with ether, and the aqueous layer was neutralized with dilute hydrochloric acid (10%). The aqueous solution was then extracted with ether three times. The combined organic solution was dried over anhydrous sodium sulfate and filtered, and the filtrate was evaporated in vacuo to give the oily product **39** (59 mg, 39%), which did not exhibit any optical rotation. The spectroscopic properties are consistent with the structure of **39**.[19]

**Desulfurization of (*R*)-(−)-Methyl 2-Phenyl-2-(phenylthio)propionate (40).** Accordiung to the general procedure, a mixture of **40**[18] (544 mg, 2.0 mmol) and $W(CO)_6$ (710 mg, 2.0 mmol) in chlorobenzene (20 mL) was heated under reflux for 30 h. After being cooled to room temperature, the mixture was filtered and the filter cake was washed with ether. The combined organic solution was evaporated in vacuo, and the residue was chromatographed on silica gel and eluted with hexane–ethyl acetate (20:1) to give the first portion, **41a** (138 mg, 43%): mp 113–115 °C; $^1$H NMR $\delta$ 1.85 (s, 6 H), 3.60 (s, 6 H), 6.60–7.20 (m, 10 H); MS, *m/e* 326. The second portion was isolated as oil **41b** (115 mg, 35%): $^1$H NMR $\delta$ 1.77 (s, 6 H), 3.67 (s, 6 H), 6.60–7.20 (m, 10 H); MS, *m/e* 326. The high-melting compound **41a** would be the more symmetric isomer or the meso form.

**Desulfurization of Methyl 2-Phenyl-2-(phenylthio)-butyrate (42).** A mixture of **42** (858 mg, 3 mmol) and $W(CO)_6$ (1.1 g, 3 mmol) in chlorobenzene (20 mL) was treated according to the general procedure described above to give a mixture of three products **43**, **44**, and **45** in a ratio of 5:4:1 based on the NMR spectrum of the crude mixture. After careful thromatography on silica gel using hexane–ethyl acetate (30:1) as eluent, **43** (120 mg, 23%) was obtained as the first portion: $^1$H NMR $\delta$ 0.90 (t, 3 H), 2.04 (dq, 2 H), 3.70 (dd, 1 H), 3.77 (s, 3 H), 7.50 (m, 5 H).[20] The second portion was a mixture of **43**, **44**, and **45**. The third portion afforded pure **45** (100 mg, 19%): $^1$H NMR $\delta$ 1.68 (d, 3 H), 3.67 (s, 3 H), 7.04 (m, embodied in the aromatic absorptions), 7.05–7.40 (m, 5 H). **44**: $^1$H NMR $\delta$ 2.06 (d, 3 H), 3.60 (s, 3 H), 6.10 (q, 1 H), 7.00–7.30 (m, 5 H).[20]

**Desulfurization of 1-Naphthylmethyl 2-Naphthylmethyl Sulfide (19).** Following the same procedure as described above, we refluxed a mixture of **19** (507 mg, 1.6 mmol) and $W(CO)_6$ (616 mg, 1.7 mmol) in chlorobenzene (10 mL) for 48 h. After filtration and evaporation of the solvent, the residue was subject to NMR and GC/MS analyses. The yields of the products are as follows: **8** (14%), **9** (27%), **10** (28%), **11** (18%), and 1-(1-naphthyl)-2-(2-naphthyl)ethane (11%).

**Desulfurization of 2-(Phenylthio)styrene (20).** According to the general procedure, a chlorobenzene solution (10 mL) of **20** (639 mg, 3.0 mmol) and $W(CO)_6$ (1.81 g, 5.1 mmol) was allowed to react. After chromatographic separation, *trans*-stilbene (98 mg, 18%) was the only product which was identified by comparing its physical properties with those of an authentic sample.

**Desulfurization of 2-Naphthylmethanethiol-*d* (37).** A mixture of **37** (387 mg, 2.2 mmol) and $W(CO)_6$ (804 mg, 2.3 mmol) in chlorobenzene (5 mL) was allowed to react according to the general procedure to afford 2-methylnaphthalene-*d* (186 mg, 59%); MS, *m/e* 143.

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# $S_N2$ Displacement on 2-(Alkylthio)ethyl Derivatives

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We have studied the reaction mechanism of various 2-(alkylthio)ethyl and 2-(arylthio)ethyl derivatives with strong nucleophiles in an attempt to overcome powerful neighboring sulfur participation and shift reaction to a direct displacement $S_N2$ mechanism. The 2,4-dinitrophenolate derivative of specifically deuteriated 2-(methylthio)ethanol reacts by an aromatic substitution mechanism ($S_NAr$) when exposed to amines in aprotic solvents. Use of sulfonate esters avoids competition from the $S_NAr$ mechanism. The rate of reaction of these esters in dimethyl sulfoxide (DMSO) or acetonitrile is independent of concentration of added methylamine, thiourea, urea, or iodide, thus indicating continued $S_N1$ reaction with neighboring sulfur participation. As would be expected on this basis, but in contrast to previous mechanistic suggestions, the product for reaction with iodide in acetone shows complete scrambling of methylene groups. In contrast, reaction with thiophenolate ions in DMSO proceeds by direct nucleophilic displacement (an $S_N2$ mechanism), as shown by second-order kinetics and unrearranged product. This is the first demonstration of $S_N2$ displacement on a 2-(alkylthio)ethyl or 2-(arylthio)ethyl derivative.

## Introduction

One of the prime concerns of physical organic chemistry has been to understand the processes whereby reactions shift from one mechanism to another.[1] We have been investigating this question using 2-(alkylthio)ethyl compounds, which may react with nucleophiles by neighboring-group participation, elimination, or direct nucleophilic substitution. Reaction of 2-(alkylthio)ethyl derivatives with several nucleophiles and bases under a variety of conditions has shown these substrates to be extremely resistant to direct nucleophilic displacement (an $S_N2$ mechanism) because of the dominant competition from powerful neighboring sulfur participation ($k_\Delta$ pathway), eq 1.[2-4] For example, solvolysis in water or alcohols

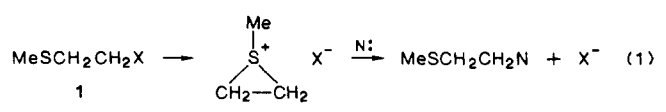

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**Table I. Rates and β-Deuterium Isotope Effects for Reaction of 2-(Methylthio)ethyl Dinitrophenolate with Various Nucleophiles at 25 °C**

| nucleophile[a] | solvent | $10^3k_2$, $M^{-1}$ $s^{-1}$ | runs | β-d[b] |
|---|---|---|---|---|
| ethanolamine | DMF | 4.65 ± 0.31 | 15 | 1.00 |
| | $CH_3CN$ | 0.465 ± 0.006 | 4 | 1.03 |
| | formamide | 0.435 ± 0.016 | 4 | 1.02 |
| | DMSO | 11.9 ± 0.4 | 4 | 1.02 |
| | methoxyethanol | 0.133 ± 0.003 | 4 | 1.02 |
| $CH_3NH_2$ | $CH_3CN$ | 3.54 ± 0.07 | 2 | 1.04 |
| 5% NaOH | water | 0.643 ± 0.061[c] | 4 | 0.98 |
| 2% NaOH | water | 0.226 ± 0.018[c] | 4 | 1.02 |
| none | water | 0.000 499[c,d] | | |

[a] Substrate concentration 1 × $10^{-4}$ M, and nucleophile concentrations 0.037–0.10 M. [b] Error limits on the isotope effects were ±0.02 except for the water runs where limits of ±0.09 were observed (insolubility problems here). [c] First order rates, $s^{-1}$. [d] Extrapolated. $T$ (°C)/$10^5k$ ($s^{-1}$): 100/56.1, 80.0/10.9, 70.0/5.86, and 62.9/2.29.

proceeds rapidly (greater than a million times faster than *n*-butyl chloride)[5] with complete equilibration of methylene carbons in the product, thus showing the absence of direct displacement ($k_s$ pathway).[2] Addition of more powerful nucleophiles (such as thiourea) fails to alter the $k_\Delta$ mechanism.[3] Even reaction with acetate anion under phase-transfer conditions (KOAc/benzene/PEG) proceeds by the $k_\Delta$ pathway.[4]

An estimate of the power of the β-sulfur as a neighboring group can be derived by using the observation that 2-(methylthio)ethyl chloride (**1-Cl**) undergoes hydrolysis 6 × $10^6$ times as fast as does *n*-butyl chloride.[5] Since *n*-butyl chloride is reacting by a nucleophilically assisted $k_s$ process in which water provides a $10^5$ rate acceleration,[6] neighboring sulfur must provide additional assistance to bond cleavage (6 × $10^6$ in rate terms) beyond that provided by the nucleophilic solvent. We can see from this analysis that an enhancement of nucleophilicity of approximately $10^7$ relative to the nucleophilicity of water and alcohols will be required for an external nucleophile to become competitive with the internal sulfur nucleophile.

A proven means of achieving enhancements of this magnitude is to perform substitutions with anionic nucleophiles in "dipolar aprotic" solvents such as dimethyl sulfoxide (DMSO) and acetonitrile.[7] The present paper describes mechanistic studies of this type for reaction of various 2-(alkylthio)ethyl and 2-(arylthio)ethyl substrates.

## Results and Discussion

**Dinitrophenolate Studies.** Our previous mechanistic study of solvolysis of β-sulfur derivatives was aided by the availability of deuterium-labeled 2,4-dinitrophenolates **2-ODNP** and **3-ODNP**.[2] We attempted to use these same labeled compounds in the present experiments with strong nucleophiles, but as could be expected, nucleophilic attack on the aromatic ring by an $S_NAr$ mechanism intervenes. Four pieces of evidence for this mechanism were obtained for reaction of **1-ODNP** with several nucleophiles in several solvents: (1) second-order kinetics (Table I); (2) absence of a deuterium kinetic isotope effect for **2-ODNP**

**Table II. Rates for Reaction with Ethanolamine of 2-Methoxyethyl and 2-(Methylthio)ethyl 2,4-Dinitrophenolates under the Same Conditions at 25 °C**

| compd[a] | solvent | $10^2k_2$, $M^{-1}$ $s^{-1}$ |
|---|---|---|
| $MeOCH_2CH_2ODNP$ | DMSO | 1.19 ± 0.02 |
| | DMF | 0.362 ± 0.002 |
| | $HCONH_2$ | 0.0435 ± 0.0016 |
| $MeSCH_2CH_2ODNP$ | DMSO | 1.16 ± 0.01 |
| | DMF | 0.360 ± 0.003 |
| | $HCONH_2$ | 0.0457 ± 0.0004 |

[a] Duplicate runs; [substrate] (1–3) × $10^{-4}$ M, [nucleophile] = 0.0275–0.0370 M.

**Table III. First-Order Rate Constants for Reaction of 2-(Phenylthio)ethyl Brosylate and 2-Naphthalenesulfonate with Various Nucleophiles in DMSO and Acetonitrile**

| compd[a] | solvent | nucleophile[b] | $10^4k$,[c] $s^{-1}$ | runs |
|---|---|---|---|---|
| OBs | DMSO | $CH_3NH_2$ | 4.41 ± 0.34 | 4 |
| | | none | 2.08 ± 0.54 | 3 |
| | $CH_3CN$ | $CH_3NH_2$ | 1.89 ± 0.16 | 10 |
| | | thiourea | 1.66 ± 0.04 | 4 |
| ONps | $CH_3CN$[d] | thiourea | 0.544 ± 0.058 | 6 |
| | | urea | 0.522 ± 0.004 | 2 |
| | DMSO | none | 1.56 ± 0.04 | 2 |
| | | KI | 1.56 | 1 |
| | | $(CH_3)_4NI$ | 1.68 ± 0.00 | 2 |
| | | *n*-$Bu_4NI$ | 1.57 ± 0.01 | 2 |

[a] [Brosylate] = (3.08–20.0) × $10^{-4}$ M; [naphthalenesulfonate] = (5.12–8.32) × $10^{-4}$ M. [b] [Methylamine] = 0.0095–0.318 M; [urea] = 0.026 M; [thiourea] = 0.00525–0.058 M; [$I^-$] = 0.005 97–0.009 94 M except KI, which is 0.160 M. [c] At 25 °C unless noted otherwise. [d] 35 °C.

(Table I);[8,9] (3) identical rates for **1-ODNP** and its oxygen analogue 2-methoxyethyl dinitrophenolate (Table II); and (4) formation of $S_NAr$ products for reaction of **3-ODNP** and methylamine (unscrambled alcohol **3-OH** and *N*-methyl-2,4-dinitroaniline).[10]

$$\underset{\mathbf{2}}{CH_3SCHDCH_2X} \qquad \underset{\mathbf{3}}{CH_3SCH_2CD_2X}$$

These results emphasize the difficulty of performing an $S_N2$ reaction on β-sulfur derivatives. Improving nucleophilicity relative to solvolytic media by reacting **1-ODNP** with aqueous hydroxide or amines in nonhydroxylic solvents produced a shift in mechanism to attack on the aromatic ring of the leaving group rather than a shift to direct nucleophilic attack on saturated carbon.

**Studies of Sulfonate Esters.** To avoid the complicating $S_NAr$ mechanism that occurs with the dinitrophenolates, we have examined the corresponding brosylate (OBs) and 2-naphthalenesulfonate (ONps) of 2-(phenylthio)ethanol, **4-OH**.

$$\underset{\mathbf{4},\ X = OBs,\ ONps,\ Cl,\ OH}{C_6H_5SCH_2CH_2X}$$

In our search for specifically labeled derivatives we had initially avoided sulfonate esters because we had assumed that they would be too reactive; the chlorides are quite reactive and tosylate–chloride rate ratios are frequently in the thousands.[5] However, this assumption was later shown to be incorrect when the β-sulfur derivatives were found to have low tosylate–chloride ratios similar to those for $S_N2$ reactions.[5] Thus the way is open to product studies

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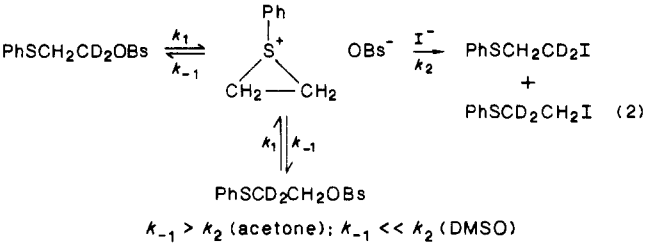
with deuterium-labeled sulfonates which are much less likely to react via the $S_NAr$ mechanism than the dinitrophenolates.

Initially we examined the kinetics of reactions in DMSO or acetonitrile of **4-OBs** and **4-ONps** with methylamine and thiourea, two moderately strong nucleophiles (Table III). As shown in Table III, these nucleophiles give first-order reactions. Slight differences in the rates result, we believe, from alteration of the solvent by the nucleophile. Consistent with the lack of kinetic effect of these nucleophiles is the observation that the weak nucleophile urea gives the same rate as the strongly nucleophilic thiourea.[3] Finally we measured the reaction rate for iodide in DMSO (Table III) and found an unaltered first-order rate (no shift to second-order kinetics). Obviously an even more powerful nucleophile is required to compete with neighboring sulfur participation.

The observation of first-order kinetics for reaction of iodide ion with **4-ONps** in DMSO requires comment on an important earlier work of Bordwell and Brannen on the kinetic effects of a large number (40) of Y groups in Y-$(CH_2)_n$Cl on reaction with potassium iodide in acetone.[11] Included in this study was $PhSCH_2CH_2Cl$, **4-Cl**. Obviously, a detailed mechanistic study was not done on the large number of substrates, and it was assumed that all reacted by an $S_N2$ mechanism because second-order kinetics were observed. However, our observation of first-order kinetics for **4-ONps** with iodide in DMSO is inconsistent with an $S_N2$ mechanism for **4-Cl** in acetone. It is our view that the second-order kinetics observed by Bordwell and Brannen do not derive from $S_N2$ displacement. Rather we suggest that the rate dependence observed for iodide in acetone derives from removal of a return process (either ion-pair return or external-ion return) and possibly from alteration of the solvent.

There are two reasons why return would be expected to be much more important for **4-Cl** in acetone than for **4-ONps** in DMSO or acetonitrile. First, chloride is a better nucleophile than sulfonate and return is known to be much more important for chlorides than for the sulfonates.[12] Specifically, Bartlett and Swain observed a common ion rate depression for reaction of mustard chlorohydrin in 5% acetone/95% water,[13] and we have observed the same effect for **1-Cl** in pure alcohols,[14] yet **4-OBs** shows no return in aqueous acetone.[2] Secondly, return processes are known to be very important in pure acetone and relatively unimportant in more polar solvents such as aqueous acetone, DMSO, or acetonitrile.[12]

Unfortunately, the specifically labeled chloride is not available.[2] Therefore, to test this proposal we have used NMR to determine the extent of deuterium scrambling during reaction of deuterium labeled **4-OBs**, $PhSCH_2CD_2$-OBs, with KI in acetone. As expected on the basis of our observed first-order kinetics for **4-ONps** in DMSO and acetonitrile, the iodide product for reaction of **4-OBs** in acetone is completely scrambled; methylene peaks of equal areas are observed at 3.35 and 3.40 ppm (see the Experimental Section). Also in keeping with the expected greater importance of return in acetone than in DMSO, the starting brosylate scrambles more rapidly than product is formed (a qualitative estimate of $k_{-1}/k_2$ of 4 can be calculated from the spectra; a much larger value would be expected for **4-Cl**). If iodide is not added, rapid deuterium scrambling is seen in the brosylate, along with very slow formation of a second product that is presumed to derive from capture of the sulfonate by acetone. Thus, if the state of ion pairing is ignored (i.e., tight ion pair, solvent separated ion pair, or free cation), reaction takes place as shown in eq 2.




$k_{-1} > k_2$ (acetone); $k_{-1} << k_2$ (DMSO)

Consistent with this mechanism, addition of thiourea (a nucleophile similar in reactivity to iodide) to reaction of **1-Cl** in acetone gives a rate acceleration and second-order kinetics, as would be expected for competition with $k_{-1}$ ($k^{obsd} = (5.41 \pm 0.93) \times 10^{-3}$ $M^{-1}$ $s^{-1}$ at 89.6 °C, [thiourea] = 0.04–0.22 M);[3] recall that the same nucleophile gives no rate enhancement for reactions in DMSO or acetonitrile (Table III). We did not examine the kinetic effect of iodide in acetone because we feel our evidence for mechanism (2) is very strong and because kinetic methods other than those in standard use in our laboratory would be required; UV (at 325 nm) and conductivity methods are not suitable for reactions of concentrated salts in acetone.

As a final point regarding the justifiability of basing mechanistic conclusions on kinetics in iodide/acetone reactions, we refer to some earlier comments by Streitwieser.[15] Streitwieser noted that KI is incompletely dissociated in acetone and that it is likely that specific interactions between KI and polar organic molecules could affect rates. In view of this complication, Streitwieser states that it is not justifiable to draw mechanistic conclusions from kinetics without accompanying studies, in particular product determination. Our studies provide strong support for this general conclusion.

**Observation of an $S_N2$ Reaction. Arenethiolate Nucleophiles.** Bordwell and his co-workers have published a series of papers relating basicity and nucleophilicity in DMSO in which nucleophiles are generated by reacting the "dimsyl" ion, $CH_3SOCH_2^-$, with various acids such as phenols, alkanes, and thiophenols.[16] This system provides a graded series of increasingly powerful nucleophiles, which are directly related by their $pK_a$ values and nucleophilic center. Some of the nucleophiles studied by Bordwell and co-workers are much stronger than those discussed in the preceding section. Therefore, we have used this chemistry developed by the Bordwell group to generate the 2-naphthalenethiolate ion, **5**, for reaction with **4-OBS** and **1-Cl**. Disappearance of this nucleophile can be easily monitored by following its ultraviolet absorption at 444 nm.

Adding thiolate **5** to the solvolytic reaction of **4-OBs** or **1-Cl** in DMSO gives rapid disappearance of the thiolate. If **5** is assumed to be reacting with the substrate (confirmed below), then addition of thiolate is producing a dramatic acceleration in loss of substrate. Whereas the half-life for substrate loss in DMSO without a nucleophile or with methylamine (still first-order) approaches 1 h at 25 °C, addition of **5** gives essentially complete disappearance of

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**1-Cl** in a few minutes by a second-order process ($k_2$ = (2.66 ± 0.15) × $10^{-2}$ $M^{-1}$ $s^{-1}$). Interestingly, we observed a rate for reaction of **5** with *n*-butyl chloride ($k_2$ = (2.56 ± 0.06) × $10^{-2}$ $M^{-1}$ $s^{-1}$) that is very close to that of **1-Cl**; this result, along with the second-order kinetics, indicates (but does not prove) that reaction is occurring by an $S_N2$ mechanism and that the inductive effect of a β-sulfur atom is slight.

Product studies with proton NMR confirm reaction by an $S_N2$ mechanism. First we describe reaction of 1,1-dideuterio-2-(phenylthio)ethyl brosylate (**4-$D_2$-OBs**) in DMSO without a nucleophile. The reactant alkyl absorptions are 4.12 ($C_1$-H; absent in the deuteriated derivative) and 3.12 ppm ($C_2$-H), and the product absorptions are 4.41 ($C_1$-H) and 3.34 ppm ($C_2$-H). When the reaction is started with **4-$D_2$-OBs** in DMSO, a single alkyl peak at 3.12 ppm is observed; as the reaction proceeds, this peak is replaced by two peaks of equal areas at 4.41 and 3.34 ppm. This result is consistent with rate-determining neighboring sulfur participation to give the sulfonium ion, which is then rapidly destroyed by nucleophilic attack, presumably by DMSO, to give a product in which the 1- and 2-carbons have scrambled. No vinyl absorptions are seen, indicating no elimination. Also, no return from sulfonium ion to give scrambled reactant (absorption at 4.12 ppm) is seen (complete spectral data are given in the Experimental Section). Although we were unable to isolate or identify this product, the spectrum is consistent with DMSO acting as nucleophile to give $PhSCH_2CH_2OS(CD_3)_2^+$.

If reaction of **4-$D_2$-OBs** with thiolate **5** proceeds by an $S_N2$ mechanism, as the kinetics for **1-Cl** suggest, then the substitution product should exhibit no deuterium rearrangement. This result is indeed observed in NMR experiments monitoring reaction of **4-$D_2$-OBs** with **5** in DMSO-$d_6$ as a function of time. At time zero the alkyl portion of the spectrum reveals the single 3.12 ppm $C_2$-H absorption (sharp singlet), which is rapidly replaced by a single absorption at 3.20 ppm (sharp singlet) (eq 4).

$$\underset{3.12}{PhS-CH_2-}\underset{4.12}{CH_2-}OBs + 2\text{-Naph-}S^- \xrightarrow[\mathbf{5}]{} \underset{3.20}{PhS-CH_2-}\underset{3.27}{CH_2-}S(2\text{-Naph}) \quad (3)$$

$$\underset{3.12\text{ ppm only}}{PhS-CH_2-}CD_2OBs + 2\text{-Naph-}S^- \xrightarrow[\mathbf{5}]{} \underset{3.20\text{ ppm only}}{PhS-CH_2-}CD_2-S(2\text{-Naph}) \quad (4)$$

Isolation of the product for reaction of nondeuteriated **4-OBs** with anion **5** permits assignment of the alkyl proton absorptions, with the $PhSCH_2$ protons at 3.20 ppm and the 2-Naph-S-$CH_2$ protons at 3.27 ppm (eq 3); elemental analysis of this product is consistent with the substitution product. Although the product alkyl absorptions are quite close together, the two peaks can be clearly resolved by 200-MHz proton NMR. The peak at 3.27 ppm is absent for the product from reaction of **4-$D_2$-OBs**. Thus it is apparent that substitution by **5** on **4-OBs** occurs by direct displacement without rearrangement, i.e., by a typical $S_N2$ mechanism.

To confirm this conclusion we have performed a similar experiment for reaction of **4-$D_2$-OBs** with the *p*-aminothiophenolate anion **6**; in this case the product alkyl NMR absorptions are farther apart than in the product of reaction with **5**. Reaction of **6** with protiated **4-OBs** gives the expected substitution product (from elemental analysis) with the $PhSCH_2$ protons at 3.03 ppm and the $H_2NPhSCH_2$ protons at 2.85 ppm (eq 5). As would be expected for the $S_N2$ mechanism, reaction of **6** with **4-$D_2$-OBs** shows the 3.12 ppm $PhSCH_2$ absorption of the brosylate being rapidly replaced by a single sharp peak at 3.03 ppm (eq 6); no brosylate scrambling (4.12 ppm peak) or product scrambling (2.85 ppm peak) is observed.

$$\underset{3.12}{PhS-CH_2-}\underset{4.12}{CH_2-}OBs + H_2N\text{-Ph-}S^- \rightarrow \underset{3.03}{PhS-CH_2-}\underset{2.85}{CH_2-}S\text{-Ph-}NH_2 \quad (5)$$

$$\underset{3.12\text{ ppm only}}{PhS-CH_2-}CD_2-OBs + \mathbf{6} \rightarrow \underset{3.03\text{ ppm only}}{PhS-CH_2-}CD_2-S\text{-Ph-}NH_2 \quad (6)$$

It is possible that the observed results could arise by base-catalyzed elimination from **4-OBs** followed by addition of thiophenolate to give unscrambled substitution product (eq 7). As a control experiment we combined

$$PhSCH_2CD_2OBs + \mathbf{6} \rightarrow PhSCH{=}CD_2 \xrightarrow{\mathbf{6}} PhSCH_2CD_2SC_6H_4NH_2 \quad (7)$$

thiophenolate ion **6** with the alkene $PhSCH{=}CH_2$ in DMSO-$d_6$ and found (by NMR) the alkene to be unreactive toward thiophenolate ion after a time greater than 10 half-lives of the substitution reaction. Thus, since the second step of eq 7 does not occur under these conditions, we can assume that the overall process of eq 4 is not contributing to our observed product studies.

## Conclusions

In summary, we have found that 2-(methylthio)ethyl dinitrophenolate reacts by an $S_NAr$ mechanism when exposed to nucleophilic systems considerably more powerful than hydroxylic solvolytic media. Use of sulfonate esters (brosylate and 2-naphthalenesulfonate) avoids competition from the $S_NAr$ mechanism and permits specific deuterium labeling (e.g., in the synthesis of $PhSCH_2CD_2OBs$, **4-OBs**). Reaction of these esters with methylamine, thiourea, urea, potassium iodide, and tetrabutylammonium iodide in DMSO or acetonitrile proceeded at approximately the same rate (depending on solvent) by a first-order process. Although products were not isolated, reaction presumably proceeds by rate-determining neighboring sulfur participation. Consistent with this interpretation, reaction of deuterium-labeled **4-OBs** with iodide in acetone gave substitution products in which the methylene groups were completely scrambled. This study suggests that the earlier conclusion of Bordwell and Brannen[11] that **4-Cl** reacts with iodide/acetone by an $S_N2$ mechanism may be incorrect.

In sharp contrast, reaction in DMSO of **4-OBs** or **1-Cl** with 2-naphthalenethiolate ion or *p*-aminothiophenolate ion does proceed by direct nucleophilic displacement (an $S_N2$ mechanism), as shown by second-order kinetics and lack of rearrangement. This is the first demonstration of $S_N2$ displacement on a 2-(alkylthio)ethyl or 2-(arylthio)ethyl derivative.

Previous work has shown that 2-(alkylthio)ethyl derivatives will give elimination under phase-transfer conditions with hydroxide/benzene.[4] We now see that extremely powerful nucleophiles can give $S_N2$ displacement. Our future efforts will be directed toward the complex issue of better defining the transitions from neighboring sulfur participation to elimination or to direct displacement for 2-(alkylthio)ethyl derivatives; at this point, the interactions of solvent, substrate, neighboring group, and nucleophile are not sufficiently well understood to permit predictions on these transitions.

## Experimental Section

Solvents and reagents of the highest available purity were purchased from Aldrich or Sigma and used without further purification unless noted otherwise. Proton NMR spectra were obtained on an IBM-Bruker AFT-200 (200 MHz) spectrometer

(chemical shifts given are for the center of the multiplet), and UV spectra were obtained on a Varian DMS-90 spectrophotometer with a thermostated cell changer.

**Materials. Deuteriated Alcohols.** The $\alpha$-$d_2$ forms of the alcohols 2-(methylthio)ethanol and 2-(phenylthio)ethanol were obtained by lithium aluminum deuteride reduction in diethyl ether of ethyl 2-(methylthio)acetate (Aldrich) and ethyl 2-(phenylthio)acetate (prepared from the corresponding acid, Aldrich). The $\beta$-deuterio form of 2-(methylthio)ethanol was prepared by hydroboration[17] of methyl vinyl sulfide with $BD_3$.[4]

$^1$H NMR spectral data of the protiated alcohols follow (in ppm). $PhSCH_2CH_2OH$ (DMSO-$d_6$): $CH_2S$, 3.04 (t, 2 H); $CH_2O$, 3.56 (q, 2 H); OH, 4.96 (t, 1 H); PhS, 7.26 (m, 5 H). $CH_3SCH_2CH_2OH$ (DMSO-$d_6$): $CH_3S$, 2.15 (s, 3 H); $CH_2S$, 2.60 (t, 2 H); $CH_2O$, 3.60 (t, 2 H).

**2-(Methylthio)ethyl and 2-Methoxyethyl Dinitrophenolates.** These compounds were prepared by a general procedure of Sinnott and Whiting[18] for reaction of 2,4-dinitrofluorobenzene with the appropriate alcohol.

$CH_3SCH_2CH_2ODNP$: mp 55–56 °C. $^1$H NMR ($CDCl_3$) (in ppm) $CH_3S$, 2.04 (s, 3 H); $CH_2S$, 2.79 (t, 2 H); $CH_2O$, 4.25 (t, 2 H); 6-Ar-H, 7.07 (d, 1 H); 5-Ar-H, 8.26 (q, 1 H); 3-Ar-H, 8.51 (d, 1 H). The $\alpha$-$d_2$ form gave a singlet at 2.79 ppm (2 H) and no peak at 4.25 ppm. The $\beta$-$d$ form gave a triplet at 2.79 ppm (1 H) and a doublet at 4.25 ppm (2 H).

$CH_3OCH_2CH_2ODNP$: mp 35.8–36.2 °C. $^1$H NMR ($CDCl_3$) (in ppm) $CH_3O$, 2.85 (s, 3 H); $CH_2O$, 3.24 (t, 2 H); $CH_2ODNP$, 3.80 (t, 2 H); 6-Ar-H, 6.70 (d, 1 H); 5-Ar-H, 7.85 (q, 1 H); 3-Ar-H, 8.15 (d, 1 H).

**2-(Phenylthio)ethyl Brosylate and 2-Naphthalenesulfonate 4.** These sulfonate esters were prepared by the standard reaction of alcohol with the appropriate sulfonyl chloride in dry pyridine,[19] and they were recrystallized from hexane.

$PhSCH_2CH_2OBs$: mp 58–59 °C. $^1$H NMR ($CD_3CN$) (in ppm) $CH_2S$, 3.12 (t, 2 H); $CH_2O$, 4.12 (t, 2 H); PhS, 7.25 (m, 5 H); OBs, 7.73 (m, 4 H). The $\alpha$-$d_2$ form had a singlet at 3.12 ppm and no peak at 4.12 ppm.

$PhSCH_2CH_2ONps$: mp 31–32 °C. $^1$H NMR ($CDCl_3$) (in ppm) $CH_2S$, 3.13 (t, 2 H); $CH_2O$, 4.16 (t, 2 H); PhS, 7.16 (m, 5 H); ONps, 7.67–8.44 (m, 7 H).

**Product Analysis. Reaction of Dintrophenolates with Methylamine.** Methylamine (Matheson) was passed over a column of potassium hydroxide and then bubbled through the solvent. Concentrations were determined by diluting with water and titrating with acid. Solutions of 1-**ODNP** and methylamine in DMSO-$d_6$ were mixed, and product formation was followed by $^1$H NMR; the following spectral data of an equimolar mixture of $CH_3SCH_2CH_2OH$ and *N*-methyl-2,4-dinitroaniline were obtained (in ppm): $CH_3S$, 2.06 (s, 3 H); $CH_2S$, 2.53 (t, 2 H); $CH_2O$, 3.54 (t, 2 H); $CH_3N$, 3.06 (s, 3 H); 6-Ar-H, 7.13 (d, 1 H); 5-Ar-H, 8.28 (m, 1 H); 3-Ar-H, 8.83 (d, 1 H). The NMR spectrum obtained by reacting the $\alpha$-$d_2$ form (**2**) with methylamine was identical except that the 2.53 ppm peak was a singlet and the 3.54 ppm peak was absent. To confirm the presence of *N*-methyl-2,4-dinitroaniline, this compound was prepared by reacting methylamine with 2,4-dinitrofluorobenzene in acetonitrile; the NMR spectrum of this isolated material was identical with that described above.

**Reaction of Brosylate 4 with Thiophenolate Ions.** Ten milliliters of DMSO containing 12 mmol of 2-naphthalenethiol or *p*-aminothiophenol was added to a 20 mL solution of 0.44 M potassium dimsyl ($KCH_2SOCH_3$, prepared according to the procedure of Bordwell and Hughes[16]) to produce the thiophenolate anions. Brosylate 4 (2.7 g, 9 mmol) was added to either of the anions, and the reaction mixture was shaken for about 2 h. The solution was poured into cold water and extracted with ether. The ether solution was washed with water and dried over magnesium sulfate. Evaporation of the ether gave the white solid product. The products were then recrystallized several times from methanol/water.

2-Naphthalenethiolate product: $^1$H NMR (DMSO-$d_6$) (in ppm) $CH_2$-S-Naph, 3.27 (m, 2 H); $CH_2SPh$, 3.20 (m, 2 H); aromatic protons, 7.25–7.93 (m, 12 H). Mp 64–66 °C. Anal. Calcd: C, 73.93; H, 5.44. Obsd: C, 73.39; H, 5.19. Yield >90%.

*p*-Aminothiophenolate product: $^1$H NMR (DMSO-$d_6$) (in ppm) $CH_2SPhNH_2$, 2.85 (t, 2 H); $CH_2SPh$, 3.03 (t, 2 H); NH, 5.3 ppm (m, 2 H); Ar, 6.57–7.26 (m, 9 H). Mp 41–43 °C. Anal. Calcd: C, 64.33; H, 5.78; N, 5.36. Obsd: C, 63.44; H, 5.95; N, 5.33. Yield >90%.

The lack of methylene scrambling in this reaction was corroborated by direct NMR observation (without product isolation) of the reaction. Deuteriated potassium dimsyl ($KCD_2SOCD_3$, 1.14 M) was prepared by adding KH to DMSO-$d_6$. To 10 mL of this solution was added a slight excess (12 mmol) of thiol in 10 mL of DMSO-$d_6$. The brosylate $PhSCH_2CD_2OBs$ (11.5 mmol) was added to this thiolate solution, and after about 5 min the NMR spectrum was obtained. Observed chemical shifts are given in the Discussion.

For the reaction in DMSO without added thiophenolate ion, the product aryl absorption was in the range of 7.37–7.56 ppm. The alkyl region is described in the Discussion.

**Reaction of 4-OBs with Iodide in Acetone.** One milliliter of acetone-$d_6$ containing 0.06 mmol of potassium iodide and 0.054 mmol of $PhSCH_2CD_2OBs$ was reacted at 60 °C and the $^1$H NMR spectrum obtained. The alkyl region of the spectrum at time zero showed a single absorbance at 3.25 ppm ($SCH_2CD_2OBs$). After reaction for 0.5 h, the peak for scrambled brosylate ($SCD_2CH_2OBs$) appeared at 4.21 ppm (area 0.44 relative to $SCH_2CD_2OBs$ as unity), along with a pair of singlets for scrambled iodide ($CH_2CD_2I$ and $CD_2CH_2I$) at 3.35 and 3.40 ppm (relative areas 0.11 for each peak). At longer reaction times (3 h, 60 °C), or in the absence of iodide ion, a pair of peaks attributed to 2-(phenylthio)ethanol or possibly $PhSCH_2CD_2$ and $PhSCD_2CH_2OC(CD_3)CD_2$ appear at 3.70 and 3.08 ppm; GC analysis showed some alcohol even in carefully dried acetone, and we hypothesize that this product may derive from the alkene. The aromatic region between 7.18 and 7.85 ppm consisted of complex overlapping multiplets and was not analyzed further.

**Kinetics.** Rates for brosylate 4 were measured conductimetrically as described previously.[3] All other rates were measured spectrophotometrically in stoppered cells in a thermostated cell changer (Varian DMS-90; ±0.1 °C) under an inert atmosphere. DMSO used was Aldrich "anhydrous" with 0.005% water. Acetonitrile was dried with calcium hydride. The following wavelengths were used: 2,4-dinitrophenol appearance at 360 nm, 2-naphthalenesulfonate disappearance at 325 nm, *p*-aminothiophenolate disappearance at 570 nm, and 2-naphthalenethiolate disappearance at 444 nm. All reported rate constants are the result of at least duplicate determinations; error limits reported are standard deviations. In the case of reaction of the 2-naphthalenethiolate anion in DMSO, kinetic accuracy was confirmed by obtaining the rate constant for reaction at 25 °C with *n*-butyl chloride ($k_2 = (2.56 \pm 0.06) \times 10^{-2}$ $M^{-1}$ $s^{-1}$) that had been measured previously by Bordwell and Hughes ($2.54 \times 10^{-2}$).[16] Second-order rate constants were obtained by first determining a pseduo-first-order rate constant for reaction with excess substrate and then dividing this constant by the substrate concentration.

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