Provided all substituent parameters are known, eq 13 does not need any experimental data for the calculation (prediction) of log K/K^0 and $\Delta\Delta G_p$; eq 14 requires only an experimental determination of ρ; eq 15 in addition relies on the experimental determination of (at least) one exalted σ value to evaluate r; eq 16 only separates "normal" and through-resonance effects, and provides $\Delta\Delta G_p$ values only as far as the exalted σ values are determined experimentally. Which of these equations is most profitable depends on the specific problem involved; the accuracy of the results obtained will, of course, increase from eq 13 to eq 16.

Returning, finally, to the systems I, these are rather exceptional in that the reaction center is the same in all series, in that this reaction center is mesomerically insulated from the aromatic ring, and in that no charged substituents are involved in the comparisons.[5,6] As to eq 3, holding for these systems, the above treatment would suggest that the term $\Delta\sigma_R^+(XCH_3)$ should be replaced by $[\Delta\sigma_R^+(XCH_2COOH) - \Delta\sigma_R^+(XCH_2COO^-)]$. The applicability of eq 3 then means that these two quantities are proportional, which would seem to be not unreasonable. Further details of the behavior of the systems I are discussed in a separate paper [2]

Acknowledgment. This paper was composed at the University of California at Santa Cruz while the author was on sabbatical leave.

Nucleophilic Substitution Reactions Involving Sulfenic Acids and Sulfenyl Derivatives. The Nucleophile- and Acid-Catalyzed Oxygen-18 Exchange of Phenyl Benzenethiolsulfinate[1a,2]

John L. Kice*[1b] and James P. Cleveland[1c]

Contribution from the Department of Chemistry, Oregon State University, Corvallis, Oregon 97331. *Received June 23, 1972*

Abstract: The acid- and nucleophile-catalyzed oxygen-18 exchange of phenyl benzenethiolsulfinate-^{18}O has been studied in 60% dioxane using *n*-butyl sulfide, bromide ion, and chloride ion as the nucleophilic catalysts. Comparison of the rates for the exchange with the rates for the acid- and nucleophile-catalyzed racemization of (+)-PhS(O)SPh under the same conditions shows that benzenesulfenic acid (PhSOH) is orders of magnitude more reactive than water as a nucleophile toward reactive sulfenyl derivatives such as PhSCl, PhSBr, or $PhSS^+R_2$. The rapidity with which PhSOH performs a nucleophilic substitution on such sulfenyl compounds explains why sulfenic acids are never isolated as hydrolysis products of sulfenyl halides and related compounds. The relatively high reactivity of sulfenic acids as nucleophiles in displacements at dicoordinate sulfur would appear to have other significant ramifications for a number of aspects of sulfur chemistry.

Sulfenic acids, RSOH, are thought to be important intermediates in a variety of organosulfur reactions,[3-6] but only in a few very special cases have they proved capable of actual isolation.[7,8] One typical example of their elusiveness is the following. Although sulfenic acids are almost certainly produced during the hydrolysis of arylsulfenyl chlorides, ArSCl, Vinkler and Klivenyi found[9] that the first isolable product of the hydrolysis of such sulfenyl halides was invariably not the sulfenic acid but the corresponding sulfenic anhydride (or thiolsulfinate), ArS(O)SAr. Clearly, because of their probable importance as intermediates in many organic sulfur reactions, it is desirable for us to learn as much as we can about the chemical behavior and reactivity of sulfenic acids, but clearly also, since one is seldom going to be able to isolate a sulfenic acid and study its chemistry directly, almost all of this information is going to have to be derived in an indirect manner.

Ever since the pioneering review by Foss[10] sulfur chemists have recognized that reactions involving nucleophilic substitution at sulfur play a central role in organic sulfur chemistry and, in particular, that much of the chemistry of sulfenyl derivatives can be understood in terms of reactions, or reaction sequences, involving nucleophilic displacements at dicoordinate sulfur, which can be represented in a generalized sense as shown in eq 1.

$$Nu^- + R\text{-}S\text{-}Y \longrightarrow R\text{-}S\text{-}Nu + Y^- \qquad (1)$$

The studies described in the present paper, which are

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(1) (a) This research was supported by the National Science Foundation, Grant GP-10732X; (b) to whom correspondence should be addressed: Department of Chemistry, University of Vermont, Burlington, Vt. 05401; (c) National Institutes of Health Postdoctoral Fellow, 1969–1970.

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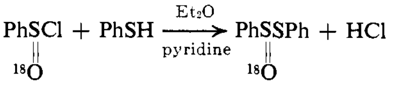
concerned with the acid- and nucleophile-catalyzed oxygen-18 exchange of phenyl benzenethiolsulfinate-^{18}O, PhS(^{18}O)SPh, when considered in conjunction with certain earlier investigations[11,12] of other acid- and nucleophile-catalyzed reactions of PhS(O)SPh, turn out to provide some interesting insight into various aspects of the behavior of sulfenic acids in nucleophilic substitution reactions with other sulfenyl derivatives. In particular they reveal the high reactivity of a sulfenic acid, in this case PhSOH, as a nucleophile toward dicoordinate, or sulfenyl, sulfur. This high reactivity is not only of interest from a purely theoretical point of view but also provides a simple practical explanation for why thiolsulfinates, and not sulfenic acids, are the first isolable intermediate in the hydrolysis of sulfenyl chlorides and other easily hydrolyzable sulfenyl derivatives.

Results

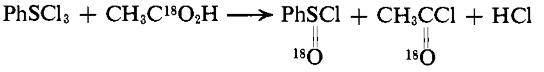
Synthesis of Oxygen-18 Labeled Phenyl Benzenethiolsulfinate. The labeled thiolsulfinate was prepared by the reaction of oxygen-18 labeled benzenesulfinyl chloride with thiophenol (eq 2) in the manner described



$$\mathrm{Ph}\underset{\underset{^{18}\mathrm{O}}{\|}}{\mathrm{S}}\mathrm{Cl} + \mathrm{PhSH} \xrightarrow[\text{pyridine}]{\mathrm{Et_2O}} \mathrm{Ph}\underset{\underset{^{18}\mathrm{O}}{\|}}{\mathrm{S}}\mathrm{SPh} + \mathrm{HCl} \qquad (2)$$

by Backer and Kloosterziel[13] for the preparation of the unlabeled compound. The necessary labeled sulfinyl chloride was obtained by chlorinating thiophenol in methylene chloride in the presence of ^{18}O-labeled acetic acid (eq 3 and 4). This general proce-

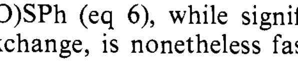
$$\mathrm{PhSH} + 2\mathrm{Cl_2} \xrightarrow[\mathrm{CH_2Cl_2}]{-70^\circ} \mathrm{PhSCl_3} + \mathrm{HCl} \qquad (3)$$



$$\mathrm{PhSCl_3} + \mathrm{CH_3C^{18}O_2H} \longrightarrow \mathrm{Ph}\underset{\underset{^{18}\mathrm{O}}{\|}}{\mathrm{S}}\mathrm{Cl} + \mathrm{CH_3}\underset{\underset{^{18}\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{Cl} + \mathrm{HCl} \qquad (4)$$

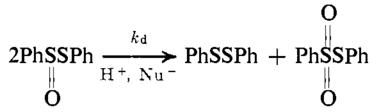
dure for converting mercaptans to the corresponding sulfinyl chlorides is one that was developed by Douglass and his associates.[14]

Acid- and Nucleophile-Catalyzed Oxygen-18 Exchange of Phenyl Benzenethiolsulfinate. The exchange (eq 5) of ^{18}O-labeled PhS(^{18}O)SPh in 60% aqueous



$$\mathrm{Ph}\underset{\underset{^{18}\mathrm{O}}{\|}}{\mathrm{S}}\mathrm{SPh} \xrightarrow[60\%\ \text{dioxane}]{\mathrm{H^+,\ Nu^-}} \mathrm{Ph}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{S}}\mathrm{SPh} \qquad (5)$$

dioxane (v/v) was followed by recovering samples of thiolsulfinate from the reaction medium after varying lengths of time and determining their oxygen-18 content. At the thiolsulfinate concentrations (0.0125–0.05 *M*) that must be used in order to recover adequate sized samples of thiolsulfinate conveniently, the rate of the acid- and nucleophile-catalyzed disproportionation[15] of PhS(O)SPh (eq 6), while significantly slower than that of exchange, is nonetheless fast enough that



$$2\mathrm{Ph}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{S}}\mathrm{SPh} \xrightarrow[\mathrm{H^+,\ Nu^-}]{k_d} \mathrm{PhSSPh} + \mathrm{Ph}\overset{\overset{\mathrm{O}}{\|}}{\underset{\underset{\mathrm{O}}{\|}}{\mathrm{S}}}\mathrm{SPh} \qquad (6)$$

1

some disproportionation occurs during the time period over which the exchange is followed. Recrystallization of the crude recovered thiolsulfinate, particularly that obtained at longer reaction times, does not satisfactorily remove the thiolsulfonate impurity PhSO$_2$SPh from these samples. We had, therefore, to resort to a purification procedure involving preparative thin layer chromatography of the crude recovered thiolsulfinate on silica gel using benzene–1% acetic acid as solvent. Control experiments with pure thiolsulfinate of known oxygen-18 content demonstrated that PhS(^{18}O)SPh does not undergo any loss of oxygen-18 during this chromatographic procedure. Other control experiments using known mixtures of disulfide, thiolsulfonate, and thiolsulfinate had earlier demonstrated that the chromatographic procedure did separate the thiosulfonate completely from the thiosulfinate and the disulfide.

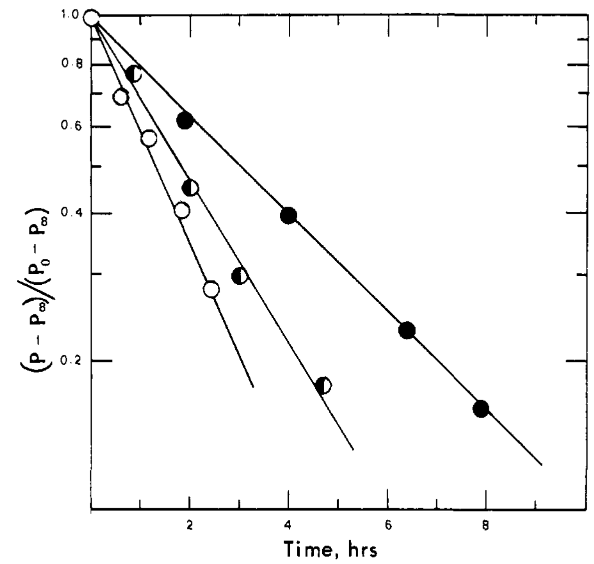


Figure 1. Kinetics of oxygen-18 exchange of phenyl benzenethiolsulfinate. Plot of log $(P - P_\infty)/(P_0 - P_\infty)$ *vs.* time, where *P* = atom % oxygen-18 in the thiolsulfinate: (●) *n*-Bu$_2$S 0.002 *M*, HClO$_4$ 0.10 *M*, **1** 0.025 *M*; (○) KBr 0.03 *M*, HClO$_4$ 0.50 *M*, **1** 0.05 *M*; (◐) NaCl 0.10 *M*, HClO$_4$ 0.40 *M*, **1** 0.05 *M*. All runs in 60% dioxane at 39.6° at an ionic strength of 0.50.

Three different nucleophiles—*n*-butyl sulfide, bromide ion, and chloride ion—were used as nucleophilic catalysts for the exchange. Perchloric acid was the acid catalyst in each instance, and all runs were carried out at a constant ionic strength of 0.50. Figure 1 shows first-order plots of the data for several representative runs. One can see that, as expected,[16] the loss of oxygen-18 from PhS(^{18}O)SPh follows good first-order kinetics. The slopes of the plots in Figure 1 are equal to k_{exch}, the experimental first-order rate constant for the exchange under that particular set of reaction conditions. The values of k_{exch} for the various reaction conditions investigated are tabulated in Table I. Also listed in Table I are values of k_α, the experimental first-order

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[11] J. L. Kice and G. B. Large, *J. Amer. Chem. Soc.*, **90**, 4069 (1968).

[12] J. L. Kice, C. G. Venier, and L. Heasley, *ibid.*, **89**, 3557 (1967); J. L. Kice and G. B. Large, *J. Org. Chem.*, **33**, 1940 (1968).

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[14] (a) I. B. Douglass and B. S. Farah, *J. Org. Chem.*, **23**, 330 (1958); (b) I. B. Douglass and D. R. Pool, *ibid.*, **22**, 536 (1957); (c) I. B. Douglass, B. S. Farah, and E. C. Thomas, *ibid.*, **26**, 1996 (1961).

[15] J. L. Kice and J. P. Cleveland, *J. Amer. Chem. Soc.*, **95**, 109 (1973).

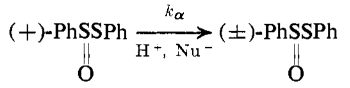
[16] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, pp 192–193.

Table I. Rate of Oxygen-18 Exchange of Phenyl Benzenethiolsulfinate-^{18}O in 60% Dioxane[a]

Nucleophile	$[\mathbf{1}\text{-}^{18}O]_0$, M	$10^2\cdot[\mathrm{Nu^-}]$, M	$[\mathrm{HClO}^4]$, M	$10^4\cdot k_{\mathrm{exch}}$, sec^{-1}	$10^4 k_\alpha$,[b] sec^{-1}	$k_\alpha/k_{\mathrm{exch}}$
n-Bu$_2$S	0.050	1.0	0.50	7.0	2.4×10^2	34
			0.10	1.5	47	31
		0.20	0.50	1.5	47	31
	0.025	0.20	0.10	0.63	9.4	15
	0.0125	0.20	0.10	0.83	9.4	11.3
Br$^-$	0.050	3.0	0.50	1.5	30	20
		1.0	0.50	0.60	10	17
Cl$^-$	0.050	10.0	0.40	1.0	3.2[c]	3.2

[a] All runs at 39.6°. Ionic strength maintained constant at 0.50 by addition of lithium perchlorate where needed. [b] Rate of racemization of (+)-**1** under same conditions; data from ref 11, except where indicated. [c] This work.

rate constant for the acid- and nucleophile-catalyzed racemization (eq 7) of optically active PhS(O)SPh



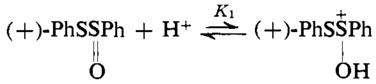
$$(+)\text{-Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}\mathrm{SPh} \xrightarrow[\mathrm{H^+,\ Nu^-}]{k_\alpha} (\pm)\text{-Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}\mathrm{SPh} \qquad (7)$$

(+)-**1**

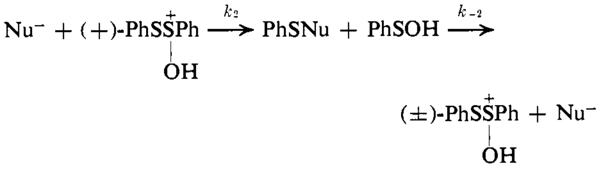
under the same conditions, either as calculated from the data reported earlier by Kice and Large,[11] or, in the case of chloride ion, from a direct measurement in conjunction with the present work.[17] In the last column of Table I is given the value of $k_\alpha/k_{\mathrm{exch}}$ for each set of reaction conditions.

Discussion

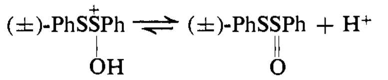
Mechanism of the Acid- and Nucleophile-Catalyzed Oxygen-18 Exchange. In aqueous dioxane optically active phenyl benzenethiolsulfinate undergoes a relatively rapid acid- and nucleophile-catalyzed racemization (eq 7).[11] Previous work[11] has demonstrated that the mechanism for this racemization is as shown in eq 8–10, with step k_2 being rate determining. Several other acid- and nucleophile-catalyzed reactions of **1** are known which also have step k_2 as their rate-determining step.[12]



$$(+)\text{-Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}\mathrm{SPh} + \mathrm{H^+} \overset{K_1}{\rightleftharpoons} (+)\text{-Ph}\underset{\overset{|}{\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh} \qquad (8)$$



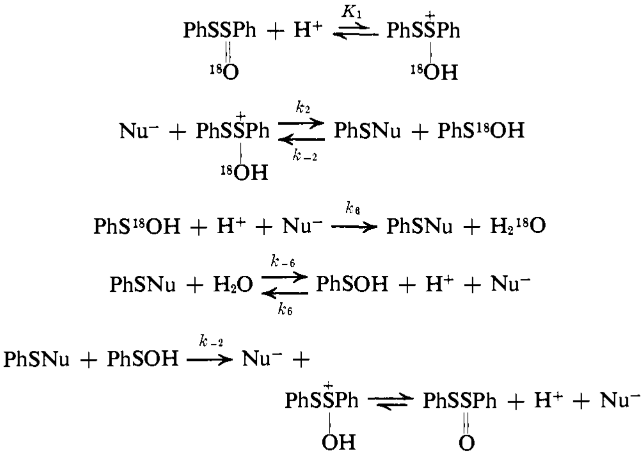
$$\mathrm{Nu^-} + (+)\text{-Ph}\underset{\overset{|}{\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh} \xrightarrow{k_2} \mathrm{PhSNu} + \mathrm{PhSOH} \xrightarrow{k_{-2}} (\pm)\text{-Ph}\underset{\overset{|}{\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh} + \mathrm{Nu^-} \qquad (9)$$



$$(\pm)\text{-Ph}\underset{\overset{|}{\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh} \rightleftharpoons (\pm)\text{-Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}\mathrm{SPh} + \mathrm{H^+} \qquad (10)$$

Given these facts the expectation is that any acid- and nucleophile-catalyzed oxygen-18 exchange of **1**-^{18}O in the same medium would presumably take place by the mechanism shown in Chart I. Our first task is to determine whether the actual exchange of **1**-^{18}O follows the kinetics expected of such a mechanism.

Chart I. Mechanism of the Acid- and Nucleophile-Catalyzed Oxygen-18 Exchange of Phenyl Benzenethiolsulfinate-^{18}O



$$\mathrm{Ph}\underset{\overset{\|}{^{18}\mathrm{O}}}{\mathrm{S}}\mathrm{SPh} + \mathrm{H^+} \overset{K_1}{\rightleftharpoons} \mathrm{Ph}\underset{\overset{|}{^{18}\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh}$$

$$\mathrm{Nu^-} + \mathrm{Ph}\underset{\overset{|}{^{18}\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{PhSNu} + \mathrm{PhS^{18}OH}$$

$$\mathrm{PhS^{18}OH} + \mathrm{H^+} + \mathrm{Nu^-} \xrightarrow{k_6} \mathrm{PhSNu} + \mathrm{H_2{}^{18}O}$$

$$\mathrm{PhSNu} + \mathrm{H_2O} \underset{k_6}{\overset{k_{-6}}{\rightleftharpoons}} \mathrm{PhSOH} + \mathrm{H^+} + \mathrm{Nu^-}$$

$$\mathrm{PhSNu} + \mathrm{PhSOH} \xrightarrow{k_{-2}} \mathrm{Nu^-} + \mathrm{Ph}\underset{\overset{|}{\mathrm{OH}}}{\overset{+}{\mathrm{S}}}\mathrm{SPh} \rightleftharpoons \mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{S}}\mathrm{SPh} + \mathrm{H^+} + \mathrm{Nu^-}$$

For the mechanism in Chart I the experimental rate constant for loss of oxygen-18 label should be given by eq 11.

$$k_{\mathrm{exch}} = k_2K_1a_{\mathrm{H^+}}[\mathrm{Nu^-}]\left[\frac{k_6a_{\mathrm{H^+}}[\mathrm{Nu^-}]}{k_{-2}[\mathrm{PhSNu}] + k_6a_{\mathrm{H^+}}[\mathrm{Nu^-}]}\right] \qquad (11)$$

If one assumes a steady state in the concentrations of both PhSNu and PhSOH, as has been done in successfully treating the kinetics of the other acid- and nucleophile-catalyzed reactions of **1**,[11,12] then

$$\frac{\mathrm{d[PhSOH]}}{\mathrm{d}t} = k_2K_1a_{\mathrm{H^+}}[\mathrm{Nu^-}][\mathbf{1}] + k_{-6}[\mathrm{PhSNu}][\mathrm{H_2O}] - k_{-2}[\mathrm{PhSOH}][\mathrm{PhSNu}] - k_6a_{\mathrm{H^+}}[\mathrm{Nu^-}][\mathrm{PhSOH}] \cong 0$$

$$\frac{\mathrm{d[PhSNu]}}{\mathrm{d}t} = k_2K_1a_{\mathrm{H^+}}[\mathrm{Nu^-}](\mathbf{1}) - k_{-6}[\mathrm{PhSNu}][\mathrm{H_2O}] - k_{-2}[\mathrm{PhSOH}][\mathrm{PhSNu}] + k_6a_{\mathrm{H^+}}[\mathrm{Nu^-}][\mathrm{PhSOH}] \cong 0$$

and by (1) addition and (2) subtraction of these two equations, one obtains the two relationships

$$[\mathrm{PhSOH}][\mathrm{PhSNu}] = k_2K_1a_{\mathrm{H^+}}[\mathrm{Nu^-}][\mathbf{1}]/k_{-2}$$

$$[\mathrm{PhSOH}] = (k_{-6}[\mathrm{H_2O}]/k_6a_{\mathrm{H^+}}[\mathrm{Nu^-}])[\mathrm{PhSNu}]$$

from which one obtains

$$[\mathrm{PhSNu}] = [k_2K_1k_6/k_{-2}k_{-6}(\mathrm{H_2O})]^{1/2}a_{\mathrm{H^+}}[\mathrm{Nu^-}][\mathbf{1}]^{1/2}$$

Upon substitution of this expression into eq 11 for [PhSNu] there results

$$k_{\mathrm{exch}} = k_2K_1a_{\mathrm{H^+}}[\mathrm{Nu^-}]\left[\frac{1}{1 + [k_2K_1k_{-2}[\mathbf{1}]/k_6k_{-6}[\mathrm{H_2O}]]^{1/2}}\right] \qquad (12)$$

Since k_α, the rate constant for the acid- and nucleophile-catalyzed racemization of (+)-**1**, is equal to $k_2K_1a_{\mathrm{H^+}}[\mathrm{Nu^-}]$, $k_\alpha/k_{\mathrm{exch}}$ should be given by

$$k_\alpha/k_{\mathrm{exch}} = 1 + [k_2K_1k_{-2}/k_6k_{-6}[\mathrm{H_2O}]]^{1/2}[\mathbf{1}]^{1/2} \qquad (13)$$

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[17] The value of k_α found for Cl$^-$ in the present work, 3.2×10^{-4} sec^{-1}, is somewhat higher than that reported for 0.10 M Cl$^-$, 0.40 M HClO$_4$ by Kice and Large[11] ($k_\alpha = 2.3 \times 10^{-4}$). Since checks of certain of their other runs showed excellent agreement with their previously reported k_α values in every case, we believe the difference is due to the fact that sodium chloride, rather than lithium chloride, was used in the present work. Unlike the other nucleophilic catalysts, rather large concentrations of alkali metal chloride (0.10 M) are used in comparison to the total ionic strength (0.50), so that a difference in the nature of the alkali metal cation could have an influence on the effective ionic strength of the solution. Since the rates of all of the acid- and nucleophile-catalyzed reactions of 1 in 60% dioxane are known[11] to be quite sensitive to ionic strength, this could indeed make a difference in the measured k_α.

The mechanism in Chart I accordingly predicts that the exchange should be first order in both acid and catalyzing nucleophile, so that k_α/k_{exch} for a given nucleophile should be independent of both acid and nucleophile concentration. Although the data in Table I are limited, due to the amount of effort required to carry out each kinetic experiment, they definitely appear to be consistent with this requirement. The mechanism also predicts that k_α/k_{exch} should be dependent on total thiolsulfinate concentration. The experiments with n-Bu_2S as catalyst at varying initial thiolsulfinate concentrations indicate that this is indeed true. Equation 13 predicts that $[(k_\alpha/k_{\text{exch}}) - 1]$ should vary as the half-power of thiolsulfinate concentration. While this is true for the change from 0.0125 to 0.025 *M* **1**, the change from 0.025 to 0.05 *M* **1** leads to a larger increase in k_α/k_{exch} than expected.

Does this mean that Chart I is not the correct mechanism for the exchange? We think not. Rather we feel that it results from the fact that particularly at higher thiolsulfinate concentrations the rate of acid- and nucleophile-catalyzed disproportionation of **1** becomes sufficiently comparable to the rate of exchange to lead to certain complications.

What we are measuring *vs.* time in each exchange is (^{18}O-labeled **1**)/(total **1**). The mechanism in Chart I assumes there is no change in the total amount of thiolsulfinate during the period while the rate of exchange is being followed, only a decrease in the fraction which is labeled. As long as the exchange is much faster than the disproportionation of **1** this is an adequate approximation. However, when the rate of disproportionation is more nearly comparable to the rate of exchange, it is no longer completely satisfactory, and the disappearance of thiolsulfinate due to disproportionation during the course of an exchange experiment will cause the measured value of (^{18}O-labeled **1**)/(total **1**) to be larger at any given time than it would if disproportionation were not occurring. Since the magnitude of the effect depends on the amount of disproportionation that has occurred it becomes progressively larger with time in any given experiment. The net result is that a plot of log (^{18}O-labeled **1**)/(total **1**) *vs.* time, while apparently still adequately linear, will have a smaller slope, or experimental value of k_{exch}, than the true value of k_{exch} for the particular reaction conditions.

Since the rate of disproportionation depends on the three-halves power of thiolsulfinate concentration,[15] this error in the measurement of k_{exch} for a given catalyst will be larger the higher the initial thiolsulfinate concentration. This will tend to make the measured values of k_α/k_{exch} increase more rapidly with increasing thiolsulfinate concentration than the half-power dependence predicted by eq 13.[18]

While we therefore believe that the exchange does indeed proceed by the mechanism in Chart I, we also recognize that the k_α/k_{exch} values in Table I for 0.05 *M* **1** are probably somewhat larger than the true values of this ratio because of the complications just outlined. However, the magnitude of the error is small enough that meaningful conclusions can still be drawn from both these data and those at 0.0125 and 0.025 *M* **1**, where the error introduced by concomitant disproportionation is significantly less.

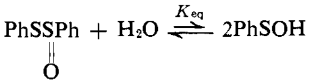
Implications of Results for the Chemistry of Sulfenic Acids. Let us concentrate our attention initially on the results for n-Bu_2S as catalyst, for this is where we have the most extensive data. At the lowest thiolsulfinate concentration employed (0.0125 *M*), where there should be negligible interference with an accurate determination of k_α/k_{exch} from any disproportionation of **1**, k_α/k_{exch} for this catalyst has a value of 11.3. From eq 13

$$\left(\frac{k_2K_1}{k_6}\right)\left(\frac{k_{-2}}{k_{-6}}\right) = [(k_\alpha/k_{\text{exch}}) - 1]^2\frac{[\mathrm{H_2O}]}{[\mathbf{1}]}$$

Since in 60% dioxane $(H_2O) \cong 20$ *M*, this means that for this particular system

$$\left(\frac{k_2K_1}{k_6}\right)\left(\frac{k_{-2}}{k_{-6}}\right) = (10.3)^2\frac{20}{0.0125} = 1.7 \times 10^5$$

The equilibrium constant K_{eq} for the equilibrium



$$\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{PhSSPh}} + \mathrm{H_2O} \overset{K_{\text{eq}}}{\rightleftharpoons} 2\mathrm{PhSOH}$$

can be expressed as

$$\frac{[\mathrm{PhSOH}]^2}{[\mathbf{1}][\mathrm{H_2O}]} = K_{\text{eq}} = \left(\frac{k_2K_1}{k_6}\right)\left(\frac{k_{-6}}{k_{-2}}\right)$$

Now we know from other work[11] that at equilibrium in such systems (PhSOH) ≪ (**1**), as was also suggested earlier by the results of Vinkler and Klivenyi.[9] That being the case, K_{eq} must be very much smaller than one; a value no larger than 10^{-6} seems indicated.[19] Thus we have the situation that

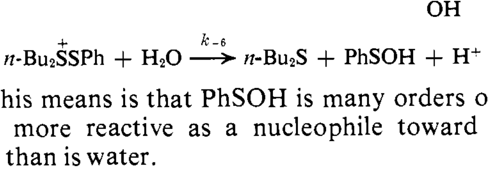
$$[k_2K_1/k_6][k_{-2}/k_{-6}] = 1.7 \times 10^5$$

$$[k_2K_1/k_6][k_{-6}/k_{-2}] \leqq 10^{-6}$$

Obviously the only way that both these relationships can be met is for k_{-2}/k_{-6} to have a very large value, *i.e.*

$$k_{-2}/k_{-6} \geqq 4 \times 10^5$$

Since these two rate constants refer to the following pair of reactions



$$n\text{-}\mathrm{Bu_2}\overset{+}{\mathrm{S}}\mathrm{SPh} + \mathrm{PhSOH} \xrightarrow{k_{-2}} n\text{-}\mathrm{Bu_2S} + \mathrm{PhS}\underset{\underset{\displaystyle \mathrm{OH}}{|}}{\overset{+}{\mathrm{S}}}\mathrm{Ph}$$

$$n\text{-}\mathrm{Bu_2}\overset{+}{\mathrm{S}}\mathrm{SPh} + \mathrm{H_2O} \xrightarrow{k_{-6}} n\text{-}\mathrm{Bu_2S} + \mathrm{PhSOH} + \mathrm{H^+}$$

what this means is that PhSOH is many orders of magnitude more reactive as a nucleophile toward n-Bu_2S^+SPh than is water.

One can use the same procedure and the appropriate k_α/k_{exch} data in Table I to estimate values of k_{-2}/k_{-6} for the systems involving Br^- and Cl^- as catalysts, *i.e.*, the cases where PhSNu equals PhSBr and PhSCl, respectively. The estimated values of k_{-2}/k_{-6} are the following: for PhSBr, 3×10^5; for PhSCl, 4×10^4. (Nat-

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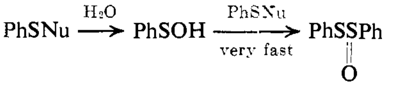
[18] Because of the extreme complexity of the kinetic situation when exchange and disproportionation have roughly comparable rates, we have not been able, despite numerous attempts, to obtain an *explicit* solution for how the measured $(k_\alpha/k_{\text{exch}})$ would be expected to vary with [1] in such situations. Qualitatively, however, it is clear that it will behave as indicated.

[19] A value of K_{eq} of 10^{-6} would correspond to an equilibrium concentration of PhSOH equal to about 4% of the concentration of **1**. This is larger than we actually suspect is present, and so K_{eq} is probably in reality smaller than 10^{-6}. To the extent that K_{eq} is smaller than 10^{-6} this will only serve to require that k_{-2}/k_{-6} have an even larger value than the one calculated.

urally, because of the problems introduced by accompanying disproportionation of **1** discussed earlier, these estimated values of k_{-2}/k_{-6} for PhSBr and PhSCl are likely to be somewhat larger than the true values, although in no case is the difference likely to be much greater than a factor of 2.)

Two points regarding these results are worth mention at this juncture. First, although the values of k_{-2}/k_{-6} show some variation with leaving group, they are in every instance much larger than one. In other words, regardless of whether the leaving group in PhSNu is n-Bu_2S^+–, Br–, or Cl–, PhSOH is much more reactive as a nucleophile toward PhSNu than is water. Second, because of the high concentration of water in 60% dioxane and the very small value of K_{eq}, even a modest value of k_α/k_{exch}, such as 3.2 for Cl^- as catalyst, corresponds to a value of k_{-2}/k_{-6} which is much, much larger than unity. As a matter of fact, k_α/k_{exch} will not be significantly larger than one unless k_{-2}/k_{-6} itself is greater than about 5×10^3.

The fact that benzenesulfenic acid, PhSOH, is much more reactive than water as a nucleophile toward the various sulfenyl derivatives, PhSNu (Nu = S^+Bu_2, Br, Cl) provides an explanation for Vinkler and Klivenyi's[9] observation that thiolsulfinates, and not sulfenic acids, are invariably the first isolable products of the hydrolysis of reactive sulfenyl derivatives. Since $k_{-2} \gg k_{-6}$, as soon as any PhSOH is formed by the hydrolysis of PhSNu it will react with some of the remaining PhSNu much faster than the latter undergoes hydrolysis. Thus the fact that sulfenic acids cannot be isolated from the hydrolysis of compounds like sulfenyl chlorides may well be due not so much to any particular instability of sulfenic acids, but rather because they are so reactive as nucleophiles toward labile sulfenyl compounds.



$$\text{PhSNu} \xrightarrow{H_2O} \text{PhSOH} \xrightarrow[\text{very fast}]{\text{PhSNu}} \text{Ph}\underset{\underset{\displaystyle O}{\|}}{S}\text{SPh}$$

We have seen that compared to water PhSOH is very reactive as a nucleophile in substitutions at sulfenyl sulfur, $k_{-2}/k_{-6} \geqq 4 \times 10^4$–$4 \times 10^5$ depending on the nature of the leaving group. Unfortunately such data do not tell us exactly how PhSOH compares in nucleophilicity to such sulfur nucleophiles as PhSH, for example, although from the extremely large magnitude of the k_{-2}/k_{-6} values it is tempting to suggest that the nucleophilic reactivity of PhSOH is probably not too much less than that of PhSH and could perhaps even equal or exceed it. In any event, the results of the present work clearly establish that sulfenic acids, even when undissociated, are good nucleophiles toward dicoordinate sulfur, a finding which definitely has important ramifications for a number of areas of sulfur chemistry.

It is interesting to speculate whether part of the nucleophilic reactivity of PhSOH could be due to the fact that it is a possible α-effect nucleophile, in that there are two unshared pairs of electrons on the oxygen adjacent to the sulfur. However, a definitive answer on this point must await the advent of systems that permit the nucleophilicity of a sulfenic acid to be compared directly with that of such compounds as mercaptans and sulfides.

Pearson and Songstad[20] have investigated the effect of an increase in the "softness" of the leaving group as a base on the relative reactivity of hard *vs.* soft nucleophiles in SN2 displacements on CH_3X. They found that an increase in the softness of the leaving group (from Br– to I–) led to a greater rate increase for displacements involving soft nucleophiles than for those involving hard ones and termed this the "symbiotic effect." Benzenesulfenic acid is presumably a much softer nucleophile than water, while Br– and n-Bu_2S^+– are softer base leaving groups than Cl–. A symbiotic effect could therefore perhaps be the reason that k_{-2}/k_{-6} for the displacements on PhSCl is significantly smaller than for the same displacements on PhSBr and $PhSS^+Bu_2$.

Experimental Section

Preparation of Phenyl Benzenethiolsulfinate-^{18}*O*. Oxygen-18 labeled sodium acetate was prepared by the procedure described by Oae and coworkers.[21] Oxygen-18 labeled acetic acid was then prepared from this labeled acetate in the following manner. The labeled $CH_3C^{18}O_2Na$ (8.2 g, 0.1 mol) was placed in a 200-ml three-necked flask equipped with a mechanical stirrer and a reflux condenser with drying tube. Anhydrous ether (100 ml) was added, stirring was begun, and anhydrous hydrogen chloride was passed into the flask for several minutes. The gas flow was then shut off and vigorous stirring was continued for several hours with periodic checks being made to ensure there was still free hydrogen chloride in the flask. After 3–5 hr the mixture was filtered. The ether was then removed by distillation and the residual $CH_3C^{18}O_2H$ distilled. There was obtained 5.1 g (85%) of acetic acid-$^{18}O_2$, bp 118°.

Thiophenol (2.2 g, 0.02 mol) and $CH_3C^{18}O_2H$ (1.2 g, 0.02 mol) were dissolved in 75 ml of methylene chloride and placed in a 200-ml three-necked flask equipped with a drying tube, mechanical stirrer, and gas inlet tube. The solution was cooled in a Dry Ice–acetone bath while being stirred vigorously. Dry chlorine (1.8 ml, 0.04 mol), which had been collected and measured earlier in a trap connected to the gas inlet tube, was allowed to vaporize and recondense in the thiophenol–$CH_3C^{18}O_2H$–methylene chloride solution, which first turned red, and then yellow. Finally, as the last of the chlorine was added a pale yellow slush formed. The Dry Ice–acetone bath was then removed and replaced with an ice-salt bath cooled to $-15°$. As the reaction mixture warmed to this temperature a rapid reaction occurred with the evolution of a large amount of hydrogen chloride. The solution was then warmed to room temperature and purged with dry air to remove any excess chlorine and any remaining hydrogen chloride formed in the reaction. At this point the solvent and the acetyl chloride formed in the reaction were removed under reduced pressure at 50°. The residual oxygen-18 labeled benzenesulfinyl chloride left in the flask was used in the next step without further purification.

The labeled sulfinyl chloride was dissolved in 50 ml of anhydrous ether and placed in a three-necked flask equipped with a drying tube and a mechanical stirrer. To this was added a solution of 2.2 g of thiophenol (0.02 mol) and 1.58 g of pyridine in 50 ml of anhydrous ether. The precipitate of pyridinium hydrochloride which formed was filtered off and the ether removed from the filtrate by evaporation under reduced pressure. The residue after removal of the ether was dissolved in chloroform and washed first with dilute sulfuric acid, then with 5% sodium bicarbonate, and finally twice with water. The chloroform solution was then dried over magnesium sulfate and the chloroform was removed under reduced pressure. The residue was recrystallized twice by dissolving it in the minimum amount of chloroform at room temperature, adding hexane until a slight turbidity appeared, and then cooling the solution to $-20°$. Bright yellow crystals of phenyl benzene thiolsulfinate-^{18}O, 1.9 g (40%), mp 69° (lit.,[13] 69–70°), were obtained (1.48 atom % ^{18}O).

Purification of Other Materials. Dioxane was purified by the method described by Wiberg.[22] Anhydrous reagent grade lithium perchlorate, potassium bromide, and sodium chloride were

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(20) R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

(21) S. Oae, T. Kitao, and Y. Kitaoka, *ibid.*, **84**, 3359 (1962).

(22) K. B. Wiberg, "Laboratory Techniques in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, pp 245–246.

used without further purification. The *n*-butyl sulfide was fractionally distilled before use.

Procedure for Measurement of Exchange Rates. Standard solutions of perchloric acid, the catalyzing nucleophile, and lithium perchlorate in 60% dioxane (v/v) were prepared as described in the accompanying paper.[15] To initiate a run a weighed amount of **1**-^{18}O was dissolved in 60% dioxane, the proper amounts of the various stock solutions were added, and the solution was made up to volume with additional 60% dioxane. The final solution was then transferred to a reaction vessel of a type described previously[23] and the solution was deaerated by passing prepurified nitrogen through it for 5 min. Solutions were kept under nitrogen during the course of the exchange.

At appropriate times aliquots of the reaction solution were removed and the aliquot was added to a large volume of water. The resulting mixture was extracted several times with portions of chloroform. The combined chloroform extracts were washed with water and dried over magnesium sulfate, and the solvent was removed under reduced pressure.

The thiolsulfinate was then separated in a pure state from the residue by means of preparative thin-layer chromatography on silica gel (1 mm thickness, 1% acetic acid in benzene as solvent). Clean separations were achieved in all cases with the disulfide showing the largest and the thiolsulfinate the smallest R_f value. After development of the tlc plate was complete and the developing solvent had been allowed to evaporate, the thiolsulfinate was removed from the plate using dry ether. The ether was removed under reduced pressure and the thiolsulfinate residue was recrystallized from warm hexane to which just enough chloroform had been added to effect solution of the thiolsulfinate. The use of this isolation and work-up procedure on a sample of ^{18}-O-labeled **1**, which had not been subjected to exchange, led to no detectable loss of ^{18}O label, provided that care was taken to use scrupulously dry ether for the removal of the chromatographed thiolsulfinate from the tlc plate.

The oxygen-18 content of the thiolsulfinate samples was determined by using the Doering and Dorfman[24] procedure. The ratio of mass 46:44 in the samples of CO_2 resulting from the pyrolyses was measured using an Atlas CH-7 mass spectrometer. The atom percentage of oxygen-18 in the thiolsulfinate, P, was then calculated using the equation given by Doering and Dorfman[24]

$$P = \frac{0.00408R - 0.00204}{0.9959 + 0.00408R} \times 10^2$$

where

$$R = (I_{46}/I_{44})/(I^0{}_{46}/I^0{}_{44})$$

and I^0 represents the intensity of a particular mass peak in a sample of standard (or tank) carbon dioxide and I represents the intensity of the same mass peak in the sample of carbon dioxide from the pyrolysis of the thiolsulfinate.

The rate of the exchange reaction (eq 5) was then determined by plotting log $(P - P_\infty)/(P_0 - P_\infty)$ *vs.* time, where P_0 = atom % oxygen-18 in the starting thiolsulfinate and P_∞ that which would be present after exchange was complete. Since there is from 400 to 1600 times more water than **1**-^{18}O present, depending on the initial thiolsulfinate concentration, P_∞ was taken in all runs as being equal to 0.204, the natural abundance of oxygen-18.

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[23] J. L. Kice and K. W. Bowers, *J. Amer. Chem. Soc.*, **84**, 605 (1962).

[24] W. von E. Doering and E. Dorfman, *ibid.*, **75**, 5595 (1953).

The Nucleophile- and Acid-Catalyzed Disproportionation of Phenyl Benzenethiolsulfinate in Aqueous Dioxane. Confirmation of a Previously Suggested Mechanism for the Disproportionation[1a]

John L. Kice*[1b] and James P. Cleveland[1c]

Contribution from the Department of Chemistry, Oregon State University, Corvallis, Oregon 97331.

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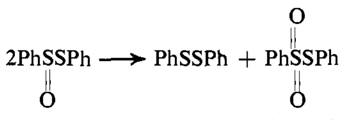
Abstract: In 60% dioxane the acid- and nucleophile-catalyzed disproportionation of phenyl benzenethiolsulfinate exhibits a three-halves-order dependence on thiolsulfinate concentration, in contrast to the first-order dependence on thiolsulfinate observed in acetic acid–1% water. In both media the reaction is first order in both acid and catalyzing nucleophile. It is shown that this is exactly the change in kinetics that would be expected for the mechanism shown in Chart I upon transfer of the reaction from a medium of very low water content to one of much higher water content. The results therefore constitute important evidence for the probable correctness of this mechanism.

One of the important reactions of thiolsulfinates (sulfenic anhydrides) is their disproportionation into thiolsulfonates and disulfides (eq 1).[2] It has been found[3] that in acetic acid–1% water as solvent the disproportionation can be dramatically accelerated *via*



$$2\text{Ph}\underset{\text{O}}{\underset{\|}{\text{S}}}\text{SPh} \longrightarrow \text{PhSSPh} + \text{Ph}\overset{\text{O}}{\overset{\|}{\underset{\underset{\text{O}}{\|}}{\text{S}}}}\text{SPh} \qquad (1)$$

catalysis by added strong acid and nucleophiles. Kinetic study of this acid- and nucleophile-catalyzed disproportionation showed that in AcOH–1% H_2O the reaction was first order in both thiolsulfinate and nucleophile and had the same dependence of rate on acidity as other[4] acid- and nucleophile-catalyzed reactions of thiolsulfinates, but exhibited a significantly

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[1] (a) This research was supported by the National Science Foundation, Grant GP-10732X; (b) to whom correspondence should be addressed: Department of Chemistry, University of Vermont, Burlington, Vt. 05401; (c) National Institutes of Health Postdoctoral Fellow, 1969–1970.

[2] (a) H. J. Backer and H. Kloosterziel, *Recl. Trav. Chim. Pays-Bas*, **73**, 129 (1954); (b) D. Barnard, *J. Chem. Soc.*, 4675 (1957); (c) D. Barnard and E. J. Percy, *Chem. Ind. (London)*, 1332 (1960).

[3] J. L. Kice, C. G. Venier, G. B. Large, and L. Heasley, *J. Amer. Chem. Soc.*, **91**, 2028 (1969).

[4] (a) J. L. Kice, C. G. Venier, and L. Heasley, *ibid.*, **89**, 3557 (1967); (b) J. L. Kice and G. B. Large, *J. Org. Chem.*, **33**, 1940 (1968).