slowly than primary amines. Primary amines, *e.g.*, *n*-butylamine and *n*-heptylamine, react approximately at the same rate.[29] Thus the possibility that undetected amounts of nucleophiles could disturb the kinetics was ruled out.

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Substitution Reactions at Sulfenyl Sulfur. The Extremely Rapid Exchange Reaction between Dimethyl Sulfide and a Dimethylmethylthiosulfonium Salt[1]

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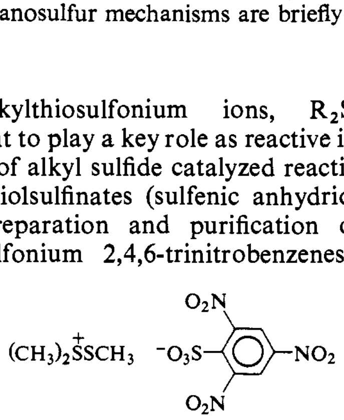
Abstract: The nmr spectra of methyl sulfide, $MeSS^+Me_2$, and mixtures of the two in acetonitrile-d_3 show that the exchange reaction $Me_2S + MeSS^+Me_2 \rightarrow Me_2S^+SMe + Me_2S$ takes place extremely rapidly, k_s being at least $10^5\ M^{-1}\ sec^{-1}$. This is several orders of magnitude faster than the exchange of MeS^- with the corresponding disulfide, and, since MeS^- is a considerably better nucleophile than Me_2S, must be due entirely to the fact that Me_2S^+– is a very much better leaving group than MeS– in a substitution at sulfenyl sulfur. The rate for k_s is also compared to that for an appropriate nucleophilic displacement by Me_2S on an sp^3 carbon, and it is concluded that the displacement at the sulfenyl sulfur of $MeSS^+Me_2$ is at least 10^9–10^{10} faster. Some general implications for organosulfur mechanisms are briefly discussed.

Dialkylalkylthiosulfonium ions, R_2S^+SR', are thought to play a key role as reactive intermediates in a number of alkyl sulfide catalyzed reactions of disulfides[2] and thiolsulfinates (sulfenic anhydrides).[3,4] The successful preparation and purification of dimethylmethylthiosulfonium 2,4,6-trinitrobenzenesulfonate (**1**)



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by Helmkamp, *et al.*,[5] makes it possible for one to study a number of important aspects of the chemistry of such thiosulfonium ions directly. In the present paper we

$$(CH_3)_2S + CH_3S\overset{+}{S}(CH_3)_2 \rightarrow (CH_3)_2\overset{+}{S}SCH_3 + (CH_3)_2S \quad (1)$$

will show that the rate constant for the exchange reaction in eq 1 is orders of magnitude larger than the rate con-

$$CH_3S^- + CH_3SSCH_3 \rightarrow CH_3SSCH_3 + CH_3S^- \quad (2)$$

stant[6] for the exchange in eq 2 and that thiosulfonium ions such as Me_2S^+SMe can undergo nucleophilic substitution reactions incredibly rapidly.

Results and Discussion

Curve A in Figure 1 shows the nmr spectrum of **1** in CD_3CN at 0°. The largest singlet corresponds to the resonance of the two methyl groups attached to the sulfonium sulfur, the smaller singlet at higher field to the resonance of the methyl attached to the sulfenyl sulfur. Curve B in the same figure is the nmr spectrum of dimethyl sulfide in CD_3CN. Curve C is the spectrum of a 1:1 mixture of **1** and dimethyl sulfide in CD_3CN at 0° with both sulfide and thiosulfonium salt present at a concentration of 0.15 *M*. One sees that the separate resonances due to the methyl groups of the sulfide and the sulfonium methyl groups, $(CH_3)_2S^+$–, have collapsed into a single very sharp resonance centered exactly halfway between the original positions of the $(CH_3)_2S^+$– and $(CH_3)_2S$ resonances. Obviously the methyl groups of the sulfide and those attached to the sulfonium sulfur are undergoing exchange of environment *via* eq 1 at a rate which is rapid on the nmr time scale. Since the original resonances of the Me_2S and Me_2S^+– protons are separated by 60 cps, and since the width at half-height of the collapsed peak in curve C is *only 1 cps*, the average time required for exchange to occur must be very short, no more than 7×10^{-5} sec.[7] This means that the first-order rate constant for the exchange reaction, k_1, has a value of $k_1 \geqq 1.5 \times 10^4\ sec^{-1}$.

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[1] This research supported by the National Science Foundation, Grant GP-6952.

[2] J. L. Kice and E. H. Morkved, *J. Am. Chem. Soc.*, **86**, 2270 (1964).

[3] J. L. Kice, C. G. Venier, and L. Heasley, *ibid.*, **89**, 3557 (1967).

[4] (a) J. L. Kice and G. B. Large, *ibid.*, **90**, 4069 (1968); (b) *J. Org. Chem.*, **33**, 1940 (1968).

[5] G. K. Helmkamp, H. N. Cassey, B. A. Olsen, and D. J. Pettitt, *ibid.*, **30**, 933 (1965).

[6] A. Fava, A. Ilceto, and E. Camera, *J. Am. Chem. Soc.*, **79**, 833 (1957).

[7] This represents an *upper limit* on the average lifetime before exchange. The actual lifetime is almost certainly shorter than this because the figure of 7×10^{-5} sec was calculated using the equation given by Allerhand, Gutowsky, Jonas, and Meinzer[8] (eq 6 of ref 8) assuming that the line width at half-maximum intensity in the absence of exchange was 0.6 cps. Since it seems highly likely that the line width in the absence of exchange is larger than this,[9] 2τ is almost certainly smaller than 7×10^{-5} sec, although by how much one cannot say at this time.

[8] A. Allerhand, H. S. Gutowsky, J. Jonas, and R. A. Meinzer, *J. Am. Chem. Soc.*, **88**, 3185 (1966).

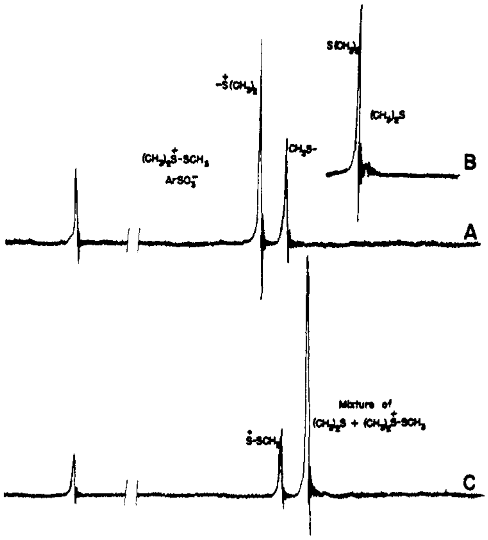
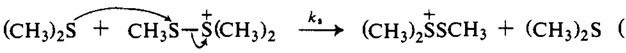


Figure 1. Nmr spectra of **1** (curve A), methyl sulfide (curve B), and an equimolar mixture of **1** and Me_2S (curve C) in CD_3CN at 0°

A priori the exchange process depicted in eq 1 could be taking place either by a direct nucleophilic attack of Me_2S on the sulfenyl sulfur of **1** (eq 3) or by a two-step process (eq 4) analogous to an SN1 substitution. Although the present results do not provide a decision

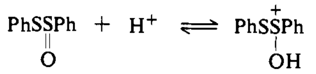


$$(CH_3)_2S + CH_3S-\overset{+}{S}(CH_3)_2 \xrightarrow{k_s} (CH_3)_2\overset{+}{S}SCH_3 + (CH_3)_2S \quad (3)$$

$$CH_3S\overset{+}{S}(CH_3)_2 \xrightarrow[\text{determining}]{\text{rate}} CH_3S^+ + S(CH_3)_2 \quad (4a)$$

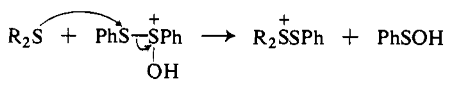
$$CH_3S^+ + S(CH_3)_2 \xrightarrow[\text{fast}]{\text{very}} CH_3S\overset{+}{S}(CH_3)_2 \quad (4b)$$

between these two alternatives,[10] arguments using the principle of microscopic reversibility and based on known behavior of reactions involving R_2S^+SR' ions in other systems[3,4] allow one to show that the mechanism in eq 3 must be the correct one. Specifically, the formation of R_2S^+SPh from phenyl benzenethiolsulfinate (**2**) and an alkyl sulfide in acid solution is known to involve rate-determining nucleophilic attack of the sulfide on the protonated thiolsulfinate (eq 5b). Furthermore, studies[4a]



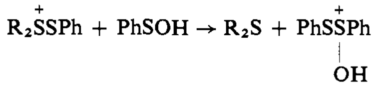
$$\underset{\underset{O}{\|}}{PhSSPh} + H^+ \rightleftharpoons \underset{\underset{OH}{|}}{Ph\overset{+}{S}SPh} \quad (5a)$$

2



$$R_2S + \underset{\underset{OH}{|}}{PhS-\overset{+}{S}Ph} \longrightarrow R_2\overset{+}{S}SPh + PhSOH \quad (5b)$$

of the sulfide- and acid-catalyzed racemization of optically active **2**[11] have demonstrated that the reverse of reaction 5b, also occurs readily under the same conditions.



$$R_2\overset{+}{S}SPh + PhSOH \rightarrow R_2S + \underset{\underset{OH}{|}}{Ph\overset{+}{S}SPh} \quad (5c)$$

The principle of microscopic reversibility requires that eq 5c take place *via* nucleophilic attack of PhSOH on the sulfenyl sulfur of R_2S^+SPh. If this is the manner in which such a thiosulfonium salt undergoes substitution by PhSOH it seems almost certain that substitution by Me_2S, which is presumably a better nucleophile, should also proceed by a direct displacement (eq 3) rather than by eq 4.

Given that the exchange presumably proceeds by the mechanism shown in eq 3, k_1 will be related to k_s, the actual bimolecular rate constant for eq 3, in the following manner

$$k_1 = k_s C_{Me_2S}$$

and therefore

$$k_s \geqq \frac{1.5 \times 10^4}{0.15} \geqq 1 \times 10^5 \, M^{-1}\,\text{sec}^{-1}$$

We would stress that the figure of $1 \times 10^5 \, M^{-1}\,\text{sec}^{-1}$ represents only a *lower limit* for k_s. Given the fact that fivefold dilution of the solution used for curve C does not lead to appreciable broadening of the collapsed resonance peak, *the true value of* k_s *could easily be several orders of magnitude larger than this.*

A rate constant of at least $10^5 \, M^{-1}\,\text{sec}^{-1}$ for a bimolecular reaction, while still a few orders of magnitude smaller than the rate constants ($\sim 10^9 \, M^{-1}\,\text{sec}^{-1}$) for extremely rapid bimolecular reactions, such as free-radical termination, which are essentially diffusion controlled, is nonetheless very large, and, in particular, it is at least 3×10^5 larger than the rate constant for the related exchange reaction of a mercaptide with a disulfide[6] (eq 6)

$$n\text{-Bu*S}^- + n\text{-BuSSBu-}n \xrightarrow{k_M'} n\text{-Bu*SSBu-}n + n\text{-BuS}^- \quad (6)$$

where $k_M' = 0.3 \, M^{-1}\,\text{sec}^{-1}$ at 25° in EtOH.[6] From the known effect of changes in the steric bulk of R on the rates of both the mercaptide–disulfide exchange[6] and the exchange reaction[12] shown in eq 7 one can estimate that

$$\text{*}SO_3^{2-} + RSSO_3^- \rightarrow R\overset{*}{S}SO_3^- + SO_3^{2-} \quad (7)$$

the rate constant for the exchange reaction between CH_3S^- and methyl disulfide (eq 8) would be no greater than 0.6–1.0 $M^{-1}\,\text{sec}^{-1}$ in ethanol at 25°. Thus even

$$CH_3\overset{*}{S}^- + CH_3SSCH_3 \xrightarrow{k_M} CH_3\overset{*}{S}SCH_3 + CH_3S^- \quad (8)$$

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(9) Line widths at half-maximum intensity for the methyl groups of dimethyl sulfide alone (curve B) or the sulfonium methyls of **1** alone (curve A) are about 1 cps, which suggests that 0.4 cps is a very generous estimate for any exchange broadening of the combined resonance in curve C and that something like 0.10 cps or less is probably more realistic.

(10) In principle the two mechanisms could be distinguished experimentally by determining whether or not variations in the concentration of methyl sulfide have any effect on k_1; for the case in eq 3 k_1 is equal to $k_s(Me_2S)$, while, if the exchange were to involve the mechanism in eq 4, k_1 would be independent of the concentration of methyl sulfide. A fivefold dilution of the solution used for curve C of Figure 1 led to at best only a very modest broadening of the collapsed resonance peak. (Study of more dilute solutions than this was precluded by (1) unfavorable signal to noise ratios and (2) the fact that slow disappearance of a significant fraction of **1** through irreversible reactions with impurities in the solvent becomes important at these high dilutions.) In view of other evidence indicating that the exchange almost certainly occurs by eq 3, we think that the failure of the fivefold dilution to lead to appreciable broadening of the collapsed peak should not be construed as evidence for the mechanism in eq 4 but only as indicative of such a very rapid rate of exchange even in 0.03 *M* solution that the exchange process leads to very little broadening of the resonance peak.

(11) (a) J. L. Kice and G. B. Large, *Tetrahedron Letters*, 3537 (1965); (b) W. E. Savige and A. Fava, *Chem. Commun.*, 417 (1965).

(12) A. Fava and A. Ilceto, *J. Am. Chem. Soc.*, **80**, 3478 (1958).

making allowance for the difference in alkyl groups in eq 3 and 6, the rate constant for the sulfide–thiosulfonium salt exchange in CH_3CN is still *at least* 10^5 faster than the rate constant for the mercaptide–disulfide exchange in ethanol.[13]

Methanethiolate (CH_3S^-) is without question a considerably more reactive nucleophile than $(CH_3)_2S$, even in substitutions involving attack on very soft electrophilic centers.[15] Thus the difference in the intrinsic reactivity of the two nucleophiles involved in eq 3 and 8 can in no way be responsible for the much faster rate observed for eq 3.

The much faster rate for eq 3 is therefore entirely the result of the greater ease with which the thiosulfonium ion undergoes nucleophilic substitution, and this, in turn, is presumably primarily due to the fact that $(CH_3)_2S^+$– represents a much better leaving group in such a substitution than does CH_3S–. In fact the present results strongly suggest that $(CH_3)_2S^+$– is such a good leaving group that nucleophilic substitutions (eq 9) involving the thiosulfonium ion and considerably better "soft" nucleophiles than $(CH_3)_2S$, such as Et_3P, $C_6H_5S^-$,

$$Nu^- + CH_3S\overset{+}{S}(CH_3)_2 \rightarrow CH_3SNu + (CH_3)_2S \quad (9)$$
$$(Nu^- = Et_3P,\ C_6H_5S^-,\ \text{or}\ CN^-)$$

or CN^-,[15] *would probably have rate constants very close to diffusion controlled* in CH_3CN as solvent.

It has long been realized that, in general, nucleophilic substitution at sulfenyl sulfur occurs much more readily than similar substitutions at sp^3 carbon. However, the present results drive home in a particularly forceful way just how fantastically rapid nucleophilic substitution at sulfenyl sulfur can easily be. Although no data are

$$(CH_3)_2S^* + CH_3\overset{+}{S}(CH_3)_2 \rightarrow (CH_3)_2\overset{+}{S}{}^*CH_3 + (CH_3)_2S \quad (10a)$$

available on the rate of the exchange reaction in eq 10a, Pearson and co-workers[15] have measured the rate of reaction 10b. Assuming that I^- is not too much better

$$(CH_3)_2S + CH_3I \xrightarrow{k_c} (CH_3)_2\overset{+}{S}CH_3 + I^- \quad (10b)$$

or worse a leaving group than $(CH_3)_2S^+$–, their value for k_c of $4.5 \times 10^{-5}\ M^{-1}\ sec^{-1}$ at 25° in methanol shows that the analogous displacement on sulfenyl sulfur in eq 3 is *at least 10^9–10^{10}* faster than the displacement at sp^3 carbon. This incredible rapidity of appropriate substitution reactions at sulfenyl sulfur is one of the things that must be kept carefully in mind in all thinking about sulfur mechanisms and is certainly one of the features which serves to set organosulfur mechanisms apart from other types of reactions.[16]

Experimental Section

Preparation and Purification of Reagents. Dimethylmethylthiosulfonium 2,4,6-Trinitrobenzenesulfonate. The thiosulfonium salt **1** was prepared by alkylation of freshly distilled dimethyl disulfide with trimethyloxonium 2,4,6-trinitrobenzenesulfonate[17] in anhydrous nitromethane using the procedure described by Helmkamp and coworkers.[5] The cream-colored product melted at 164–165° (lit.[5] 164–165°). The nmr spectrum of **1** in acetonitrile-d_3 showed two singlets in the aliphatic proton region at τ 7.17 and 6.88 with an intensity ratio of 1:2. Goodrich and Treichel[18] have measured the nmr spectrum of $(CH_3)_2S^+SCH_3\ PF_4^-$ and report two singlets at τ 7.20 and 6.90 in the ratio of 1:2.

Methyl sulfide (Matheson Coleman and Bell) was purified by fractional distillation through a spinning-band column under nitrogen. The fraction boiling at 37–39° was collected and stored over Molecular Sieve (Linde, Type 4A).

Acetonitrile-d_3 (Diaprep Inc.) was refluxed over and distilled from phosphorus pentoxide through a short Vigreux column.

Procedure for Nmr Runs. A 0.30 *M* stock solution of methyl sulfide in acetonitrile-d_3 was prepared by dissolving 0.22 ml of purified methyl sulfide in acetonitrile-d_3, adding 0.10 ml of tetramethylsilane, and then making the solution up to 10 ml with additional acetonitrile-d_3. More dilute solutions were prepared by appropriate dilution of aliquots of this solution with acetonitrile-d_3.

A weighed amount of dimethylmethylthiosulfonium 2,4,6-trinitrobenzenesulfonate (**1**) was dissolved in an acetonitrile-d_3 solution containing an equimolar amount of methyl sulfide. Spectra of freshly made 0.10–0.20 *M* solutions were taken at 10° intervals from −30 to +20°. The 0.10 *M* and more concentrated solutions showed no change in the appearance of the spectrum for at least 4 hr. However, considerably more dilute solutions (0.03 *M*) of **1** either alone or with methyl sulfide gave extraneous peaks after 10–15 min at 0°.

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(13) We realize, of course, that the transfer of the mercaptide–disulfide exchange from the protic solvent, ethanol, to the aprotic one, acetonitrile, will lead to an increase in k_M. However, Parker's studies[14] indicate that the magnitude of the increase is usually fairly modest ($\sim 2 \times 10^2$) when the anionic nucleophile is a highly polarizable one like SCN^- or CH_3S^-. For this reason it is clear that, even taking into account such a protic to aprotic solvent transfer, the rate constant for eq 8 will still be *at least* 10^3 smaller than that for eq 3.

(14) A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962); A. J. Parker, *J. Chem. Soc.*, 1328, 4398 (1961).

(15) R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, **90**, 319 (1968). These authors find $C_6H_5S^-$ to be ~300 times more reactive than $(CH_3)_2S$ in a nucleophilic substitution at Pt^{II}. In a nucleophilic substitution at sp^3 carbon $C_6H_5S^-$ is 2.4×10^4 more reactive than $(CH_3)_2S$. The ion CH_3S^- should, of course, in each instance be somewhat more reactive than $C_6H_5S^-$.

(16) A referee has pointed out that one might make an analogous statement about nucleophilic substitutions at some *other* second-row elements as well, since many of these are also very fast compared to substitutions at carbon.

(17) D. J. Pettitt and G. K. Helmkamp, *J. Org. Chem.*, **29**, 2702 (1964).

(18) R. A. Goodrich and P. M. Treichel, *J. Am. Chem. Soc.*, **88**, 3509 (1966).