$) is first order in sulfoxide, $k_{rac}^{25} = (1.8 \pm 0.3) \times 10^{-6}$ sec^{-1}. As indicated in Table I, only a portion of the sulfoxide was recovered, extensive cleavage to arene having taken place. Under the reaction conditions employed, conversion of sulfoxides to arenes takes place in yields upward of 30% (Table I).[18] As might be ex-

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(2) Presented at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, Abstracts, p O-103.

(3) U. S. Public Health Service Postdoctoral Fellow, 1966–1967.

(4) D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon, and K. Mislow, *J. Am. Chem. Soc.*, **88**, 3138 (1966).

(5) K. Mislow, M. Axelrod, D. R. Rayner, H. Gotthardt, L. M. Coyne, and G. S. Hammond, *ibid.*, **87**, 4958 (1965).

(6) K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *ibid.*, **86**, 1452 (1964).

(7) S. Oae, T. Kitao, and Y. Kitaoka, *Chem. Ind.* (London), 291 (1961).

(8) J. Day and D. J. Cram, *J. Am. Chem. Soc.*, **87**, 4398 (1965).

(9) C. R. Johnson and D. McCants, Jr., *ibid.*, **86**, 2935 (1964); **87**, 1109 (1965); S. Oae, N. Kunieda, and W. Tagaki, *Chem. Ind.* (London), 1790 (1965).

(10) S. Oae and M. Kise, *Tetrahedron Letters*, 1409 (1967).

(11) D. J. Cram and S. H. Pine, *J. Am. Chem. Soc.*, **85**, 1096 (1963).

(12) D. J. Cram and S. H. Pine, unpublished work cited in ref 11, footnote 12.

(13) Y. H. Khim, W. Tagaki, M. Kise, N. Furukawa, and S. Oae, *Bull. Chem. Soc., Japan*, **39**, 2556 (1966). It was subsequently shown by S. Oae, M. Kise, N. Furukawa, and Y. H. Khim. [*Tetrahedron Letters*, 1415 (1967)] that ^{18}O-labeled methyl *p*-tolyl sulfoxide suffers oxygen-isotope exchange in potassium *t*-butoxide–*t*-butyl alcohol or potassium hydroxide–aqueous methanol at 150°, but these authors did not report on the fate of optically active sulfoxide under these vigorous conditions.

(14) The optically active sulfoxides listed in Table I were prepared by reaction of menthyl methanesulfinate[15] with the corresponding arylmagnesium bromides. Since reaction with *p*-tolylmagnesium bromide (see Experimental Section) yields (+)-(*R*)-methyl *p*-tolyl sulfoxide,[16] and since the Grignard reaction is known to proceed with inversion,[17] it follows that the menthyl methanesulfinate prepared by this procedure is enriched in the diastereomer which has the *R* configuration at sulfur and that all five (+)-aryl methyl sulfoxides listed in Table I have the *R* configuration.

(15) K. K. Andersen, *J. Org. Chem.*, **29**, 1953 (1964); M. M. Green, Ph.D. Dissertation, Princeton University, 1965.

(16) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **87**, 1958 (1965).

(17) P. Bickart, M. Axelrod, J. Jacobus, and K. Mislow, *ibid.*, **89**, 697 (1967).

Table I. Racemization and Cleavage of Aryl Methyl Sulfoxides by Reaction with Methyllithium[a]

R in $RSOCH_3$	Reaction time, hr	Reagent ratio[b]	$[\alpha]D$ of sulfoxide, deg[c] Starting	Recovered	Fraction of sulfoxide, % Racemized	Recovd[d]	Cleaved[e]
α-Naphthyl	2	2	+119	+112	5.9	50	50
β-Naphthyl	2	2	+15.5	+11.5	25.8	20	60
p-Biphenylyl	2	2	+43.5	+35.0	19.5	61	31
Mesityl	2	2	+43.0	+41.7	3.0	78	..
Phenyl	2	2	+24.2	+18.4	24.0	65	..
Phenyl	20	1	+24.9	+21.6	13.3	66	..
Phenyl	76	1	+24.9	+15.1	39.4	9	..

[a] In dimethoxyethane containing *ca.* 4% ether (see Experimental Section) at room temperature. [b] Molar ratio of methyllithium to sulfoxide. [c] In absolute ethanol. [d] By isolation from the reaction mixture after hydrolysis. [e] Fraction of sulfoxide cleaved to give arene = moles of arene isolated from the reaction mixture after hydrolysis/moles of starting sulfoxide.

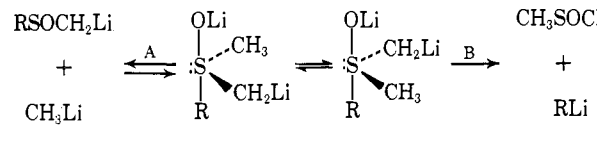
pected, an increase in the molar ratio of methyllithium to methyl phenyl sulfoxide or an increase in reagent contact time increases the extent of racemization and/or cleavage.

The reaction of dimethyl sulfoxide (DMSO) with butyllithium is reported[19] to give the conjugate base of DMSO; that the reaction of aryl methyl sulfoxides with methyllithium also produces the conjugate base was demonstrated as follows. First, reaction of methyllithium with (+)-methyl α-naphthyl sulfoxide in DME at −50°, followed by carbonation, gave a 43% yield of (+)-1-naphthalenesulfinylacetic acid[20] with 17% racemization. Second, reaction of methyllithium with methyl phenyl sulfoxide (molar ratio 2:1) in ether at room temperature, followed (after 2 min) by hydrolysis with deuterium oxide, gave recovered sulfoxide whose mass spectrum showed the following composition: 21.1% d_0, 58.4% d_1, 16.4% d_2, 3.2% d_3, and 0.8% d_4. The presence of methyl phenyl sulfoxide-d_4 reveals the presence of ring-deuterated molecules[22] but the rough agreement of the mass-spectral analysis, which gives a total deuterium content of 1.04 atoms per molecule, with the nmr analysis, which gives a deuterium content of 0.9 atom per methyl group on the assumption that there is *no* ring deuteration,[23] indicates that base-catalyzed removal of the aromatic proton is a minor process. The heterogeneity of the isotopically enriched mixture probably results from exchange reactions *following* quenching of the reaction mixture with deuterium oxide: the initially formed $C_6H_5SOCH_2D$ should be capable of further base-catalyzed exchange in a medium containing deuterium oxide and lithium deuterioxide.[11,13] Similar results were obtained with (+)-methyl *p*-tolyl sulfoxide having $[\alpha]D$ +33.6° (ethanol): reaction of methyllithium with the sulfoxide (molar ratio 1:1) in ether at room temperature, followed (after 30 min) by hydrolysis with deuterium oxide, gave recovered sulfoxide with $[\alpha]D$ +27.1° (ethanol), whose nmr spectrum revealed extensive hydrogen isotope exchange in both methyl groups.[13]

The previous failure to observe racemization[11,13] is accounted for by the circumstance that sulfinylmethide ions are generated *irreversibly* by reaction of sulfoxides with methyllithium, whereas under conditions employed by the previous workers the reversible formation of such ions in protic solvents keeps the concentration low enough to preclude significant racemization at sulfur yet high enough to cause extensive deuterium exchange on α-carbon; from our measurements a conservative estimate of the ratio of rate constants for the two processes is $k_{exch}/k_{rac} > 10^4$.

If the first step in the reaction sequence leading to racemization and cleavage is formation of lithium arenesulfinylmethide, then the rate of racemization should be independent of the lithium reagent. However, reaction of phenyl methyl sulfoxide with phenyllithium (1:1) in DME for 22 hr leads to 50% racemization, whereas under identical conditions for 20 hr methyllithium leads to 13.3% racemization. We shall now turn to a discussion of the steps of the mechanism or mechanisms which need be invoked to account for the observed results.

First to be considered is a mechanism which involves reversible addition of methyllithium to lithium arenesulfinylmethide, a reaction which might produce an intermediate of bipyramidal geometry. This hypothetical intermediate could suffer inter- or intramolecular hydrogen exchange between methyl and methide groups or rapid scrambling of ligands (*i.e.*, pseudorotation) and could cleave either to give starting materials (reaction A) or to give lithium methanesulfinylmethide and aryllithium (reaction B).



The above mechanism would in principle be capable of accounting for our observations: the cleavage reaction is represented by B, and the racemization reaction by A, provided that hydrogen exchange between the enantiomeric intermediates is rapid and/or that scram-

(18) The presence of benzene and mesitylene as cleavage products of methyl phenyl and mesityl sulfoxides was demonstrated by glpc analysis, but no quantitative estimate was made. In the other three cases, the arene was isolated following separation from the sulfoxide.

(19) J. I. Brauman and N. J. Nelson, *J. Am. Chem. Soc.*, **88**, 2332 (1966).

(20) Since reaction of (+)-(*R*)-methyl α-naphthyl sulfoxide[14] gives (+)-1-naphthalenesulfinylacetic acid (1), the *R* configuration is established for (+)-1. This provides an absolute standard for several ring-substituted derivatives of **1** which were individually resolved by Janczewski and co-workers. Janczewski[21] arbitrarily assigned the L configuration to (−)-**1** and, by correlations through use of the Freudenberg rule of shift and asymmetric oxidation, assigned the L configuration also to the following (−)-acids, listed as derivatives of **1**: 4-bromo [M. Janczewski, *Roczniki Chem.*, **35**, 601 (1961)], 5-bromo [M. Janczewski, L. Bilczuk, T. Bartnik, and H. Szczeklik, *ibid.*, **38**, 399 (1964)], 2-bromo-[M. Janczewski, *ibid.*, **39**, 391 (1965)], 2-methoxy [M. Janczewski and T. Bartnik, *ibid.*, **40**, 1919 (1966)], 4-methoxy [M. Janczewski and T. Bartnik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **10**, 271 (1962)]. Since it has now been established that L corresponds to *S*, all of the above compounds have the *S* configuration.

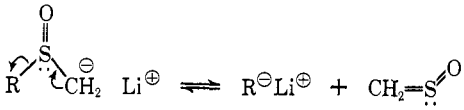
(21) M. Janczewski, *Roczniki Chem.*, **35**, 585 (1961).

(22) Precedent for the ring metallation of an aryl sulfoxide is provided by the work of D. A. Shirley and E. A. Lehto, *J. Am. Chem. Soc.*, 77, 1841 (1955).

(23) The integrated intensity ratio of aromatic to aliphatic protons is 5.0:2.1.

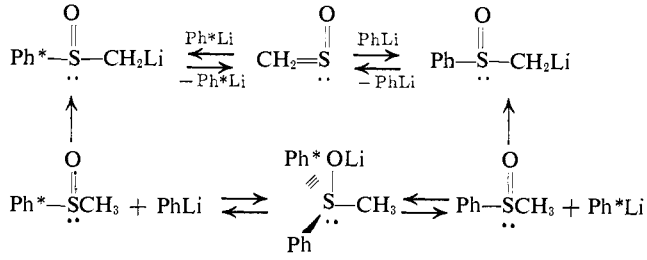
bling of the ligands on sulfur is facile.[24] The addition mechanism appeared especially attractive to us because it had been reported by Franzen[25] that "DMSO reacts with organolithium compounds...to a considerable extent according to the following exchange reaction: $Me_2SO + RLi \rightarrow SOMeR + MeLi$. This exchange reaction is common for the sulfoxides." Nevertheless, we were able to rule out this mechanism unambiguously because reaction of $^{13}CH_3$-enriched methyl phenyl sulfoxide with $^{12}CH_3Li$ under conditions sufficient to give at least 13% racemization yields recovered sulfoxide with unaltered ^{13}C content.

A plausible alternative mechanism in the methyllithium reaction involves reversible cleavage of lithium arenesulfinylmethide into methylene sulfine and aryllithium.

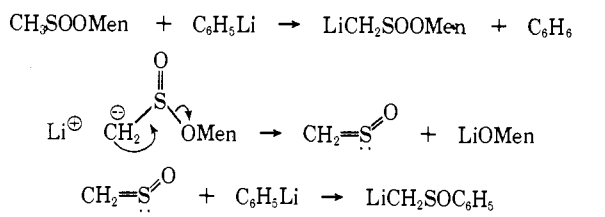


Methylene sulfine is an achiral intermediate, and recombination with aryllithium would result in formation of racemic starting material. However, we have been unable to adduce any *direct* evidence for the formation of this intermediate, which is the parent compound in the family of sulfines.[26,27] While certain derivatives of methylene sulfine are sufficiently stable to be isolable,[26,27] the only simple alkyl derivative reported, isopropylidene sulfine,[26] is "too unstable for isolation or handling at room temperature." An unsuccessful attempt to prepare and trap methylene sulfine has been recorded previously;[28] our own efforts to demonstrate the presence of this compound, either by direct isolation or by trapping *in situ*, also resulted in failure. We ascribe our lack of success to the presumed ease with which methylene sulfine decomposes, and to its extreme reactivity with organolithium reagents as judged by the reaction of fluorenylidene sulfine[26] with methyllithium which results in extensive decomposition of the sulfine (Experimental Section).

However, a mechanism involving intervention of an adduct of RLi[25] is indicated by an exchange reaction observed between phenyl-^{14}C methyl sulfoxide and phenyllithium. Reaction of phenyl-^{14}C methyl sulfoxide (28.84 ± 0.36 counts min^{-1} $\mu mole^{-1}$) with phenyllithium under conditions identical with those employed in the above-mentioned racemization reaction (22 hr, DME solvent) afforded recovered sulfoxide with 25.61 ± 0.60 counts min^{-1} $\mu mole^{-1}$, corresponding to a loss of $11.2 \pm 2.0\%$ of the ^{14}C label. This result indicates that there are at least two mechanisms operative in this racemization–exchange reaction. Nevertheless, since racemization exceeds exchange by a factor of five, only a minor portion of of the racemization can arise from the intervention of a phenyllithium adduct



Sulfines may be similarly invoked as intermediates in the reaction of organolithium reagents with sulfinate esters of the type $R_2CHSOOR$, containing an α-hydrogen which can be abstracted by base. This suggestion is supported by our finding that reaction of a mixture (60.7:39.3) of diastereomeric *l*-menthyl methanesulfinates with phenyllithium gives largely or even completely racemic methyl phenyl sulfoxide (Experimental Section), whereas reaction with phenylmagnesium bromide[15] gives 20.7% optically pure product. In contrast to the highly stereospecific Grignard displacement reaction which proceeds by a direct inversion mechanism,[16,17] the reaction with phenyllithium appears to proceed in part or even entirely by an elimination–addition mechanism.



In the absence of an acidic α-hydrogen, the elimination–addition mechanism becomes inoperative and the intermediacy of sulfines is ruled out. In this case a direct displacement of alkoxide by the organolithium reagent becomes the major reaction pathway, as demonstrated by the observation that reaction of diastereomerically pure menthyl benzenesulfinate[29] with methyllithium gives methyl phenyl sulfoxide of 97.3% optical purity The 3% loss in optical purity may be due to racemization of the produced sulfoxide by methyllithium.

Methylene sulfine has also been recently suggested[30] as an intermediate in the base-catalyzed elimination of N-methanesulfinylmorpholine. In sulfinamides as in sulfinate esters, the intervention of sulfine intermediates is ruled out in the absence of an acidic α-hydrogen, and reaction with the organolithium reagent would in that case be expected to occur by direct displacement. The reaction of N-benzenesulfinylmorpholine with methyl-

(24) The depicted geometry is one of several asymmetric regular or distorted trigonal bipyramidal structures which may be written, any one of which is capable of fulfilling one of the stated conditions, *i.e.*, that hydrogen exchange has the effect of interconverting the enantiomers. For example, this would also be the case if the methyl and methide groups occupied the two apical positions. However, even if the methide and methyl groups were to occupy basal and apical positions, respectively, rapid scrambling (pseudo-rotation) of the ligands on sulfur would also result in interconversion of the enantiomers. For a relevant discussion of related structures, see R. J. Gillespie, *Inorg. Chem.*, **5**, 1634 (1966); L. S. Bartell, *ibid.*, **5**, 1635 (1966); D. Hellwinkel, *Chem. Ber.*, **99**, 3628 (1966).

(25) V. Franzen, "Synopses of Papers Read at an International Symposium on Organic Reaction Mechanisms Held at Cork, Ireland, July 1964," Special Publication, No. 19, The Chemical Society, London, 172 (1965). No experimental details are given in this abstract.

(26) W. A. Sheppard and J. Diekmann, *J. Am. Chem. Soc.*, **86**, 1891 (1964).

(27) W. Walter and K. D. Bode, *Ann.* **660**, 74 (1962); J. F. King and T. Durst, *J. Am. Chem. Soc.*, **85**, 2676 (1963); *Can. J. Chem.*, **44**, 819 (1966); J. Strating, L. Thijs, and B. Zwanenburg, *Rec. Trav. Chim.*, **83**, 631 (1964); *Tetrahedron Letters*, 65 (1966); *Rec. Trav. Chim.*, **86**, 641 (1967); B. Zwanenburg, L. Thijs, and J. Strating, *ibid.*, **86**, 577 (1967).

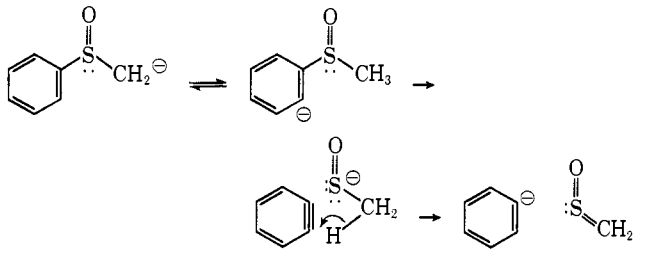
(28) W. E. Truce and J. R. Norell, *J. Am. Chem. Soc.*, **85**, 3231 (1963).

(29) H. F. Herbrandson and R. T. Dickerson, Jr., *ibid.*, **81**, 4102 (1959).

(30) E. J. Corey and T. Durst, *ibid.*, **88**, 5656 (1966).

lithium, which produces methyl phenyl sulfoxide (Experimental Section), is a case in point.

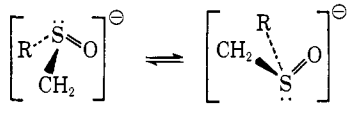
Since cleavage of diphenyl sulfoxide by phenyllithium is reported to proceed *via* a benzyne mechanism,[31] precedent exists for a hypothetical detour route to methylene sulfine by which the initially formed arenesulfinylmethide ion undergoes proton exchange with the hydrogen atoms on the aromatic ring, followed by benzyne elimination and hydride transfer to give methylene sulfine and aryl anion, *e.g.*



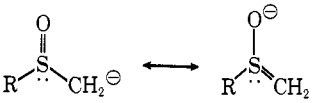
However, this cleavage mechanism may be ruled out for at least one sulfoxide, mesityl methyl sulfoxide, which suffers racemization and cleavage to mesitylene (Table I) yet which is constitutionally incapable of undergoing benzyne elimination.

The possibility was entertained that the cleavage products might at least in part arise by reduction of the sulfoxides to sulfides,[32] followed by quantitative cleavage of the sulfides. However, since under conditions sufficient to cleave 75% of a sample of methyl β-naphthyl sulfoxide (2 hr) no cleavage of methyl β-naphthyl sulfide[33] was observed, and since no aryl sulfides were detected among the reaction products, it may be concluded that the cleavage products do not to any significant extent arise *via* this route.

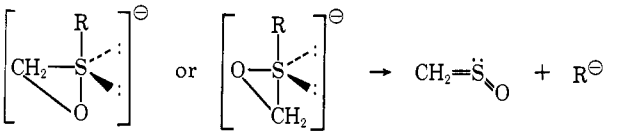
Although the sulfine mechanism has the virtue of accommodating all of our observations, some alternative pathways which also lead to racemization cannot at present be excluded and may play a significant role. For example, arenesulfinylmethide ions may conceivably suffer relatively rapid pyramidal inversion and may thus racemize more readily than the corresponding sulfoxides.



Arenesulfinylmethide ions are isoelectronic with sulfoxides, which are normally resistant to pyramidal inversion at room temperature.[4] However the comparison between the two systems is less than strict because delocalization of the unshared electron pairs on oxygen[34] *and* carbon, involving the 3d orbital on sulfur, changes the bonding character in the ion, as compared to its conjugate acid (*i.e.*, the sulfoxide), and may to an important extent affect the inversional energy barrier which separates the pyramidal enantiomers.



Taking this argument a step further, σ bonding between oxygen and methylene carbon, with concomitant promotion of the electrons to the 3d orbital of sulfur and rehybridization, may result in a planar and thus achiral ion of C_s geometry which could function as a transition state or intermediate in the racemization and possibly also in the cleavage reaction.



The studies of racemization and cleavage described in this paper have been restricted to aryl *methyl* sulfoxides, *i.e.*, to sulfoxides containing labile α-hydrogens but lacking β-hydrogens; under strongly basic conditions sulfoxides containing β-hydrogens undergo E2 elimination.[35]

It is interesting to contrast the results of the present work with those of Horner, *et al.*,[36] who recently reported that the reaction of optically active methyl phenyl-*n*-propylphosphine with *t*-butyllithium, followed by carbonation, gave optically active carboxymethyl-phenyl-*n*-propylphosphine with complete retention of configuration. This result is not surprising: the mechanistic pathways discussed above for sulfinylmethide ions are not open to the phosphinemethide ion, and the sole remaining alternative is the relatively slow pyramidal inversion mechanism. The alternative discussed[36] by Horner, *et al.*, that 2p–3p π bonding would also result in a flattening of the ion by virtue of bringing the ligands on carbon and phosphorus into a common plane, is less likely since such an arrangement would require promotion of a nonbonding electron pair into one of the upper energy states, *e.g.*, a 3d orbital.

Experimental Section[37]

Preparation of Menthyl (*R*)-Methanesulfinate.[38] A solution of 1 mole of methyllithium in ether was transferred under nitrogen to a 2-l three-necked flask equipped with a mechanical stirrer, a calcium chloride drying tube, a gas inlet tube, and contained in a Dry Ice immersion bath. After the solution has been cooled to approximately −70° a *nitrogen-diluted* stream of sulfur dioxide was introduced through the gas inlet tube; care was taken that the inlet was above the surface of the methyllithium solution to avoid clogging. A fine white solid began to form immediately. Addition was continued until approximately 70 g of sulfur dioxide (1.1

(31) K. K. Andersen and S. A. Yaeger, *J. Org. Chem.*, **28**, 865 (1963).

(32) It has been reported that sulfoxides can be reduced to sulfides by organometallic reagents; *cf.* E. P. Kohler and H. Potter, *J. Am. Chem. Soc.*, **57**, 1316 (1935), and ref 22.

(33) F. Kehrmann and G. A. Sava, *Chem. Ber.*, **45**, 2895 (1912).

(34) A. B. Burg, "Organic Sulfur Compounds," Vol. 1, N. Kharasch, Ed., Pergamon Press, Inc., New York, N. Y., 1961, pp 35, 36.

(35) J. E. Hofmann, T. J. Wallace, P. A. Argabright, and A. Schriesheim, *Chem. Ind.* (London) 1243 (1963); T. J. Wallace, J. E. Hofmann, and A. Schriesheim, *J. Am. Chem. Soc.*, **85**, 2739 (1963); J. E. Hofmann, T. J. Wallace, and A. Schriesheim, *ibid.*, **86**, 1561 (1964).

(36) L. Horner, W. D. Balzer, and D. J. Peterson, *Tetrahedron Letters*, 3315 (1966).

(37) Elemental analyses by Schwarzkopf Microanalytical Laboratories, Woodside, N. Y. Optical rotatory dispersions were measured on a Cary 60 recording spectropolarimeter. All reported specific rotations refer to *ca.* 1% solutions in absolute ethanol, unless otherwise specified. Nmr spectra were measured on a Varian A-60A spectrometer and refer to approximately 10% solutions in deuteriochloroform unless otherwise specified, with tetramethylsilane as internal standard. Methyllithium (prepared from methyl bromide) was obtained in ether solution from Foote Chemical Co.

(38) We report herein a modification of Andersen's procedure[15] which consistently leads to ester of significantly higher diastereomeric purity. The prefix *R* refers to the configuration at sulfur[14] in the predominant diastereomer.

Table II. Properties of Optically Active Aryl Methyl Sulfoxides

R in RS(=O)CH$_3$[a]	Bp,[b] °C (mm)	Melting range, °C	[α]D, deg	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S
Phenyl[c]	90 (0.2)	...	+45.8[d]	59.97	5.75	22.86	60.19	5.96	22.83
α-Naphthyl	140 (0.5)	58–65	+119[e]	69.44	5.29	16.85	69.17	5.25	16.77
β-Naphthyl	135 (0.25)	103–108	+15.5	69.44	5.29	16.85	69.61	5.39	16.83
p-Biphenylyl	140 (0.5)	132–139	+43.5	72.18	5.59	14.82	72.15	5.81	14.90
Mesityl	100 (0.03)	...	+43.0	65.89	7.74	17.59	65.80	8.10	17.44

[a] All sulfoxides of *R* configuration; *cf.* ref 14. Optical purity in all cases is 30.3% as judged by the diastereomeric ratio (65.15:34.85) in the starting menthyl methanesulfinate. [b] Approximate boiling points (Kugelrohr). [c] Previously reported by Andersen[15] in a state of lower optical purity. [d] ORD corrected to optical purity (*c* 0.07–0.005, isooctane): $[\phi]_D$ +209°, $[\phi]_{270}$ +18,000° (pk), $[\phi]_{256}$ 0°, $[\phi]_{230}$ −78,250° (tr), $[\phi]_{218}$ 0°. [e] ORD corrected to optical purity (*c* 0.131–0.005, isooctane): $[\phi]_D$ +385°, $[\phi]_{319}$ +12,120° (pk), $[\phi]_{317}$ +11,660° (tr), $[\phi]_{305}$ +17,040° (pk), $[\phi]_{286}$ 0°, $[\phi]_{274}$ −5510° (tr), $[\phi]_{264}$ 0°, $[\phi]_{244}$ +39,850 (pk), $[\phi]_{231}$ 0°.

mole) had been introduced. The addition of sulfur dioxide was stopped and stirring was continued for 0.5 hr. Nitrogen flushing was continued as 600 g (5 moles) of thionyl chloride was added to the ether slurry of lithium methanesulfinate; the reaction mixture was maintained at −15 to −20° during the addition. The slurry changes in color from white to yellow (solid dissolves and precipitation of lithium chloride occurs) during the addition as methanesulfinyl chloride is produced. After the addition was completed, the Dry Ice bath was removed, and the reaction mixture was allowed to warm to room temperature. Stirring was continued at room temperature for approximately 2–4 hr. The precipitated salt (lithium chloride) was removed by filtration under nitrogen. The residue was washed with benzene to ensure complete recovery of product. The solvent (ether, benzene, and thionyl chloride) in the filtrate was removed under reduced pressure (approximately 40–70 mm) at the lowest possible temperature (preferably <40°). (*Caution:* methanesulfinyl chloride is volatile; low pressure or high temperature leads to codistillation of product.) The distillate, containing small quantities of methanesulfinyl chloride, was light yellow in color. Solvent removal was continued until the infrared spectrum of the residue showed very weak absorption at 1225 cm^{-1} ($SOCl_2$) as compared to the absorption at 1150 cm^{-1} (S–O stretch of methanesulfinyl chloride). The yield of crude, yellow methanesulfinyl chloride was approximately 50–60 g (50–60%);[39] this material was used in the next step without further purification.

A solution of 91 g (0.58 mole) of (−)-menthol in 120 ml (117 g; 1.48 moles) of anhydrous pyridine was added dropwise (at a rate sufficiently slow to maintain the temperature below −70°) to a nitrogen-flushed solution of 58.3 g (0.58 mole) of methanesulfinyl chloride in 300 ml of ether cooled to −75° (Dry Ice–acetone bath). Pyridinium hydrochloride precipitated from the reaction mixture in the course of the addition. After the addition was completed stirring was continued for 3 hr. The pyridinium hydrochloride was dissolved by adding 500 ml of water, and the ether layer was washed successively with cold water, approximately 1% aqueous hydrochloric acid until the washings were acidic, aqueous sodium bicarbonate until the washings were neutral, and finally with water. After drying the ethereal solution over anhydrous sodium sulfate, the ether was removed under reduced pressure at approximately 25°. The yield of crude menthyl methanesulfinate was approximately 87 g (62%). The viscous, crude ester was yellow-orange in color. The crude ester as isolated above was used without further purification in the preparation of sulfoxides.

Stereochemical Calibration of Menthyl Methanesulfinate.[15] A solution of 2.5 g (11.5 mmoles) of menthyl methanesulfinate in 20 ml of ether was added to the Grignard reagent prepared from 5.15 g (30 mmoles) of *p*-bromotoluene and 0.72 g (30 g-atoms) of magnesium shavings in 50 ml of anhydrous ether at such a rate that vigorous refluxing occurred. The solution became cloudy during the addition. After having been stirred for approximately 5 min, the reaction mixture was hydrolyzed with saturated aqueous ammonium chloride. The crude reaction mixture was transferred to a separatory funnel and extracted with three to five 50-ml portions of water. The combined aqueous extracts were extracted with three 50-ml portions of 30–60° petroleum ether[40] and then saturated with sodium chloride. The aqueous phase was extracted with three to five 50-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure to yield 1.08 g (61%) of sulfoxide. Kugelrohr distillation at 140° (0.07 mm) gave crystalline (+)-(*R*)-methyl *p*-tolyl sulfoxide[16] whose infrared spectrum was identical with that of authentic material. The sulfoxide had $[\alpha]^{25}D$ +47.2°; optical purity 30.3%.[41,42] The precursor therefore[16] consists of a mixture of diastereomeric menthyl menthanesulfinates, differing in configuration at sulfur, in a ratio of 65.15:34.85. The major diastereomer has the *R* configuration at sulfur.[14]

Preparation of Sulfoxides. The sulfoxides listed in Table I were prepared from menthyl methanesulfinate by the procedure given above with the following modification. Since methyl α-naphthyl, methyl β-naphthyl, and methyl *p*-biphenylyl sulfoxides could not be extracted with water from the Grignard reaction mixture, these compounds were isolated by column chromatography after solvent removal. Silica gel (approximately 20 g/g of crude reaction mixture) was washed with ethyl acetate and then with benzene. The sample was introduced onto the column in benzene and eluted with the same solvent. Elution was continued until all material (mostly menthol) with R_f values in the range 0.8–0.9 (on silica gel tlc plates with 10% MeOH in EtOAc, I_2 stain) was removed. The eluent was changed to ethyl acetate, and the sulfoxide was eluted at the solvent front. Thin layer chromatograms of eluted sulfoxides show R_f values of approximately 0.1–0.25 under testing conditions given above. The properties and elemental analyses of the isolated sulfoxides are given in Table II.

Optically pure methyl phenyl sulfoxide was prepared from diastereomerically pure (−)-menthyl (−)-benzenesulfinate, mp 50–51° (lit.[29] 50–51°), $[\alpha]^{23}D$ −206° (*c* 0.82, acetone) (lit.[29] $[\alpha]^{25}D$ −205.5°, acetone), by reaction with methylmagnesium chloride according to the procedure described above. The product, $[\alpha]^{24}D$ +149°, is presumably optically pure; this would be in accord with the calculated optical purity (30.7%) of material having $[\alpha]D$ +45.8° prepared from a mixture (65.15:34.85) of diastereomeric menthyl methanesulfinates (Table II).[43]

In a second run, ester with $[\alpha]D$ −202° (*c* 1.26, acetone) gave product sulfoxide with $[\alpha]D$ +147.5°, *i.e.*, of 99% optical purity.

A reaction of (−)-menthyl (−)-benzenesulfinate (3.6 mmoles), $[\alpha]D$ −204° (*c* 1.24, acetone), with methyllithium was carried out under conditions similar to those described for the reaction with methylmagnesium chloride. An ethereal solution of methyllithium (3.7 mmoles) was added to a solution of the ester in ether at −70°. The usual work-up gave 0.37 g (70%) of methyl phenyl sulfoxide, $[\alpha]D$ +145°.

(39) Care was taken to remove excess thionyl chloride from the product prior to esterification to avoid contamination of the ester by dimenthyl sulfite.

(40) We have found that in instances where the sulfoxide is water soluble this procedure will quantitatively remove traces of menthol and other side products from the aqueous phase, thereby making purification of the sulfoxide by column chromatography unnecessary.

(41) Calculated from the rotation of optically pure methyl *p*-tolyl sulfoxide, for which K. Mislow, M. Axelrod, D. R. Rayner, G. Gotthardt, L. M. Coyne, and G. S. Hammond, *J. Am. Chem. Soc.*, 87, 4958 (1965), report $[\alpha]^{25}D$ +156°.

(42) We have observed that menthyl methanesulfinate slowly epimerizes on storage. Thus over a period of approximately 6 months the diastereomeric composition of a sample changed from an original value of 65:35 to a value of 55:45 (calibration as above). We suggest that calibrations be run in parallel with sulfoxide preparations. The ratio of diastereomers of freshly prepared ester is consistently 2.0 ± 0.2 by the procedure given in this paper.

(43) Since the Grignard reaction goes with inversion of configuration and since the produced methyl phenyl sulfoxide has the *R* configuration,[14] it has been established that (−)-menthyl (−)-benzenesulfinate has the *S* configuration at sulfur.

Reaction of a mixture (60.7:39.3) of diastereomeric menthyl methanesulfinates (as judged by conversion to methyl *p*-tolyl sulfoxide ([α]D +33.6°)) with phenylmagnesium bromide according to the usual procedure gave methyl phenyl sulfoxide, [α]D +30.9°. The same ester was treated with phenyllithium according to the following procedure. A solution of 4.8 ml of 1.85 *M* phenyllithium in ether–benzene (Lithium Corporation of America) was added to a stirred solution of 2.0 g (8.9 mmoles) of menthyl methanesulfinate in 25 ml of ether at room temperature. Work-up by the usual procedure gave 0.133 g (11%) of methyl phenyl sulfoxide, $\alpha^{25}D$ 0.00 ± 0.02° (*l* 2, *c* 0.58, ethanol). Inverse addition (addition of ester to phenyllithium) under the same conditions afforded 0.046 g (3.8%) of methyl phenyl sulfoxide, [α]D +12.8°, *i.e.*, 8.6% optically pure. The stereospecificity is 8.6/21.4 or 40%.

Racemization and Cleavage Reactions. A 100-ml three-necked flask equipped with a nitrogen inlet, condenser with Drierite drying tube, and rubber septum was dried by flaming. Approximately 500 mg of sulfoxide was transferred to the flask containing 50 ml of dimethoxyethane (DME) distilled from calcium hydride. A predetermined volume of 1.7 *M* methyllithium in ether (generally 1–3 ml) was added to the colorless sulfoxide solution by syringe. The homogeneous solution immediately turned yellow. After stirring the reaction mixture at ambient temperatures for the desired period of time the solution was cooled to about 0° (ice bath), and water was added through the septum cap. The yellow reaction mixture was transferred to a separatory funnel and diluted with approximately 100 ml of water. The organic products were extracted with three to five 100-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure. The residue was chromatographed over silica gel (approximately 20 g of silica gel/g of residue) employing benzene as eluent. The first benzene fractions contained the cleavage products (arenes) after which no more material was eluted. The eluent was changed to ethyl acetate and the sulfoxide was eluted at the solvent front. The homogeneity of the arenes and sulfoxides was determined by nmr, infrared, and/or vapor phase chromatography. All sulfoxides were distilled (Kugelrohr) prior to polarimetric analysis.

Deuterium Exchange Reactions. The same procedure as described for racemization and cleavage studies (molar ratio of methyllithium to sulfoxide 2:1) was employed with the following modifications: solvent ether was employed, and the reactions were terminated after 2 min by addition of deuterium oxide instead of water. Deuterium content was determined by mass spectrometry; results are given in the text.

(+)-1-Naphthalenesulfinylacetic Acid. A solution of 0.50 g (2.6 mmoles) of (+)-methyl α-naphthyl sulfoxide (for properties, see Table II) in 10 ml of DME distilled from calcium hydride was cooled to −50° and 2 ml of 1.7 *M* methyllithium (3.4 mmoles) was added. After 1 min *ca.* 1 g of crushed Dry Ice was added to the reaction mixture. After warming to room temperature the mixture was poured into a separatory funnel containing 50 ml of ether and 50 ml of water. The aqueous layer was separated, acidified with dilute hydrochloric acid, and extracted with five 50-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure to give 0.263 g (43%)[44] of (+)-(*R*)-1-naphthalenesulfinylacetic acid,[20] mp 156–158°, [α]D +115°; infrared (SO stretch at 1055 cm^{-1}) and nmr [solvent acetone-d_6; aromatic multiplet at τ 1.75–2.5 (7.0 H), methylene AB quartet with τ_A 5.92, τ_B 6.28, J_{AB} = 14.0 Hz (2.0 H)] spectra were identical with those of racemic material, mp 156–157° (lit. 153–154°,[21] 151°[45]), prepared by periodate oxidation[46] of 1-naphthalenethioacetic acid.[47] Based on the highest reported rotation, [α]D ±456° (ethanol),[21,45] the material is 25.2% optically pure, corresponding to retention of 83.2% of asymmetry in the reaction sequence starting with a mixture (65.15:34.85) of diastereomeric menthyl methanesulfinates. The ORD spectrum of the (+)-(*R*) isomer, prepared by the carbonation reaction described above, is similar to that reported by Kielczewski[48] and corresponds in all respects

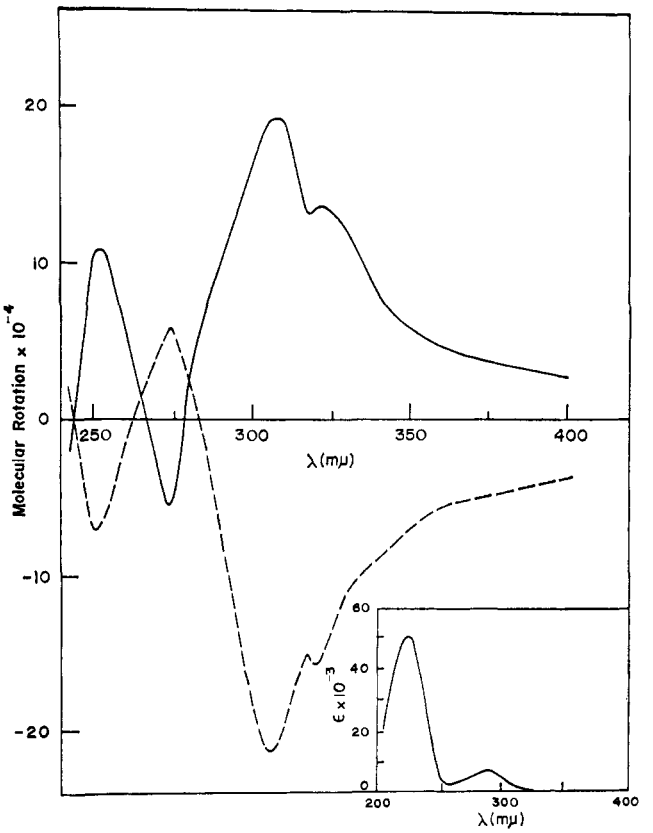


Figure 1. Optical rotatory dispersion of (+)-(*R*)- and (−)-(*S*)-1-naphthalenesulfinylacetic acids in methanol, indicated by solid and dashed lines, respectively, and corrected to optical purity. The ultraviolet absorption spectrum (methanol) is given in the lower right-hand corner.

(within experimental error) except for sign to that of the (−)-(*S*) isomer,[20] prepared by resolution of the racemic acid according to the procedure reported in the literature[21,45] (Figure 1).

Kinetics of Racemization of Methyl Phenyl Sulfoxide. Conditions for this experiment were the same as those described above for the cleavage and racemization studies (molar ratio of methyllithium to sulfoxide 1:1) with the modification that the temperature was maintained at 25 ± 2°. A separate run was performed for each time interval stated in Table III. In each case the reaction mixture was quenched with water, and the sulfoxide was isolated by column chromatography and subsequent distillation (Kugelrohr). The sulfoxide was homogeneous by infrared and glpc. The reaction mixture becomes heterogeneous after approximately 20 hr and kinetic analysis leads to large errors for long reaction times. From the data in Table III, a first-order rate constant k_{rac} = (1.8 ± 0.3) × 10^{-6} sec^{-1} was calculated.

Table III. Racemization of Phenyl Methyl Sulfoxide as a Function of Time

Time, hr	[α]D (ethanol), deg	Time, hr	[α]D (ethanol), deg
0.0	147.5	29.5	118.1
14.3	133.1	48.0	117.0
20.0	128.0	76.3	88.9

Methyl-^{13}C Phenyl Sulfoxide. A solution of 1.0 g (7.0 mmoles) of ^{13}C-enriched methyl iodide (50–60 atom % ^{13}C enrichment, Volk Radiochemical Company, Burbank, Calif.) was added to 7.0 mmoles of sodium thiophenoxide (prepared from 0.77 g of thiophenol and 0.28 g of sodium hydroxide) in 15 ml of ethanol. The resulting solution was stirred for 1 hr after the addition. The reaction mixture was poured into 50 ml of water, and the resulting solution was extracted with three 50-ml portions of

(44) Metallation and carbonation at room temperature gave only a 2% yield, due to extensive cleavage.
(45) F. Gajowczyk and J. Suszko, *Ber.*, **68**, 1005 (1935).
(46) N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).
(47) F. M. Furman, J. H. Thelin, D. W. Hein, and W. B. Hardy, *J. Am. Chem. Soc.*, **82**, 1450 (1960).
(48) M. Kielczewski, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, 12, 849 (1964).

Table IV. $^{13}CH_3$–$^{12}CH_3$ Exchange Reactions

Reagent quantities, mmoles						
Methyl-^{13}C sulfoxide	Methyllithium	Reaction time, hr	DME, ml	^{13}C enrichment, %: Starting	^{13}C enrichment, %: Recovered	Recovery of sulfoxide, %
2.60	2.72	20	50	51.7 ± 1	52.8 ± 1	68
1.58	6.32	15	30	51.7 ± 1	52.7 ± 1	14

ether. The ether extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure to give a light yellow oil. Without purification the thioanisole was oxidized with 1.5 g (7.0 mmoles) of sodium metaperiodate in 50 ml of ethanol. The reaction was stirred for 20 hr at room temperature. The precipitated sodium iodate was removed by vacuum filtration and was washed with approximately 20 ml of ethanol. The filtrate was poured into 200 ml of water. The resulting solution was extracted with one 100-ml portion of 60–70° petroleum ether, saturated with sodium chloride, and extracted with four 50-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure to give a light yellow oil. Kugelrohr distillation at 80° (0.2 mm) afforded 0.845 g (87% based on methyl iodide) of methyl-^{13}C phenyl sulfoxide. ^{13}C analysis by nmr showed 52% ^{13}C enrichment. Pmr analysis of methyl-^{13}C phenyl sulfoxide gave the following values (in Hz below internal TMS): ^{12}C-methyl protons, 162.5 (1.45 H); ^{13}C-methyl protons, 92 and 232 (1.55 H); aromatic protons, 457 (5 H). The ^{13}C–H spin coupling constant is 140 Hz.[49] The ^{13}C enrichment thus was 52%. Exchange reactions with ordinary methyllithium (assuming 1.1% natural abundance of ^{13}C) were carried out as previously described for cleavage studies, and the results are given in Table IV. No DMSO was detected in the reaction mixture by glpc analysis.

Phenyl-^{14}C Methyl Sulfoxide. The Grignard reagent was prepared from 7.48 g (4.8 mmoles) of bromobenzene-^{14}C with unspecified label (product of International Chemical and Nuclear Corp., City of Industry, Calif., diluted to an activity[50] of 28.49 ± 0.47 counts min^{-1} μmole^{-1}) and 1.10 g (4.5 g-atoms) of magnesium metal in ether. A solution of 9.81 g (4.5 mmoles) of menthyl methanesulfinate in 20 ml of ether was added to the preformed Grignard reagent. The product was isolated as described above. The infrared spectrum was identical with that of authentic phenyl methyl sulfoxide. The activity was 28.84 ± 0.36 counts min^{-1} μmole^{-1}.

Exchange Reaction between Phenyl-^{14}C Methyl Sulfoxide and Phenyllithium. The exchange reaction was run in the same manner as that described above for racemization and cleavage studies with methyllithium with the exception that 1.85 *M* phenyllithium in 70:30 benzene–ether (Alfa Inorganics, Inc.) was used and the reaction time was 22 hr. The recovered sulfoxide had an activity of 25.61 ± 0.60 counts min^{-1} μmole^{-1}.

Racemization of Phenyl Methyl Sulfoxide with Phenyllithium. This reaction was run in the same manner as the exchange reaction described above. Starting with phenyl methyl sulfoxide, $[\alpha]^{24}D$ +150° (*c* 1.46, ethanol), the recovered sulfoxide had $[\alpha]^{25}D$ +75° (*c* 2.58, ethanol).

Reaction of Methyllithium with Fluorenylidene Sulfine. The cleavage of fluorenylidene sulfine[26] with methyllithium was performed by the procedure given above for racemization and cleavage. Upon addition of methyllithium to the sulfine, the solution instantaneously developed a red color. Work-up of the usual procedure afforded no recovered sulfine (absence of infrared bands[26] at 1120 and 1019 cm^{-1}). Tlc analysis of the crude reaction mixture indicated a complex mixture of products; fluorene and bisfluorenylidene were qualitatively identified by infrared analysis.

N-Benzenesulfinylmorpholine. An ethereal solution of 18.3 g (18.3 ml, 0.21 mole) of morpholine was added dropwise at room temperature to a solution of 16.8 g (0.105 mole) of benzenesulfinyl chloride[51] in 50 ml of ether. Morpholine hydrochloride separates from the reaction mixture during the addition. The resulting slurry was poured into water and extracted with additional portions of ether until all of the solid had dissolved. The combined ether extracts were dried over anhydrous magnesium sulfate and filtered. The solvent was removed from the filtrate under reduced pressure to yield 11.3 g (51%) of crude N-benzenesulfinylmorpholine. Recrystallization of the product from ether gave 6.0 g of white powder, mp 79.5–81°.

Anal. Calcd for $C_{10}H_{13}SO_2N$: C, 56.84; H, 6.20; N, 6.63; S, 15.18. Found: C, 57.04; H, 6.05; N, 6.74; S, 15.49.

Reaction of N-Benzenesulfinylmorpholine with Methyllithium. A solution of 3 ml of 1.7 *M* methyllithium in ether (5.1 mmoles) was added dropwise to a solution of 1.0 g (4.7 mmoles) of N-benzenesulfinylmorpholine in 200 ml of ether cooled to −70° (Dry Ice bath). The reaction mixture became turbid during the addition and a white precipitate formed. The resulting mixture was stirred for 2 min at −70° and was hydrolyzed with 10 ml of a saturated aqueous solution of ammonium chloride. The reaction mixture became homogeneous during the hydrolysis process. The ether layer was extracted with three 75-ml portions of water. The combined water extracts were saturated with sodium chloride and extracted with three 50-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure to yield 0.5 g of crude product. Kugelrohr distillation at 90° (0.15 mm) afforded 0.35 g (53%) of methyl phenyl sulfoxide, identical in all respects with authentic material.

In a similar experiment employing methylmagnesium chloride (6.0 mmoles added to 4.7 mmoles of N-benzenesulfinylmorpholine at room temperature) the yield of methyl phenyl sulfoxide was 0.605 g (91%).

(49) P. Haake, W. B. Miller, and D. A. Tyssee, *J. Am. Chem. Soc.*, **86**, 3577 (1964), and N. Muller and D. Pritchard, *J. Chem. Phys.*, **31**, 1471 (1959), have reported a ^{13}C–H spin coupling constant of 138 Hz for DMSO.

(50) The determinations of relative activities were performed on a Packard Tricarb Model 3003 liquid scintillation spectrometer employing Bray's solution as the scintillation liquid.

(51) Prepared by the addition of 5 molar equiv of thionyl chloride to solid sodium benzenesulfinate (Aldrich Chemical Co.) at room temperature and isolated by the procedure given in the text for methanesulfinyl chloride.