

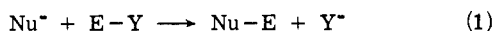
The Relative Nucleophilicity of Common Nucleophiles toward Sulfenyl Sulfur. Comparison of the Relative Reactivity of Different Nucleophiles toward Sulfenyl vs. Sulfonyl Sulfur¹

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Abstract: The rates of reaction, k_{Nu}^{S} , of 15 different nucleophiles with phenyl benzenethiolsulfonate (**2**) at 25° in 60% dioxane (eq 9) have been determined using both stopped-flow and conventional spectrophotometry. These rate constants are compared with those, $k_{\text{Nu}}^{\text{SO}_2}$, obtained earlier under identical conditions for reaction of the same nucleophiles with phenyl α -disulfone (**1**) (eq 8). A plot of $\log k_{\text{Nu}}^{\text{S}}$ vs. $\log k_{\text{Nu}}^{\text{SO}_2}$ for the data for seven nitrogen-base nucleophiles shows excellent linearity, with the slope of the correlation line being quite close to one. While the data for five anionic nucleophiles are also fairly well correlated by this same correlation line, the data for CN^- and $n\text{-BuS}^-$, the only two soft-base nucleophiles studied, are not. Both CN^- and $n\text{-BuS}^-$ are much more reactive in the substitution at the sulfenyl sulfur of **2** than would be predicted from the correlation line governing the reactivity of the rest of the nucleophiles. This behavior is in line with what the theory of hard and soft acids and bases, as applied to nucleophilic substitutions, would predict would happen on changing from SO_2 to S as the electrophilic center where the substitution occurs. Possible reasons for the failure of the N_+ function of Ritchie and Virtanen to correlate the data for **2** are discussed. Comparison of the data for **1** and **2** also reveals that the α -disulfone **1** is in general very reactive for a sulfonyl compound as regards the rates at which it undergoes substitution at an SO_2 group. This is believed to be due to significant thermodynamic destabilization of the α -disulfone due to inductive repulsion between the two adjacent sulfur atoms each bearing an appreciable partial positive charge.

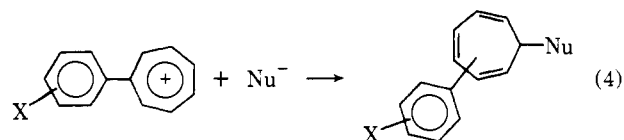
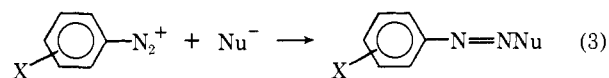
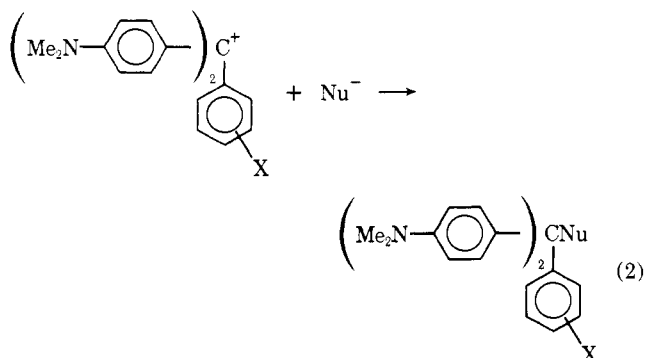
Nucleophilic substitution reactions, which can be represented in a generalized sense as shown in eq 1, play a cen-



tral role throughout chemistry. One of the important questions regarding their behavior is what factors principally determine the relative order of reactivity of a series of nucleophiles in a given substitution and whether or not there are significant changes in the reactivity order of a series of nucleophiles with a change in the nature of the electrophilic center (E) where the substitution takes place.

A series of papers by Pearson and various associates² over the course of a period of years have presented data which appeared to indicate the existence of significant changes in the reactivity pattern for nucleophiles with a change in the nature of the electrophilic center where the substitution occurred. Pearson and Songstad^{2b} suggested that many of these changes could be rationalized by the theory of hard and soft acids and bases (HSAB) if one presumed that hard electrophilic centers (acids) would react particularly well with hard nucleophiles (bases), while soft electrophilic centers would react particularly well with soft nucleophiles.

More recently Ritchie and coworkers^{3,4} have measured the reactivity of an extensive series of nucleophiles toward various triarylmethyl cations (eq 2), aryl diazonium ions



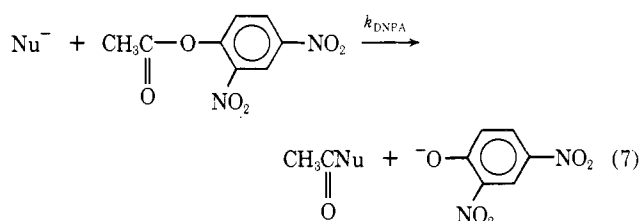
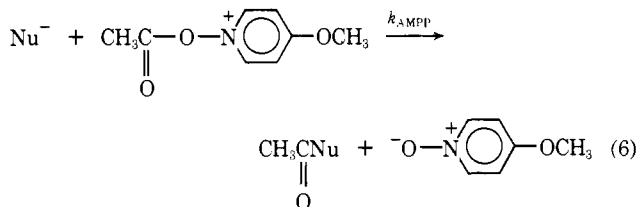
(eq 3), and tropylium ions (eq 4). Ritchie's key finding was that although the cations studied differed enormously in reactivity the entire body of data could be correlated by the equation

$$\log (k_{\text{Nu}}/k_{\text{H}_2\text{O}}) = N_+ \quad (5)$$

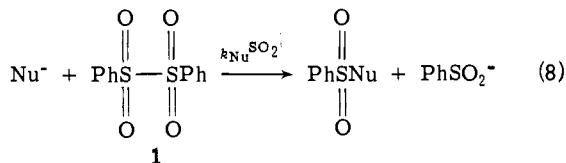
where k_{Nu} is the rate constant for reaction of a given nucleophile Nu with a particular cation, $k_{\text{H}_2\text{O}}$ is the rate constant for reaction of the same cation with water, and N_+ is a parameter characteristic of the nucleophile and independent of the cation. Values of N_+ were normally determined by measuring the reactivity of the nucleophile and water toward the reference cation *p*-nitro(Malachite Green), PNMG, and making use of the relationship $N_+ = \log k_{\text{Nu}}^{\text{PNMG}} - \log k_{\text{H}_2\text{O}}^{\text{PNMG}}$. Thus, in the reactions represented by eq 2-4, even though one might have thought that the various cations employed would differ somewhat in character as electrophilic centers, there is no detectable alteration in the pattern of nucleophile reactivity as one changes from one cationic center to another.

Ritchie and Virtanen⁴ have argued that the N_+ values are measures of the energies required to desolvate the nucleophiles, the higher N_+ , the lower the energy required, and that the reason N_+ values successfully correlate all the reactivity data for eq 2-4 is because in all these reactions the ease of desolvation of the nucleophile is the dominant factor in determining relative rates. They have suggested that other nucleophilic substitution reactions in which desolvation of the nucleophile is the dominant factor governing nucleophile reactivity might also therefore be expected

to show a good correlation of rates with N_+ values, and they have gone on to show that the extensive data on reactivity of various nucleophiles toward 1-acetoxy-4-methoxy-pyridinium perchlorate, AMPP⁺ (eq 6), and 2,4-dinitrophenyl acetate, DNPA (eq 7), obtained by Jencks and Gilchrist⁵ are also well correlated by N_+ .

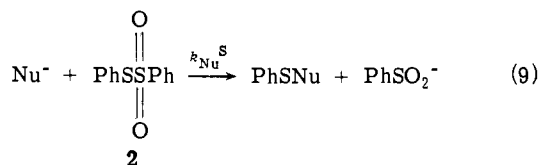


Recent work⁶ in this laboratory has shown that there is essentially a 1:1 correlation between the order of reactivity of a series of nucleophiles toward phenyl α -disulfone, **1** (eq 8), and their reactivity order toward either AMPP or



DNPA, a plot of $\log k_{\text{Nu}}^{\text{SO}_2}$ vs. $\log k_{\text{Nu}}^{\text{AMPP}}$, for example, being linear with unit slope. Given the fact that N_+ correlates the data on nucleophile reactivity toward AMPP and DNPA, this, of course, means that N_+ will also correlate the data on nucleophile reactivity toward phenyl α -disulfone. Thus N_+ appears to provide a good correlation for nucleophilic reactivity in a substitution at a sulfonyl sulfur bearing a good leaving group ($\text{p}K_a$ of $\text{PhSO}_2\text{H} = 1.2$),⁷ just as it appears to be able to correlate data for substitutions at the carbonyl carbon of highly reactive esters (eq 6 and 7).

Phenyl benzenethiolsulfonate (**2**) also undergoes simple nucleophilic substitution reactions with a wide range of nucleophiles (eq 9). These reactions can be studied kinetically



in the same solvent medium used for the reactions of the α -disulfone **1**. Since the leaving group (PhSO_2^-) is identical, the only difference between eq 8 and 9 is the nature of the electrophilic center at which the substitution takes place. In eq 8 it is a sulfonyl sulfur, while in eq 9 it is a dicoordinate, or sulfenyl, sulfur. According to the ideas of Pearson and Songstad,^{2b} the change from sulfonyl to sulfenyl sulfur should represent a change from a hard to a relatively soft electrophilic center, and should presumably lead to significant and predictable changes in the order of nucleophile reactivity toward **2** from what is observed with **1**. Alternatively, given the identity in reaction conditions, the otherwise apparent marked similarity between eq 8 and 9, and the success of N_+ in correlating nucleophile reactivity discussed above, others might predict that $\log k_{\text{Nu}}^{\text{S}}$ would correlate

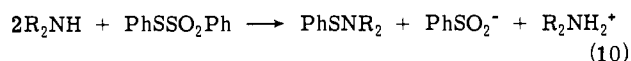
with N_+ and that one would get the same order of nucleophile reactivity toward **2** as toward **1**.

In the present work we have measured the reactivity of about 15 common nucleophiles toward **2** under exactly the same conditions used previously⁶ for these same nucleophiles with **1**. Our hope was that comparison of the results for **2** with those for **1** would contribute to a better assessment of both the value of the HSAB proposals regarding nucleophile reactivity made by Pearson and Songstad^{2b} and the breadth of applicability of the N_+ concept of Ritchie and Virtanen.⁴

In the course of carrying out this work we have also found in several cases interesting chemical behavior associated with certain of the compounds PhSNU resulting from attack of certain nucleophiles on **2**. These observations are also discussed.

Results

Reaction of Amines with 2. Dunbar and Rogers⁸ have shown that **2** reacts with primary or secondary amines to give sulfenamides (eq 10). Although the reaction is revers-



ible, the equilibrium constant is large enough ($K_{\text{eq}} = 2.2$ for reaction of **2** with morpholine in 7:1 acetonitrile: H_2O , for example) that by using a large excess of amine over **2** one can easily drive it to completion. We have measured the rate of reaction at 25° of five different representative amines with **2** in 60% dioxane in 1:1 amine:amine H^+ buffers in which the amine was present in from 25 to 100 times stoichiometric excess over **2**. The reactions were followed by observing the change in absorbance, A , at an appropriate wavelength between 270 and 275 nm, using either conventional or stopped-flow spectrophotometry, depending on the rate of the particular reaction. In every instance plots of $\log(A - A_\infty)$ vs. time were nicely linear, showing that the disappearance of **2** followed good first-order kinetics. The slope of such a plot, k_1 , is equal to the experimental first-order rate constant under those conditions. The results are tabulated in Table I. If the reaction also shows a simple first-order dependence on amine concentration, $k_1/[\text{amine}]$ should be independent of amine concentration for any given amine. Table I shows this to be the case.

Reaction of Hydrazine and Hydroxylamine with 2. The kinetics of the reaction of hydroxylamine with **2** were similar to those observed with ordinary primary and secondary amines, and the results are shown in Table I.

On the other hand, the reaction of hydrazine with **2** did not exhibit the same kinetic behavior as the reactions of the other amines, as can be seen from Figure 1, which shows a plot of $\log(A - A_\infty)$ vs. time for a typical run with hydrazine. The apparent first-order rate constant is seen to increase during the first part of the run, but finally levels off at a value approximately double what it is at the start. This is the sort of behavior that would be expected if the sulfenyl hydrazide, PhSNHNH_2 , formed initially by reaction of **2** and hydrazine, were to break down rapidly to PhSH and diimide, since PhSH , once formed, would react very fast with **2** under these conditions.⁹ The presumed sequence of reactions is shown in eq 11-13.

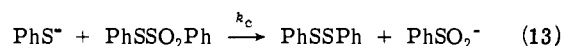
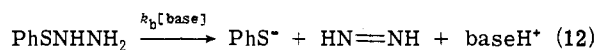
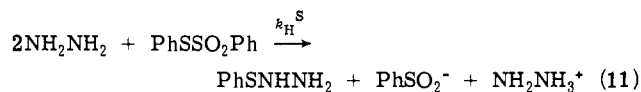


Table I. Kinetics of the Reaction of Amines and Hydroxylamine with Phenyl Benzenethiolsulfonate at 25° in 60% Dioxane^a

Amine	10 ⁴ [2] ₀ , M	10 ⁴ [amine] ₀ , M	10 ⁴ [amineH ⁺], M	10 ⁴ k ₁ , sec ⁻¹	k ₁ /[amine], M ⁻¹ sec ⁻¹
Piperidine	2.2	4.0	4.0	115	29
		2.0	2.0	54	27
		1.0	1.0	27	27
Piperazine	2.0	4.0	4.0	11.8	3.0
		2.0	2.0	5.8	2.9
		1.0	1.0	3.0	3.0
<i>n</i> -BuNH ₂	2.2	4.0	4.0	8.9	2.2
		2.0	2.0	4.3	2.1
		1.0	1.0	2.1	2.1
Morpholine	2.0	4.0	4.0	1.28	0.32
		2.0	2.0	0.67	0.33
		1.0	1.0	0.33	0.33
NH ₂ OH ^d	2.1	2.0	2.0	0.126	0.063
		1.0	1.0	0.059	0.059
		4.0	4.0	0.037	0.0092
H ₂ NCH ₂ COOEt ^{d,e}	2.1	4.0	4.0	0.037	0.0092
		2.0	2.0	0.019	0.0093

^a Except where indicated all runs with ionic strength of the solution held constant at 0.04 by addition of lithium perchlorate. ^b Solutions were prepared by adding the calculated amount of standard HClO₄ to a solution of the nitrogen base. ^c Experimental first-order rate constant for the disappearance of **2**. ^d Buffers were prepared by adding the calculated amount of standard OH⁻ to a solution of the hydrochloride of the base. ^e Ionic strength = 0.08 in all runs with glycine ethyl ester.

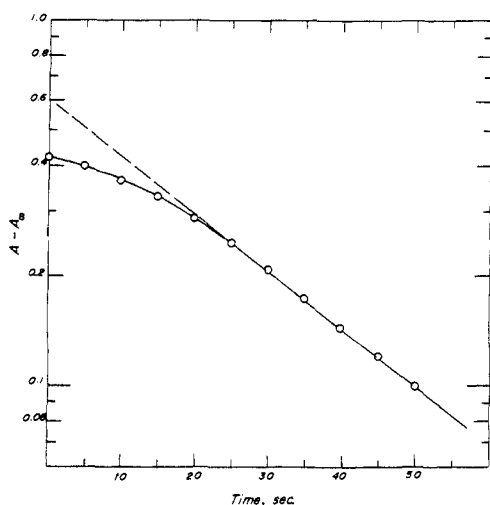


Figure 1. Plot of $\log(A - A_\infty)$ vs. time for reaction of hydrazine (0.02 M) with **2** (2×10^{-4} M) in 60% dioxane at 25°.

At the start of the reaction, before any PhS⁻ has been formed, the experimental first-order rate constant, k_1 , will be equal to $k_H^S[\text{NH}_2\text{NH}_2]$; but, as long as $k_b[\text{base}] > k_H[\text{NH}_2\text{NH}_2][\text{2}]$ and $k_c[\text{PhS}^-] > k_b[\text{base}]$, [PhS⁻] will increase and reach a steady state value before the reaction has proceeded too far. As [PhS⁻] increases k_1 will increase, finally leveling off at a value equal to $2k_H[\text{NH}_2\text{NH}_2]$ when [PhS⁻] reaches its steady state value.

When generated as an intermediate in other systems diimide (HN=NH) is known to be able to effect the reduction of olefinic double bonds.¹¹ Strong support for the proposal (eq 12) that PhSNHNH₂ decomposes readily into thiophenol and diimide is therefore provided by a series of experiments which show that mixing hydrazine and **2** together in the presence of several olefins leads to the reduction of significant amounts of the olefin. Specifically, with stilbene as the olefin, adding **2** (0.75 mmol) to a refluxing methanol solution of stilbene (0.5 mmol) and hydrazine (5 mmol) gave upon work-up a 63% yield of bibenzyl; with allyl alcohol as the olefin, the same conditions gave a 34% yield of 1-propanol; with diphenylacetylene, one got a mixture of equal amounts of *cis*-stilbene and bibenzyl, both in about 10% yield. No reduction of these compounds occurred under the same conditions in the absence of **2**.

We thus believe that the mechanism for the hydrazine-**2** reaction shown in eq 11-13 has been adequately substantiated and have accordingly estimated the reactivity of hydrazine toward **2** by taking the final slopes of plots of $\log(A - A_\infty)$ vs. time for the various runs as equal to $2k_H[\text{NH}_2\text{NH}_2]$. The results, all for 1:1 NH₂NH₂:NH₂NH₃⁺ buffers are the following: 0.04 M, 0.077 sec⁻¹; 0.02 M, 0.037 sec⁻¹; 0.01 M, 0.016 sec⁻¹. From these data k_H is estimated to be $0.9 \text{ M}^{-1} \text{ sec}^{-1}$.

Reaction of Anionic Nucleophiles with 2. The reactivity of *n*-BuS⁻, PhS⁻, and OH⁻ toward **2** has been determined in accompanying papers.^{10,12} In the present work we have examined the kinetics of the reaction of the following additional anionic nucleophiles toward **2**—CN⁻, HO₂⁻, CH₃C(O)NHO⁻, N₃⁻, and CF₃CH₂O⁻. The reactions were followed by monitoring the change in optical density with time at suitable wavelengths in the range 270-285 nm. In all cases the nucleophile was present in large stoichiometric excess over **2** so that the disappearance of **2** would follow pseudo-first-order kinetics.

The runs with cyanide ion were carried out in 1:1 CN⁻:HCN buffers. The kinetic behavior was straightforward and unexceptional, plots of $\log(A - A_\infty)$ vs. time showing excellent linearity with no drift in A_∞ with time. The results, which are shown in Table II, indicate that the experimental first-order rate constant, k_1 , varies linearly with [CN⁻].

The runs with HO₂⁻ were carried out in solutions in which H₂O₂ was present in considerable excess over HO₂⁻. That HO₂⁻ is the reactive nucleophile, however, is shown by the manner in which k_1 varies with [HO₂⁻] (see Table II). As with the cyanide runs, plots of $\log(A - A_\infty)$ vs. time were nicely linear. There was also no significant drift in A_∞ with time, at least for a period of time which was substantially longer than the time required for the initial reaction to go to completion. Since the initial substitution product, PhSOOH, is doubtless quite unstable, this observation suggests that either its breakdown is apparently rapid compared to its rate of formation under these conditions or that it and its decomposition products have essentially the same extinction coefficient at 270 nm, the wavelength at which the reaction was followed. The former explanation seems the more likely. We believed that decomposition of the persulfenic acid PhSOOH, or its anion, should lead to the corresponding sulfinic acid PhSO₂H or its anion. That this is indeed the case was shown by experiments in

Table II. Kinetics of Reaction of Selected Anionic Nucleophiles with Phenyl Benzenethiolsulfonate at 25° in 60% Dioxane^a

Nucleophile	10 ⁴ [2] ₀ , M	10 ³ [Nu ⁻], M	10 ³ [NuH], M	k ₁ , ^b sec ⁻¹	k ₁ /[Nu ⁻], M ⁻¹ sec ⁻¹
CN ⁻	2.1	2.0	2.0	151	7.6 × 10 ³
		1.0	1.0	78	7.8 × 10 ³
		0.4	0.4	32	8.0 × 10 ³
HOO ⁻	2.1	0.5	1.25	9.2	1.8 × 10 ³
		0.2	1.55	3.7	1.8 × 10 ³
		2.0	2.0	0.19	9.5
CH ₃ C(O)NHO ⁻	2.1	2.0	1.0	0.12	12
		1.0	1.0		

^a All runs with ionic strength of solution held constant at 0.04 by addition of lithium perchlorate. ^b Experimental first-order rate constant for disappearance of 2.

which both 2 and another aryl thiolsulfonate, *p*-CH₃C₆H₄SO₂SC₆H₄-*p*-CH₃, were treated with an equimolar amount of H₂O₂ in a solution made basic with excess sodium carbonate. Yields of sulfinic acid of 75–90%, based on a stoichiometry involving initial reaction according to eq 9 (Nu⁻ = HO₂⁻) followed by decomposition of the persulfenic acid to sulfinic acid, were obtained.

In the runs with CH₃C(O)NHO⁻ as the nucleophile there is a definite drift in A_∞ with time. The rate of this drift is independent of the concentration of CH₃C(O)NHO⁻ and is rapid enough to make it quite difficult to estimate an accurate value of A_∞ for runs having a CH₃C(O)NHO⁻ concentration of less than 0.01 M. The rate constants for runs having acetohydroxamate concentrations of 0.01 and 0.02 M are shown in Table II. The problem with the drifting A_∞ is doubtless responsible for the fact that k₁/[Nu⁻] shows less constancy than for the other nucleophiles.

With azide ion the breakdown of the initial substitution product PhSN₃ occurs at a rate comparable to its rate of formation from 2 and N₃⁻, even for an azide concentration of 0.04 M.¹³ In principle the system could be treated as two consecutive first-order reactions. However, since the extinction coefficient of PhSN₃ is unknown, one cannot hope to obtain very accurate rate constants for the two steps by treating the absorbance data in this manner. We have therefore simply estimated a rough value of k_{N₃} for the reaction of azide with 2 by using the initial rates as measured on a stopped-flow spectrophotometer for runs having concentrations in the range of 0.04 M N₃⁻. They indicate that k_{N₃} is 0.7 ± 0.3 M⁻¹ sec⁻¹ at 25° in 60% dioxane.

To assess the reactivity of CF₃CH₂O⁻ toward 2 stopped-flow runs were carried out in 60% dioxane solutions containing 0.10 M CF₃CH₂OH to which was added either 0.005 or 0.01 M OH⁻. Given the relative pK_a's of CF₃CH₂OH and H₂O these are conditions under which all the OH⁻ added should be converted to CF₃CH₂O⁻ by reaction with the alcohol. In these runs there was initially a modest, but rapid, increase in absorbance which was followed by a considerably slower (factor of about 7) and considerably larger (factor of about 3) decrease in absorbance. We assume that the initial increase is due to the reaction of CF₃CH₂O⁻ with 2 to form PhSOCH₂CF₃ (eq 9, Nu⁻ = CF₃CH₂O⁻), and that the subsequent slower decrease is due to a base-catalyzed decomposition of PhSOCH₂CF₃. Since we did not investigate the nature of the final reaction products, we will not speculate on the course of the latter reaction. The apparent first-order rate constant for the initial phase of the reaction was 2.5 ± 0.4 sec⁻¹ for a run 0.005 M in CF₃CH₂O⁻ and 5.0 ± 0.7 sec⁻¹ for a run 0.01 M in CF₃CH₂O⁻, indicating a second-order rate constant for reaction of CF₃CH₂O⁻ with 2 of 5 × 10² M⁻¹ sec⁻¹.

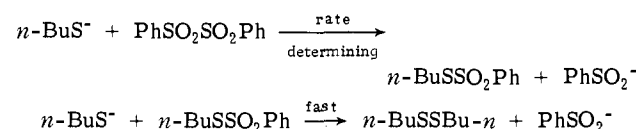
Reaction of 1-Butenethiolate Ion with 1. 1-Butenethiolate ion was not one of the nucleophiles studied in the earlier work⁶ on nucleophile reactivity toward phenyl α-disulfone (1). To permit comparison of its reactivity toward 1 vs. 2,

Table III. Summary of Rate Constants for Reaction of Nucleophiles with Phenyl Benzenethiolsulfonate (2) and Phenyl α-Disulfone (1) in 60% Dioxane at 25°^a

Nucleophile	k _{Nu^S} (eq 9), M ⁻¹ sec ⁻¹	k _{Nu^{SO₂}} (eq 8), M ⁻¹ sec ⁻¹
<i>n</i> -BuS ⁻	1.9 × 10 ⁷	4.4 × 10 ²
PhS ⁻	3.2 × 10 ⁶	
CN ⁻	7.8 × 10 ³	0.45
HOO ⁻	1.8 × 10 ³	5.4 × 10 ³
CF ₃ CH ₂ O ⁻	5 × 10 ²	230
OH ⁻	4.4 × 10 ²	75
Piperidine	27	120
CH ₃ C(O)NHO ⁻	11	870
Piperazine	3.0	48
<i>n</i> -BuNH ₂	2.1	17
NH ₂ NH ₂	0.9	16
N ₃ ⁻	0.7	0.94
Morpholine	0.33	12
NH ₂ OH	0.061	1.9
H ₂ NCH ₂ COEt	0.0093	0.26

^a Data for 2 are from the present work and ref 10 and 12; data for 1 are from ref 6, except for *n*-BuS⁻, which was measured in present work. In almost all cases the data were obtained at an ionic strength of 0.04.

we have now studied the kinetics of the disappearance of 1 in the presence of 1-butanethiol (0.10 M) in acetate buffers in 60% dioxane. Rates were determined by following the change in optical density with time at 270 nm. Since *n*-BuS⁻ reacts with thiolsulfonates much faster than 1 the reaction presumably takes the course



In a 10:1 AcO⁻:AcOH buffer the experimental first-order rate constant for the *n*-BuSH-1 reaction was 2.4 × 10⁻⁴ sec⁻¹. In a 20:1 AcO⁻:AcOH buffer, it was 5.1 × 10⁻⁴ sec⁻¹. These values are 43,000 times smaller than the rate at which this thiol would react with thiolsulfonate 2 under the same reaction conditions.¹⁰

Discussion

The second column of Table III lists the rate constants, k_{Nu^S}, for reaction of the various nucleophiles studied with phenyl benzenethiolsulfonate (2) in 60% dioxane at 25° (eq 9). The right-hand column of Table III lists the rate constants, k_{Nu^{SO₂}}, for reaction of the same nucleophiles with phenyl α-disulfone (1) under exactly the same reaction conditions (eq 8).⁶

Figure 2 shows a plot of log k_{Nu^S} vs. log k_{Nu^{SO₂}} for the data in Table III. One can see that for the seven nitrogen-base nucleophiles (open circles) there is quite a good correlation between log k_{Nu^S} and log k_{Nu^{SO₂}}, the slope of the correlation line for these data being slightly smaller than

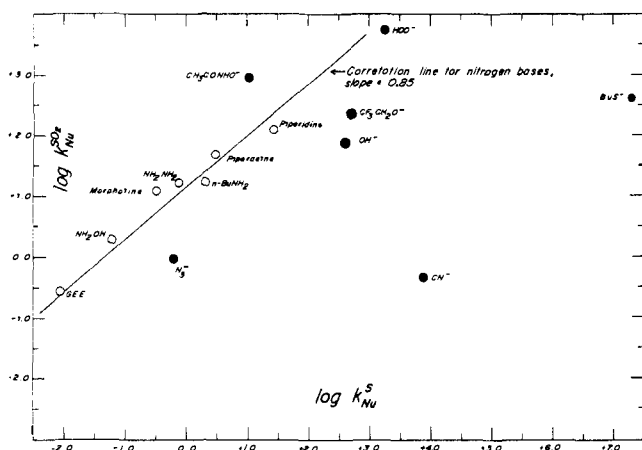


Figure 2. Plot of $\log k_{\text{Nu}}^{\text{S}}$ for reaction of nucleophiles with **2** vs. $\log k_{\text{Nu}}^{\text{SO}_2}$ for their reaction with **1** under the same reaction conditions. Anionic nucleophiles shown as solid circles, nitrogen-base nucleophiles as open circles.

one (0.85). While the data points for five of the anionic nucleophiles, although scattered, do not diverge too seriously from this line, the data points for the other two, CN^- and $n\text{-BuS}^-$, deviate *very* seriously. This deviation is in the direction that both these nucleophiles are from 10^5 to 10^6 more reactive toward the thiol sulfonate than their position in the reactivity order toward the α -disulfone would have led one to expect. These two nucleophiles, it should be noted, are the only two out of the whole group studied that are classed as soft bases by Pearson and Songstad.^{2c}

The dicoordinate, or sulfenyl, sulfur of **2** would be expected, according to the principles outlined by Pearson and Songstad,^{2c} to be a much softer electrophilic center than the sulfonyl sulfur where substitution occurs for **1**.¹⁴ According to the ideas of Pearson and Songstad,^{2c} soft-base nucleophiles should react with soft electrophilic centers particularly readily compared with their relative position in the reactivity order for a series of nucleophiles reacting with a hard electrophilic center. The behavior exhibited by CN^- and $n\text{-BuS}^-$ in Figure 2 is therefore exactly what would have been predicted by HSAB and would seem to support the contention of Pearson and Songstad^{2c} that variations in the character of the electrophilic center where substitution takes place can lead to variations in the order of nucleophile reactivity that are predictable from application of HSAB.

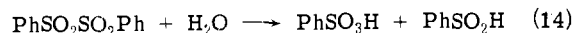
Some caution is perhaps advisable, however, as the following will show. Of the nucleophiles in Figure 2 other than CN^- and $n\text{-BuS}^-$, all but one are classed by Pearson and Songstad^{2c} as hard bases. The exception is azide ion, which is classed as being "intermediate." In accord with such a position it does react relatively faster, by about 1.2 log units, toward **2** than would be expected from the correlation line for the nitrogen-base nucleophiles and its reactivity toward **1**. However, before ascribing this to N_3^- being a softer nucleophile than the nitrogen bases, one should note that OH^- and $\text{CF}_3\text{CH}_2\text{O}^-$, both of which are hard bases, also exhibit a comparable deviation from the correlation line.

To be successfully correlated by N_+ , substitutions at different electrophilic centers must not exhibit, in a given solvent, any significant variation in the order of reactivity of a series of nucleophiles with a change in the nature of the electrophilic center. Obviously this does not hold for the behavior of CN^- and $n\text{-BuS}^-$ in the substitution at the sulfenyl sulfur of **2** (eq 9). Clearly, despite the success of N_+ in correlating the reactivity of nucleophiles toward α -disulfone **1**, it does not do at all well for the reaction of nucleo-

philes like CN^- with the sulfenyl sulfur of **2**, even though the leaving group and solvent are the same and the reactions involved (eq 8 and 9) seem to be very similar in character.

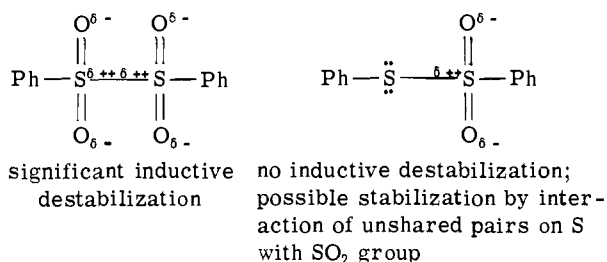
There would appear to be two positions that one can take on this failure of N_+ to correlate the data for **2** as well as it does those for **1**. The first is to point out that although N_+ successfully correlates data for substitutions at carbonyl and sulfonyl centers there is no reason that rates of nucleophilic substitutions at all electrophilic centers need be controlled primarily by the desolvation energy of the nucleophile. For those centers where the desolvation energy of the nucleophile is not the paramount factor in determining nucleophile reactivity, a correlation of rates with N_+ will almost certainly fail, as it does here for the substitutions involving **2**. The alternative is to suggest that, despite their apparent similarity in character, reactions 8 and 9 may conceivably differ significantly in mechanism in the sense that for **1** the rate-determining step always involves only the formation of the Nu-SO_2 bond, while for **2** the rate-determining step either involves formation of the Nu-S bond synchronous with the cleavage of the S-SO_2 bond, or, alternatively, that cleavage of the latter bond may in some cases be rate determining.¹⁵

Study of the spontaneous hydrolysis of phenyl α -disulfone^{17a} (eq 14) and phenyl benzenesulfinyl sulfone^{17b} (eq 15)



has indicated that, despite a large difference in rate, the reactions show virtually the same ρ value, ΔS^\ddagger , and response of rate to solvent composition. This suggests that both are of the same mechanistic type. Assuming this also holds true for other nucleophilic substitutions involving these two compounds, interpretation of the meaning of any change in the pattern of nucleophile reactivity on going from substitutions involving **1** to those involving the sulfinyl sulfone would presumably be free of the ambiguity just discussed for **2** vs. **1**. Previous study of the reaction of a very limited number of nucleophiles has suggested that going from the sulfonyl group of **1** to the sulfinyl group of the sulfinyl sulfone as the site of substitution does indeed alter the pattern of nucleophile reactivity significantly,¹⁸ but a definitive judgment and further discussion on this point would seem best deferred until a much more extensive study of nucleophile reactivity toward the sulfinyl sulfone, currently in progress in this laboratory, has been completed.

It is widely recognized¹⁹ that sulfonyl derivatives generally undergo nucleophilic substitution at the SO_2 group much less rapidly than equivalent substitution reactions occur at less highly oxidized sulfur centers. Yet, when we examine the data in Table III we are immediately struck by the fact that for the majority of the nucleophiles k_{Nu}^{S} for reaction with **2** is actually *smaller* than the rate constant at which the same nucleophile reacts with α -disulfone **1**. (Only in the case of CN^- and $n\text{-BuS}^-$ is $k_{\text{Nu}}^{\text{S}}/k_{\text{Nu}}^{\text{SO}_2}$ really significantly larger than one.) What is responsible for this, at first glance, most surprising state of affairs? We believe it is due to the fact that the α -disulfone (**1**) is unusually reactive for a sulfonyl compound,²⁰ and that its unusually high reactivity stems from the fact that it is significantly destabilized by inductive repulsion between the two adjacent sulfur atoms each bearing a substantial partial positive charge (as shown below). Such inductive destabilization is not a problem for the thiol sulfonate **2**; as a matter of fact, one can even suggest that **2** might be somewhat stabilized due to interaction of the unshared pairs on the sulfenyl sulfur with d orbitals on the sulfonyl group.



If one assumes that the rate of a typical nucleophilic substitution would normally be at least 10^5 – 10^6 faster at a sulfenyl sulfur than at a sulfonyl one,¹⁹ then the sort of ratios of $k_{\text{Nu}}^{\text{S}}/k_{\text{Nu}}^{\text{SO}_2}$ observed in Table III suggest that the combined effect of inductive destabilization of **1** plus any mesomeric stabilization of **2** must add up to at least 7–9 kcal/mol.

One final point is worth brief discussion. Several of the nucleophiles in Table III are of the class usually referred to as “ α -effect”^{2a} nucleophiles. As a class such nucleophiles exhibit greatly enhanced reactivity in many substitutions compared to that exhibited by closely related nucleophiles of comparable proton basicity. In its reaction with hydrazine **2** shows an α effect, as measured by $k_{\text{NH}_2\text{NH}_2}/k_{\text{GEE}} = 61$ (GEE = $\text{H}_2\text{NCH}_2\text{COOEt}$), very similar to that found for **1**. On the other hand, the α effect for HO_2^- , as measured by $k_{\text{HO}_2^-}/k_{\text{OH}^-} = 4.1$, is significantly smaller than those that this nucleophile gives with **1** ($k_{\text{HO}_2^-}/k_{\text{OH}^-} = 72$) or any other electrophilic centers yet studied (45 – 10^4).⁶ In the case of hydrazine the belief is that much or all of the α effect arises from the fact that ΔF° for reaction of this nucleophile with many electrophilic centers is more favorable than would be expected from its basicity toward a proton, and that this is reflected in ΔF^* for the reaction.^{22a} In the case of HO_2^- only part of the usually observed α effect can be ascribed to a more favorable ΔF° than predicted from the proton basicity of HO_2^- compared to other oxygen bases.^{22a} Aubort and Hudson^{22b} have ascribed the remainder to a decrease in the overlap integral of p orbitals on the adjacent oxygen atoms on going from HO_2^- to transition state which decreases the repulsion energy between the unshared electron pairs on the two atoms. A referee has suggested that the presence of unshared pairs on the electrophilic center in **2**, through a repulsive interaction with the approaching HO_2^- anion, might tend to largely offset the usual positive α -effect which has been observed⁶ with HO_2^- in substitutions at centers where there is no unshared electron pair on the atom serving as the electrophilic center. In this connection it is worth noting that the studies with **2** are apparently the first case where the reactivity of α -effect nucleophiles toward an electrophilic center bearing one or more unshared electron pairs has been investigated. Study of other such centers accordingly now seems indicated. An alternative explanation of the small α -effect for reaction of HO_2^- with **2** might be the following. We have noted earlier that the initial substitution product of the reaction of HO_2^- with **2**, PhSOOH , is apparently very unstable. This could cause ΔF° for reaction of HO_2^- with **2** to be less favorable than would be predicted from the basicity of HO_2^- toward a proton (*i.e.*, ΔF° for $\text{HO}_2^- + \text{H}^+ \rightarrow \text{H}_2\text{O}_2$). If this were then reflected in ΔF^* for the reaction, this could lead to a significantly smaller value of $k_{\text{HO}_2^-}/k_{\text{OH}^-}$ for **2** than those found⁶ for other substrates.

Experimental Section

Preparation and Purification of Materials. The preparation of phenyl benzenethiolsulfonate has been described in an accompanying paper¹⁰ as has the method used for purifying the dioxane

used as solvent. The purification of the nucleophiles followed the procedures of Kice and Legan.⁶

Procedure for Kinetic Runs with 2. In those cases (hydroxylamine hydrochloride, glycine ethyl ester hydrochloride, hydrogen peroxide, trifluoroethanol, and acetohydroxamic acid) in which the purified form of the nucleophile was the conjugate acid, solutions of the nucleophile of the proper concentration were prepared by adding a calculated amount of standard sodium hydroxide solution in 60% dioxane (v/v) to a known amount of the conjugate acid of the nucleophile in the same solvent. The proper amount of standard lithium perchlorate, if any, needed to bring the final ionic strength to the desired value was then added, and the solution was made up to volume. For all of the remaining nucleophiles except standard azide ion a 1:1 buffer of the nucleophile and its conjugate acid was prepared by adding a known amount of standard perchloric acid solution to a known amount of the nucleophile in 60% dioxane. Here too, if needed, the ionic strength was adjusted by the addition of standard lithium perchlorate.

The general procedures for the runs with **2**, whether followed by stopped-flow or conventional spectrophotometry, were the same as those already outlined⁶ for following the reaction of **1** with the same nucleophiles. In all cases except $\text{CH}_3\text{C}(\text{O})\text{NHO}^-$ a wavelength in the range 270–275 nm was used to follow the reaction. For $\text{CH}_3\text{C}(\text{O})\text{NHO}^-$ either 280 or 285 nm was employed.

Kinetics of the Reaction of 1 with 1-Butanethiolate Ion. 1-Butanethiol (0.10 M) was dissolved in an acetate buffer (either 10:1 or 20:1 $\text{AcO}^-:\text{AcOH}$) in 60% dioxane. The reaction of **1** with the thiol under these conditions was followed by monitoring the change in optical density with time at 270 nm using the general procedures already outlined.⁶

Reduction of Olefins by Hydrazine in the Presence of 2. A solution of 0.32 g (5.3 mmol of NH_2NH_2) of 85% hydrazine hydrate and 0.10 g (0.57 mmol) of *trans*-stilbene in 75 ml of methanol was brought to reflux and a solution containing 0.21 g (0.75 mmol) of **2** in 20 ml of methanol was added dropwise over a 1-hr period. The solution was then refluxed for an additional 4 hr. All but about 5 ml of the methanol was then removed under reduced pressure at room temperature. The residue was taken up in diethyl ether and extracted with 5% hydrochloric acid. The ether solution was then washed with water and dried over magnesium sulfate and the ether then removed under reduced pressure. A proton nmr spectrum on the residue showed it to consist of a mixture of bibenzyl and unreacted *trans*-stilbene. From the integrated intensities of the benzylic proton signal of bibenzyl at δ 2.82 and the olefinic protons of *trans*-stilbene at δ 7.1 this was shown to consist of 63% bibenzyl and 37% unreacted *trans*-stilbene. A control experiment shows that merely heating *trans*-stilbene and hydrazine in methanol under these conditions leads to only a very small amount of reduction of the olefin, consistent with the behavior reported by others.²³

Essentially the same reaction conditions were employed to reduce allyl alcohol, 0.03 g (0.52 mmol), with hydrazine (4.9 mmol) and **2** (0.72 mmol). Gas chromatography of a sample of the final reaction mixture on a 4 ft \times 0.25 in. column of Carbowax 20M on Chromosorb P at 130° indicated that 34% of 1-propanol had been formed, based on the comparison of peak areas with known samples.

In another experiment 0.11 g (0.62 mmol) of diphenylacetylene was treated analogously with hydrazine and **2** in methanol. Upon work-up there was isolated 10% of bibenzyl and 10% of *cis*-stilbene. The isolation of the latter rather than *trans*-stilbene is expected from the stereochemistry associated with diimide reductions.¹¹

Reaction of Hydrogen Peroxide Anion with 2. To a solution of 0.21 g (2.0 mmol) of sodium carbonate in 15 ml of water was added 0.05 g of 30% hydrogen peroxide (0.43 mmol of H_2O_2). To this was then added with stirring a solution of 0.12 g (0.43 mmol) of **2** in 15 ml of dioxane. The solution was allowed to stand for 4 hr at room temperature. The solvents were then removed under reduced pressure at room temperature, and the residue was treated with a known volume of glacial acetic acid. An aliquot of the glacial acetic acid solution was then titrated for sulfinic acid content using titration with standard sodium nitrite solution.²⁴ This titration method has been found to be quite specific for sulfinic acids and not to be influenced by the presence of a considerable variety of other sulfur compounds.²⁵ From the titration data, reaction of 0.43 mmol of **2** with an equimolar amount of HO_2^- gave 0.75

mmol (87%) of benzenesulfonic acid.

In another experiment 1.1 g (4.0 mmol) of *p*-tolyl *p*-toluenethiolsulfonate,¹² dissolved in 30 ml of dioxane was added with stirring to a solution of 0.52 g of 30% hydrogen peroxide (4.6 mmol of H₂O₂) and 2.2 g (20.8 mmol) of sodium carbonate in 100 ml of water and 25 ml of dioxane. The final solution was allowed to stand for 15 min. At the end of that time the still-alkaline reaction mixture was extracted with diethyl ether; the ether extracts were discarded. The water layer was then made quite strongly acid by the addition of sulfuric acid and immediately extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate and the ether was removed under reduced pressure. After drying at room temperature under high vacuum for 0.5 hr the residue was recrystallized from ether-hexane, affording 0.9 g (72%) of *p*-toluenesulfonic acid, mp 84–84.5° (lit.²⁴ 85°).

References and Notes

- (1) This research supported by National Science Foundation Grant GP-35927X.
- (2) (a) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962); (b) R. G. Pearson and J. Songstad, *ibid.*, **89**, 1827 (1967); (c) R. G. Pearson, H. Sobel, and J. Songstad, *ibid.*, **90**, 319 (1968).
- (3) (a) C. D. Ritchie and D. J. Wright, *J. Amer. Chem. Soc.*, **93**, 2425, 2429, 6574 (1971); (b) C. D. Ritchie and P. O. I. Virtanen, *ibid.*, **94**, 1589, 4963, 4966 (1972); (c) C. D. Ritchie and H. Fleischhauer, *ibid.*, **94**, 3481 (1972). For a summary of this and related work see C. D. Ritchie, *Accounts Chem. Res.*, **5**, 348 (1972).
- (4) C. D. Ritchie and P. O. I. Virtanen, *J. Amer. Chem. Soc.*, **95**, 1882 (1973).
- (5) W. P. Jencks and M. Gilchrist, *J. Amer. Chem. Soc.*, **90**, 2622 (1968).
- (6) J. L. Kice and E. Legan, *J. Amer. Chem. Soc.*, **95**, 3912 (1973).
- (7) C. D. Ritchie, J. D. Saltiel, and E. S. Lewis, *J. Amer. Chem. Soc.*, **83**, 4601 (1961).
- (8) J. E. Dunbar and J. H. Rogers, *J. Org. Chem.*, **31**, 2842 (1966).
- (9) In the NH₂NH₂-NH₂NH₃⁺ buffers PhSH should be present largely as PhS⁻. Other studies¹⁰ have shown that the rate constant for reaction of PhS⁻ with **2** in 60% dioxane at 25° is 3.2 × 10⁶ M⁻¹ sec⁻¹.
- (10) J. L. Kice and T. E. Rogers, *J. Amer. Chem. Soc.*, **96**, 8015 (1974).
- (11) S. Hunig, H. R. Muller, and W. Thier, *Angew. Chem., Int. Ed. Engl.*, **4**, 271 (1965).
- (12) J. L. Kice and T. E. Rogers, *J. Amer. Chem. Soc.*, **96**, 8009 (1974).
- (13) Use of markedly higher azide concentrations was precluded by the absorbance of azide ion at the wavelength used to follow the reaction.
- (14) J. L. Kice, "Inorganic Reaction Mechanisms. Part II," J. O. Edwards, Ed., Wiley, New York, N.Y., 1972, pp 170–171.
- (15) Ciuffarin and coworkers¹⁶ have described several substitutions involving amines and sulfonyl compounds that seem to follow this last mechanistic pattern.
- (16) E. Ciuffarin and F. Griselli, *J. Amer. Chem. Soc.*, **92**, 6015 (1970); E. Ciuffarin and G. Guaraldi, *J. Org. Chem.*, **35**, 2006 (1970).
- (17) (a) J. L. Kice and G. J. Kasperek, *J. Amer. Chem. Soc.*, **91**, 5510 (1969); (b) J. L. Kice and G. Guaraldi, *ibid.*, **89**, 4113 (1967).
- (18) J. L. Kice, G. J. Kasperek, and D. Patterson, *J. Amer. Chem. Soc.*, **91**, 5516 (1969).
- (19) Reference 14, pp 158–163.
- (20) Other evidence suggestive that **1** represents an unusually reactive sulfonyl derivative is the fact that it actually reacts slightly faster⁶ with OH⁻ at 25° than does the corresponding sulfonyl chloride,²¹ even though, *a priori*, one would probably have expected that, since Cl⁻ is presumably a considerably better leaving group than PhSO₂⁻, the sulfonyl chloride might be the more reactive of the two substrates.
- (21) O. Rogne, *J. Chem. Soc. B*, 1056 (1970).
- (22) (a) J. E. Dixon and T. C. Bruce, *J. Amer. Chem. Soc.*, **93**, 6592 (1971); **94**, 2052 (1972); (b) J. D. Aubort and R. F. Hudson, *Chem. Commun.*, 937 (1970).
- (23) J. E. Gordon and V. S. K. Chang, *J. Org. Chem.*, **38**, 3062 (1973).
- (24) J. L. Kice and K. W. Bowers, *J. Amer. Chem. Soc.*, **84**, 605 (1962).
- (25) J. L. Kice and E. H. Morkved, *J. Amer. Chem. Soc.*, **85**, 3472 (1963); **86**, 2270 (1964).

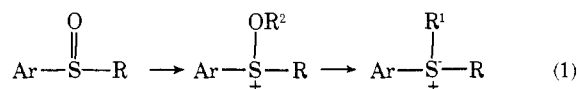
Nucleophilic Substitution at Tricoordinate Sulfur(IV). Stereochemistry of Dialkylarylsulfonium Salt Formation from Alkyl Aryl Sulfoxides¹

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Abstract: The *cis* and *trans* isomers of 2-methyl-2,3-dihydrobenzothiophene 1-oxide (**1** and **2**) were alkylated with trimethylxonium tetrafluoroborate and treated with methylmagnesium bromide at -78° or dimethylcadmium at room temperature to yield the *cis* and *trans* isomers of 1,2-dimethyl-2,3-dihydrobenzothiophenium tetrafluoroborate (**10** and **11**). The reaction proceeds with inversion of configuration at sulfur, but loss of stereospecificity may occur owing to isomerization of the starting material. The assignments of configuration to **1**, **2**, **10**, and **11** are presented.

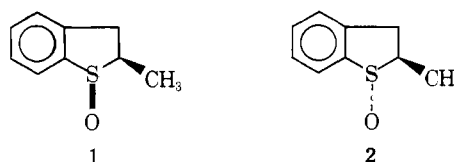
Optically active dialkylarylsulfonium salts can be prepared from optically active alkyl aryl sulfoxides by alkylation followed by reaction with a dialkylcadmium or an alkyl Grignard reagent⁴ (eq 1).



The aim of this present work was to determine the stereochemistry of this conversion, which, although assumed to proceed with inversion of configuration at sulfur analogous to most other nucleophilic substitutions on tricoordinate sulfur(IV) compounds had never been established. Nucleophilic displacement of alkoxy groups from sulfinates and alkoxy-sulfonium salts usually proceeds with inversion, thus providing the analogies to eq 1.⁵

We now wish to report the first experimental evidence concerning the stereochemical pathway followed in eq 1,

beginning with the *cis* and *trans* isomers of 2-methyl-2,3-dihydrobenzothiophene 1-oxide (**1** and **2**), the preparation



and characterization of which are described below. The diastereomeric sulfoxides, **1** and **2**, were chosen as substrates for the reaction since they not only fulfilled the basic requirement of being alkyl aryl sulfoxides but also converted the problem from one involving a determination of the absolute configuration of a chiral, acyclic sulfonium salt, with which a correlation to the starting sulfoxide could be made,⁶ into one involving the experimentally easier assignment of configuration to *cis-trans* cyclic stereoisomers. Sul-