The Reaction of Hypochlorite with Various Oxidized Derivatives of Disulfides and with Sulfinate Ions

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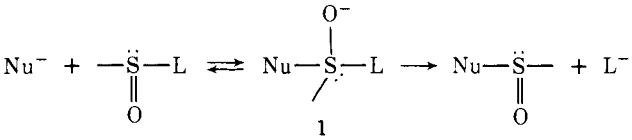
Abstract: The reaction of hypochlorite with aryl thiolsulfonates, $\mathrm{ArSO_2SAr}$, sulfinyl sulfones, $\mathrm{ArS(O)SO_2Ar}$, and α-disulfones, $\mathrm{ArSO_2SO_2Ar}$, has been investigated. In the presence of sufficient hypochlorite the products of all these reactions are 2 mol of the sulfonate $\mathrm{ArSO_3^-}$ per mol of starting sulfur compound. This transpires because any sulfinate $\mathrm{ArSO_2^-}$ formed in intermediate stages is rapidly oxidized to $\mathrm{ArSO_3^-}$ by hypochlorite. The pH-rate profile for this sulfinate-hypochlorite reaction shows that $\mathrm{OCl^-}$ reacts over 300 times faster with $\mathrm{ArSO_2^-}$ than does HOCl. The variation of the rate of the $\mathrm{ArSO_2^-}$-$\mathrm{OCl^-}$ reaction with Ar and the reaction stoichiometry suggest a mechanism where there is nucleophilic attack of $\mathrm{OCl^-}$ on the sulfur of $\mathrm{ArSO_2^-}$ to give a sulfurane-like intermediate, **5**, which then decomposes rapidly to $\mathrm{ArSO_3^-}$ and chloride ion. Similarly, the fact that a small but significant amount of phenyl α-disulfone is isolated when $\mathrm{PhS(O)SO_2Ph}$ is treated with just 1 mol of hypochlorite suggests that nucleophilic attack of $\mathrm{OCl^-}$ on the sulfinyl sulfone leads to a sulfurane-like intermediate, **6**, which breaks up either by loss of chloride ion to yield the α-disulfone, or by cleavage of the S-S bond to give sulfinate and $\mathrm{ArS(O)OCl}$, and subsequently $\mathrm{ArSO_3^-}$. After earlier inconclusive attempts to demonstrate the existence of intermediates on the reaction coordinate in simple substitutions of sulfinyl compounds, the apparent presence of **5** and **6** on the reaction coordinates of these two hypochlorite reactions is seen as providing significant support for the possible presence of sulfurane-like intermediates in many substitutions at sulfinyl sulfur, even though such intermediates may often break down so rapidly by expulsion of a leaving group as to make their detection extremely difficult.

One of the much-discussed questions regarding nucleophilic substitutions at sulfinyl (>S=O) sulfur has been whether or not bond making normally precedes bond breaking. Is an intermediate with the general structure 1 on the reaction coordinate (eq 1)? The alternative, of course, is synchronous bond making and bond breaking (eq 2), as in $\mathrm{S_N2}$ substitutions at sp^3 carbon. The successful preparation by Martin and coworkers,[1] and by others,[2] of various stable sulfuranes and related compounds clearly suggests that intermediates of the type represented by 1 are reasonable and energetically feasible. However, attempts to demonstrate their presence in a number of simple substitutions at sulfinyl sulfur using a variety of mechanistic probes have been inconclusive.[3-5]



$$\mathrm{Nu^-} + -\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\ddot{\mathrm{S}}}-\mathrm{L} \rightleftharpoons \mathrm{Nu}-\overset{\overset{\displaystyle \mathrm{O^-}}{|}}{\underset{/}{\mathrm{S}}}-\mathrm{L} \longrightarrow \mathrm{Nu}-\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\ddot{\mathrm{S}}}- + \mathrm{L^-} \qquad (1)$$

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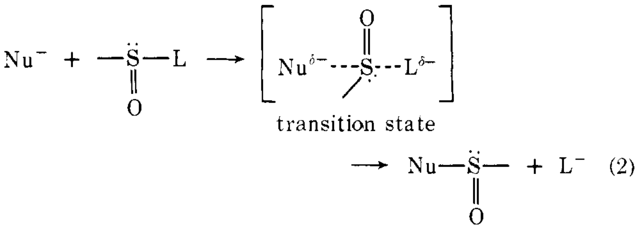


$$\mathrm{Nu^-} + -\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\ddot{\mathrm{S}}}-\mathrm{L} \longrightarrow \underset{\text{transition state}}{\left[\mathrm{Nu}^{\delta-}\cdots\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\underset{/}{\mathrm{S}}}\cdots\mathrm{L}^{\delta-}\right]} \longrightarrow \mathrm{Nu}-\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\ddot{\mathrm{S}}}- + \mathrm{L^-} \qquad (2)$$

We have been interested[6] in the reactivity of so-called[7] α-effect nucleophiles in substitutions at different oxidation states of sulfur. To better understand α effects in such systems we initiated a study of the reaction of hypochlorite with various oxidized derivatives of disulfides and with arenesulfinates.

As it turns out, certain aspects of the reaction of hypochlorite with both arenesulfinates, $\mathrm{ArSO_2^-}$, and aryl sulfinyl sulfones, $\mathrm{ArS(O)SO_2Ar}$, indicate the apparent presence of sulfurane-like intermediates on the reaction coordinate in these reactions. This will be the principal focus of attention in this paper.

Results

The Arenesulfinate-Hypochlorite Reaction. Arenesulfinates react readily with solutions containing hypochlorite in a reaction having the overall stoichiometry shown in

$$\mathrm{ArSO_2^- + OCl^- \rightarrow ArSO_3^- + Cl^-} \qquad (3)$$

The reaction has been used as an analytical method for the determination of sulfinic acids.[8,9] We have verified the stoichiometry in eq 3 and have also shown that when the sodium salt of a sulfinic acid is treated with exactly 1 mol of sodium hypochlorite the only organic product detectable is the sodium salt of the corresponding sulfonic acid.

We investigated the kinetics of the arenesulfinate-hypochlorite reaction in aqueous phosphate buffers over the pH range 5.2-9.0 at 25 °C with hypochlorite present in considerable stoichiometric excess over the sulfinate. The disappearance of the arenesulfinate followed good first-order kinetics. The reactions were generally very rapid and had to be followed by stopped-flow spectrophotometry. The kinetic results are summarized in Table I.

Runs at a fixed pH at varying stoichiometric hypochlorite concentration (first two lines of Table I) show that the experimental first-order rate constant (k_1) responds linearly to the change in hypochlorite concentration, thereby indicating that the reaction is, as expected, also first order in total hypochlorite concentration, C_{NaOCl}.

The data for the reaction of $\mathrm{PhSO_2^-}$ shown in Table I reveal that k_1/C_{NaOCl} varies markedly with pH. If hypochlorite ion, $\mathrm{OCl^-}$, and hypochlorous acid, HOCl, both react with $\mathrm{PhSO_2^-}$ but differ significantly in their reactivity, one would expect k_1 to be given by

$$k_1 = k_{\mathrm{OCl}}[\mathrm{OCl^-}] + k_{\mathrm{HOCl}}[\mathrm{HOCl}] = \left(\frac{k_{\mathrm{OCl}}K_{\mathrm{a}} + k_{\mathrm{HOCl}}a_{\mathrm{H^+}}}{K_{\mathrm{a}} + a_{\mathrm{H^+}}}\right)C_{\mathrm{NaOCl}} \qquad (4a)$$

$$k_1/C_{\mathrm{NaOCl}} = \frac{k_{\mathrm{OCl}}K_{\mathrm{a}} + k_{\mathrm{HOCl}}a_{\mathrm{H^+}}}{K_{\mathrm{a}} + a_{\mathrm{H^+}}} \qquad (4b)$$

where C_{NaOCl} is the total concentration of hypochlorite, K_{a} is the ionization constant of HOCl, and k_{OCl} and k_{HOCl} are the rate constants for reaction of $\mathrm{PhSO_2^-}$ with $\mathrm{OCl^-}$ and HOCl, respectively.

Figure 1 shows a plot of log k_1/C_{NaOCl} vs. pH. The calculated curve is for eq 4b using the known K_{a} for HOCl,[10] and assuming values for k_{OCl} and k_{HOCl} of 1.05×10^3 and $3.0\ \mathrm{M^{-1}}$

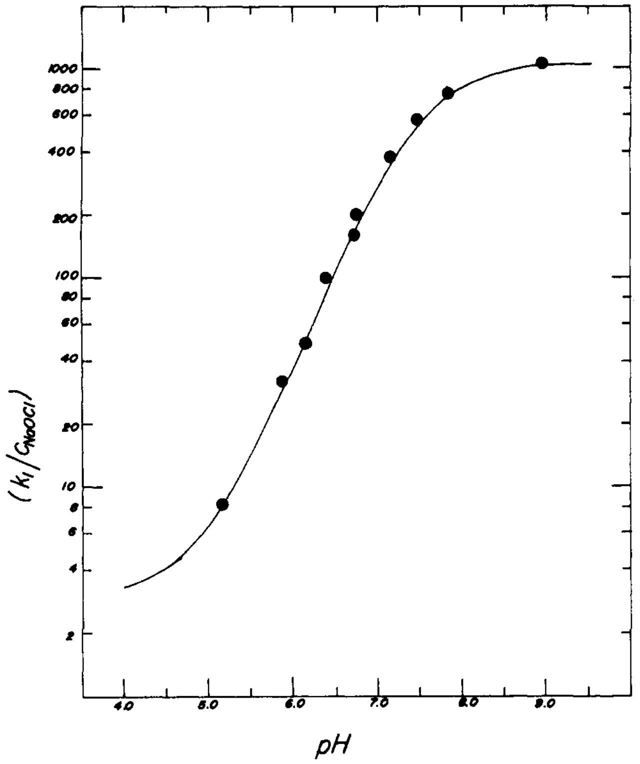


Figure 1. pH-rate profile for the reaction of sodium benzenesulfinate with hypochlorite in aqueous solution at 25 °C. Solid circles represent actual experimental data (Table I). The line drawn is the curve calculated from eq 4b using $k_{OCl} = 1.05 \times 10^3$ M^{-1} s^{-1}, $k_{HOCl} = 3$ M^{-1} s^{-1}, and K_a (for HOCl) = 3.5×10^{-8}.

s^{-1}, respectively. One can see that these values lead to an excellent fit of all the experimental data. From this we conclude that it is *hypochlorite ion*, rather than hypochlorous acid, which is the reactive species in the reaction with $PhSO_2^-$, OCl^- being over 300 times more reactive toward the sulfinate than is HOCl. This perhaps initially somewhat surprising result is of great mechanistic significance, as we shall see in the Discussion.

Table I also reveals that, at a given pH, $PhSO_2^-$ is about 2.5 times more reactive toward OCl^- than is p-$CH_3OC_6H_4SO_2^-$. These runs were made at a pH (6.7) where over 95% of the observed rate is due to the reaction of OCl^-, rather than HOCl, with the sulfinates.

Kinetics of the Reaction of Hypochlorite with Oxidized Derivatives of Aryl Disulfides. The reactions of hypochlorite with (a) phenyl α-disulfone (**2**), $PhSO_2SO_2Ph$, (b) phenyl benzenethiolsulfonate (**3**), $PhSSO_2Ph$, and (c) p-anisyl p-methoxybenzenesulfinyl sulfone (**4a**), $AnS(O)SO_2An$ (An = p-$CH_3OC_6H_4$), were examined. Because of very low solubility of the organic substrates the reactions cannot be studied in aqueous solution. In order to permit direct comparison with extensive data on the reactivity of other nucleophiles toward these three substrates already available,[6] 60% dioxane (v/v) was the solvent selected. While solutions of hypochlorite in this solvent in which all the hypochlorite is present as OCl^- show no decrease in hypochlorite titer over the period of time needed to prepare the solution and use it in a kinetic run (~30 min), the same was not true of 60% dioxane solutions of hypochlorite where a significant fraction of the hypochlorite was present as HOCl. In these during this time period there was a significant decrease in hypochlorite titer, whose magnitude depended on the length of time the solution had stood around. Presumably this is due to some reaction of hypochlorous acid with the dioxane in the solvent. Because of this problem all the kinetic runs were carried out by mixing solutions containing NaOCl *only* with solutions of the organic substrates in a stopped-flow spectrophotometer at 25 °C. The hypochlorite was always present in large stoichiometric excess over the organic substrate. Under these conditions the disappearance of **2**, **3**, or **4a** followed good first-order kinetics and runs carried out with a given hypochlorite solution at varying times after initial preparation of the solution showed no change in experimental first-order rate constant.

Table I. Kinetics of the Reaction of Arenesulfinates with Hypochlorite in Phosphate Buffers in Water at 25 °C

Ar in $ArSO_2^-$	$[ArSO_2^-]_0 \times 10^3$, M	$C_{NaOCl} \times 10^3$, M	pH of buffer[a]	k_1, s^{-1}	(k_1/C^{av}_{NaOCl})[b]
p-CH_3-OC_6H_4	0.50	5.33	6.68	0.344	67
	0.23	2.12	6.68	0.130	65
C_6H_5	0.35	2.13	5.18	0.016	8.2
			5.88	0.062	32
	0.32	2.13	6.15	0.095	48
	0.63	5.35	6.39	0.515	1.0×10^2
	0.51	2.13	6.72	0.30	1.6×10^2
		5.35	6.75	1.01	2.0×10^2
	0.32	2.13	7.16	0.74	3.8×10^2
			7.47	1.13	5.7×10^2
	0.35	2.13	7.83	1.47	7.5×10^2
			8.97	2.02	10.4×10^2

[a] Buffers prepared by mixing appropriate amounts of solutions of K_2HPO_4 and KH_2PO_4. Concentration of the major component of the buffer equal 0.08 M in all cases. [b] $C^{av}_{NaOCl} = C_{NaOCl} - \frac{1}{2}[ArSO_2^-]_0$.

Table II. Kinetics of the Reaction of Hypochlorite with Oxidized Disulfide Derivatives in 60% Dioxane at 25 °C

Substrate, concn	$C_{NaOCl} \times 10^3$, M	k_1, s^{-1} [a]	$k_{OCl} = (k_1/[OCl])$, M^{-1} s^{-1}
$PhSO_2SO_2Ph$,	4.44	3.5	8.0×10^2
3.1×10^{-5} M	8.88	6.8	7.7×10^2
$AnS(O)SO_2An$,	0.355	1.6×10^3	4.4×10^6
4.6×10^{-5} M	0.178	9.0×10^2	5.0×10^6
2.5×10^{-5} M			
$PhSSO_2Ph$,	8.88	0.107	12
3.4×10^{-5} M	17.8	0.196	11

[a] Values of k_1 listed are average of two or more runs. Rate constants were reproducible to ±5% or better.

The kinetic results for the various runs are given in Table II. The rates with sulfinyl sulfone **4a** were *extremely* fast, and the problem about the instability of solutions of HOCl in 60% dioxane prevented us from slowing the rates down by going to buffers where most of the hypochlorite would be present as HOCl rather than OCl^-. However, despite the very fast rates, the rate constants were quite reproducible, including runs made with fresh solutions on subsequent days. We therefore believe that the rate constants shown for reaction of **4a** with OCl^- are a reasonably accurate measure of the true reactivity of hypochlorite ion toward this substrate, although we recognize that they might be somewhat lower than the true value because the rates being measured are somewhat faster than those normally considered to be the upper limit for a standard stopped-flow spectrophotometer.

The variation of k_1 with $[OCl^-]$ shows that all of the reactions in Table II are, as might be expected, first order in hypochlorite. Second-order rate constants, $k_{OCl} = k_1/[OCl^-]$, for the reactivity of hypochlorite toward each of the three substrates are shown in the last column of the table.

Stoichiometry and Products of the Reaction of Oxidized

Disulfide Derivatives with Hypochlorite. In the presence of excess hypochlorite phenyl α-disulfone (**2**) was found to react rapidly with 1 mol of hypochlorite per mol of α-disulfone, while phenyl benzenethiolsulfonate (**3**) consumed 3 mol of hypochlorite per mol of **3.** The products of these two reactions were then investigated in separate experiments in which stoichiometric amounts of the substrate and hypochlorite were allowed to react. Sufficient dilute sodium hydroxide to keep the reaction solution *weakly* alkaline was added together with the hypochlorite. The only organic product produced in detectable amounts from the reaction of either **2** or **3** with a stoichiometric amount of sodium hypochlorite was sodium benzenesulfonate, $PhSO_3Na$. In both cases this was obtained in yields approaching 90% of those expected from the reaction stoichiometries shown below:

$$\underset{\mathbf{2}}{PhSO_2SO_2Ph} + NaOCl + 2NaOH \rightarrow 2PhSO_3Na + NaCl + H_2O \quad (5)$$

$$\underset{\mathbf{3}}{PhSSO_2Ph} + 3NaOCl + 2NaOH \rightarrow 2PhSO_3Na + 3NaCl + H_2O \quad (6)$$

The sulfinyl sulfone **4a** consumed 2 mol of hypochlorite per mol of **4a.** In this case the products of the reaction of 2 mol of hypochlorite with 1 mol of **4a** were not determined. Instead experiments where phenyl benzenesulfinyl sulfone (**4b**), $PhS(O)SO_2Ph$, was reacted with exactly 1 mol of hyochlorite were carried out. These are described in the next section.

Products of the Reaction of Phenyl Benzenesulfinyl Sulfone with an Equimolar Amount of Sodium Hypochlorite. Phenyl benzenesulfinyl sulfone (**4b**) was allowed to react with an exactly equimolar amount of sodium hypochlorite in 60% dioxane, and the products separated into water-soluble and water-insoluble fractions. Infrared examination showed that the only organic compounds present in the water-soluble fraction were $PhSO_3Na$ and $PhSO_2Na$, and the percentage of benzenesulfinate in the fraction was then estimated accurately by titration of a portion of the mixture with additional standard hypochlorite. The amounts of $PhSO_2Na$ and $PhSO_3Na$ found were respectively 0.54 and 0.70 mol per mol of sulfinyl sulfone **4b** reacted.

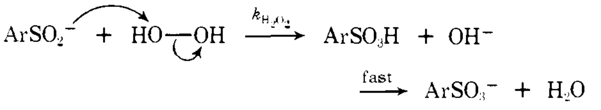
The infrared spectrum of the water-insoluble fraction showed that it contained a large amount of phenyl α-disulfone (**2**), and pure α-disulfone was isolated by crystallization of the fraction from benzene. Based on the total weight of the water-insoluble fraction of the product and the intensity of the 1355-cm^{-1} absorption band in its infrared spectrum (SO_2 group of **2**) the yield of α-disulfone **2** was estimated to be 0.10 mol/mol of **4b** reacted. The actual amount of pure crystalline **2** obtained upon crystallization of the fraction from benzene was 0.04 mol/mol of **4b.**

Discussion

The Arenesulfinate–Hypochlorite Reaction. Like hypochlorite, hydrogen peroxide also oxidizes arenesulfinates to arenesulfonates.

$$ArSO_2^- + H_2O_2 \rightarrow ArSO_3^- + H_2O \quad (7)$$

Study of this reaction[11,12] has shown that in the pH 2-9 region the reactive oxidizing agent is H_2O_2, rather than HO_2^-, and that for variations in Ar the reaction exhibits a modest negative ρ (−0.5) consistent with a mechanism in which the rate-determining step is nucleophilic attack of the arenesulfinate on H_2O_2:

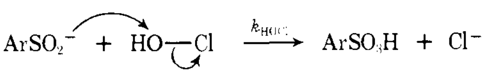


$$ArSO_2^- + HO{-}OH \xrightarrow{k_{H_2O_2}} ArSO_3H + OH^- \xrightarrow{\text{fast}} ArSO_3^- + H_2O \quad (8)$$

This oxidation of arenesulfinates by hydrogen peroxide is relatively slow, $k_{H_2O_2}$ for the reaction of $PhSO_2^-$ with H_2O_2 being only 0.02 $M^{-1}\,s^{-1}$ at 40 °C.

The pH-rate profile in Figure 1 reveals that the oxidation of arenesulfinates by hypochlorite can occur by reaction of $ArSO_2^-$ with either hypochlorite ion or hypochlorous acid, but that the rate constant for the reaction involving OCl^- anion (k_{OCl}) is over 300 times faster than the rate constant for the reaction involving HOCl (k_{HOCl}).

For $PhSO_2^-$ the rate constant for the slower reaction with hypochlorous acid (k_{HOCl} = 3 $M^{-1}\,s^{-1}$ at 25 °C) is about 100 times faster than the rate for eq 8 at 40 °C. This is not surprising if the reaction between HOCl and $PhSO_2^-$ involves a nucleophilic displacement by $PhSO_2^-$ analogous to that in eq 8, because Cl^- should be a much better leaving group, and therefore more easily displaced, than OH^-.



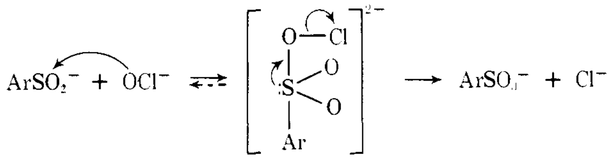
$$ArSO_2^- + HO{-}Cl \xrightarrow{k_{HOCl}} ArSO_3H + Cl^- \longrightarrow ArSO_3^- + H^+ + Cl^- \quad (9)$$

However, the really striking and noteworthy aspect of the hypochlorite–arenesulfinate oxidation is that the reaction between $ArSO_2^-$ and OCl^- (eq 10a) occurs so much more rapidly than the reaction of $ArSO_2^-$ with HOCl.

$$ArSO_2^- + OCl^- \xrightarrow{k_{OCl}} ArSO_3^- + Cl^- \quad (10a)$$

In this rapid reaction with OCl^- $PhSO_2^-$ reacts 2.5 times faster than $p\text{-}CH_3OC_6H_4SO_2^-$, a dependence of rate on aryl group structure quite opposite to that observed in eq 8, and *contrary* to what would be expected if the mechanism of eq 10a involved nucleophilic attack of $ArSO_2^-$ on the oxygen of OCl^-.[13] The greater reactivity of $PhSO_2^-$ as compared to $p\text{-}CH_3OC_6H_4SO_2^-$ in eq 10a would, however, be consistent with a mechanism in which one had nucleophilic attack by OCl^- on $ArSO_2^-$, and where the electron density on sulfur *increased* in going from reactants to transition state.

Given these observations, and the stoichiometry of the reaction, the most plausible mechanism for eq 10a would seem to be the one shown in eq 10b. This involves initial nucleophilic attack of OCl^- (known to be an excellent nucleophile) on the sulfur of the arenesulfinate to give a sulfurane-like intermediate (**5**), which then decomposes rapidly to $ArSO_3^-$ and Cl^- in the manner indicated.



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(10b)

As will be seen shortly, the reaction of hypochlorite with a sulfinyl sulfone also seems to involve a sulfurane-like intermediate on the reaction coordinate.

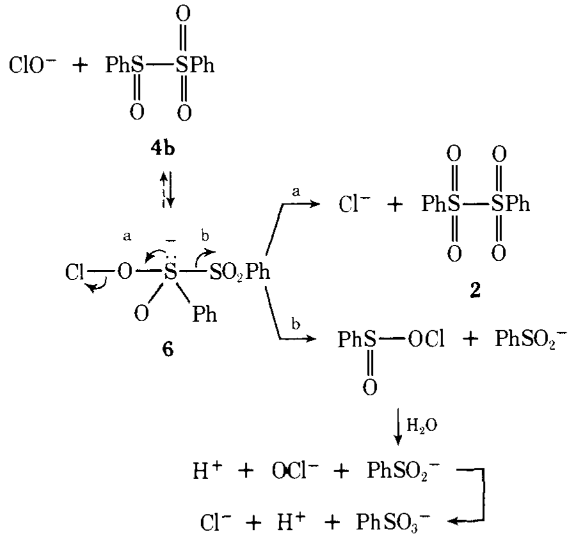
Reaction of Hypochlorite with Oxidized Derivatives of Disulfides. In the presence of sufficient hypochlorite the end products of the reaction of 1 mol of either an aryl α-disulfone (**2**), an aryl thiolsulfonate (**3**), or an aryl sulfinyl sulfone (**4**) with OCl^- are two molecules of the arenesulfonate, $ArSO_3^-$ (see eq 5 and 6, for example, for the stoichiometry of the reactions with **2** and **3**). In considering this stoichiometry one must keep in mind, of course, that any arenesulfinate, $ArSO_2^-$, formed as an intermediate at any stage during the reaction will be oxidized readily by OCl^- to the arenesulfonate (eq 3).

The kinetic data in Table II, and the kinetic data on the $ArSO_2^-$–OCl^- reaction, show that the relative order of reactivity of the different sulfur compounds toward OCl^- is sulfinyl sulfone ≫ sulfinate ion > α-disulfone ≫ thiolsulfonate.

The much greater reactivity toward OCl^- of the sulfinyl sulfone as compared to the α-disulfone allows one to determine by a suitable experiment whether any α-disulfone is formed by initial reaction of hypochlorite with the sulfinyl sulfone, or whether, alternatively, this reaction leads exclusively to cleavage of the S-S bond in the sulfinyl sulfone. The experiment involves treating the sulfinyl sulfone (**4b**) with only 1 mol of OCl^- per mol of **4b,** rather than the 2 mol of OCl^- required to oxidize the sulfinyl sulfone completely to 2 mol of $PhSO_3^-$. Since $PHS(O)SO_2Ph$ will react *much* more rapidly than $PhSO_2SO_2Ph$ with any hypochlorite remaining, any phenyl α-disulfone formed under these conditions by reaction of OCl^- with **4b** will not undergo any significant further reaction under the conditions of this experiment. We found that after treatment of 1 mol of **4b** with 1 mol of hypochlorite that $PhSO_2SO_2Ph$ had been formed in a yield of about 0.10 mol/mol of sulfinyl sulfone reacted. The remaining products, $PhSO_2Na$ and $PhSO_3Na$, were those expected from cleavage of the S-S bond of the sulfinyl sulfone by OCl^- and partial oxidation of $PhSO_2^-$ to $PhSO_3^-$.

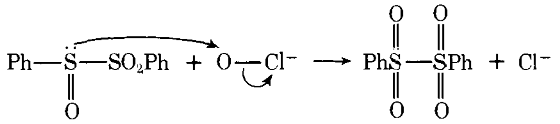
The most straightforward mechanistic explanation for this result is to assume that the reaction of hypochlorite with the sulfinyl sulfone involves initial nucleophilic attack of OCl^- on the sulfinyl group to give a sulfurane-like intermediate **6.** This intermediate can then either break up by expulsion of a chloride ion as in path a to give the α-disulfone, or by cleavage of the S-S bond to give $PhSO_2^-$ and the sulfinyl hypochlorite $PhS(O)OCl$. Hydrolysis of the latter would regenerate hypochlorite ion which could then oxidize a portion of the $PhSO_2^-$ to $PhSO_3^-$.[14]

The only alternative to eq 11, path a, for the formation of



(11)

some **2** during the reaction of **4b** with hypochlorite would be a nucleophilic attack by the unshared pair on the sulfinyl sulfur of **4b** on the oxygen of OCl^-, i.e.,



$$\mathrm{Ph{-}S(O){-}SO_2Ph + O{-}Cl^- \longrightarrow PhSO_2{-}SO_2Ph + Cl^-} \tag{12}$$

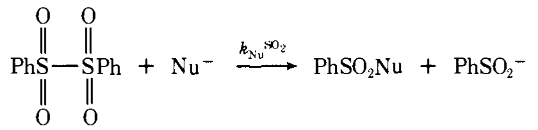
However, since we have seen in the reaction of $PhSO_2^-$ with OCl^- that a route of this type is at least 350 times slower than the path (eq 10b) involving nucleophilic attack by OCl^- on sulfur to give **5,** followed by expulsion of chloride ion, eq 12 seems a much less plausible explanation for the formation of **2** than eq 11, path a,

We therefore believe that the formation in the reaction of **4b** with hypochlorite of a small but significant amount of **2,** together with larger amounts of products resulting from the OCl^--induced cleavage of the S-S bond in **4b,** strongly suggest the presence of sulfurane-like intermediate **6** on the reaction coordinate. Furthermore, since that part of the reaction that proceeds by path b is a simple nucleophilic substitution at a sulfinyl sulfur, this means that in the hypochlorite-sulfinyl sulfone reaction we have this substitution proceeding via the general mechanistic pathway involving an intermediate on the reaction coordinate represented by eq 1. That this substitution takes place via this mechanism rather than by the synchronous bond-making and bond-breaking mechanism in eq 2, even though **4b** has an excellent leaving group ($ArSO_2$), seems particularly significant.

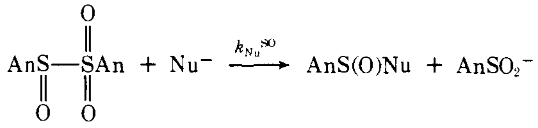
One may not, of course, extrapolate the present results to the conclusion that all nucleophilic substitutions of sulfinyl compounds proceed by the type of mechanism shown in eq 1, rather than the one shown in eq 2. Nonetheless, after the inconclusive results of earlier attempts[3-5] to demonstrate the existence of an intermediate on the reaction coordinate in simple substitutions at sulfinyl sulfur, the apparent presence of **5** and **6** on the reaction coordinate in the hypochlorite ion reactions raises a strong presumption that intermediates with structure **1** may be formed (eq 1) in many nucleophilic substitutions involving sulfinyl compounds, even though in many cases they break down so readily by expulsion of leaving group L as to make their experimental detection extremely difficult.

Reactivity of Hypochlorite toward Different Oxidation States of Sulfur as Compared with Other α-Effect Nucleophiles. Nucleophiles that exhibit greatly enhanced reactivity in a substitution compared to that exhibited by structurally closely related nucleophiles of similar proton basicity have been termed "α-effect"[7] nucleophiles because most possess an unshared pair of electrons on an atom α to the atom that actually attacks the electrophilic center of the substrate. Several classes of α-effect nucleophiles have been recognized.[15,16]

In previous work[6,17] we have examined the magnitude of the α effect for different representative α-effect nucleophiles by comparing their reactivity with that of ordinary nucleophiles in a series of substitutions involving oxidized disulfide derivatives (eq 13-15) which differed only in the oxidation state of

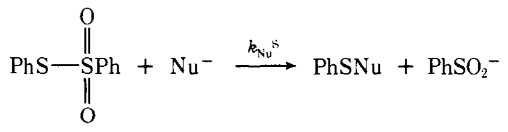


$$\mathrm{PhSO_2{-}SO_2Ph + Nu^- \xrightarrow{k_{Nu}^{SO_2}} PhSO_2Nu + PhSO_2^-} \tag{13}$$



$$\mathrm{AnS(O){-}SO_2An + Nu^- \xrightarrow{k_{Nu}^{SO}} AnS(O)Nu + AnSO_2^-} \tag{14}$$

($An = p\text{-}CH_3OC_6H_4$)



$$\mathrm{PhS{-}SO_2Ph + Nu^- \xrightarrow{k_{Nu}^{S}} PhSNu + PhSO_2^-} \tag{15}$$

sulfur at which the substitution took place. We were particularly interested in the extent to which the magnitude of the α effect might vary with the nature of the oxidation state of sulfur at which the substitution was taking place.

Hydrogen peroxide anion, HO_2^-, is considered a representative example of one class of α-effect nucleophile. In our earlier work[6,17] we found a variation in the α effect for this nucleophile with a change in the oxidation state of sulfur where substitution occurs which seemed inconsistent with expectations based on a theory regarding the origin of α effects for nucleophiles like HO_2^- recently proposed by Liebmann and Pollack.[18] Specifically this theory would have predicted that

$k_{HO_2^-}/k_{OH^-}$ would have about the same value for the substitutions at >SO_2 and >S=O, and a much smaller value for the substitution at >S. As the last column of Table III shows, $k_{HO_2^-}/k_{OH^-}$ actually is considerably smaller for the substitution at >S=O than for the one at the sulfonyl group, and the value of $k_{HO_2^-}/k_{OH^-}$ is about the same for the substitution at >S as at >S=O. While not in accord with expectations based on the Liebmann and Pollack theory, the variation of $k_{HO_2^-}/k_{OH^-}$ with oxidation state of sulfur did appear to be consistent with an alternative explanation for the origin of the α effect for HO_2^- which we had tentatively advanced.[17a]

Hypochlorite ion is supposed to be an α-effect nucleophile of the same class as HO_2^-. It would therefore have been expected that k_{OCl^-}/k_{OH^-} would show the same sort of variation with sulfur center as $k_{HO_2^-}/k_{OH^-}$. That this is emphatically not the case is evident from inspection of Table III. One sees that (k_{OCl^-}/k_{OH^-}) has about the same value for the substitutions at both >SO_2 and >S=O, and *much* smaller value for the substitution at >S. This sort of variation of α effect with variation in sulfur center is consistent with expectations based on the Liebmann and Pollack[18] proposal, and is, of course, entirely different from what we found with HO_2^-.

The dissimilarity between the reactivity pattern found with the three sulfur substrates for OCl^- vs. HO_2^-, despite the fact they are supposed to be α-effect nucleophiles of the same class, shows there is much about α effects that is not well understood. Attempts to develop a theory to explain the origin of α effects for nucleophiles of the OCl^- and HO_2^- class must wait until there are data on the reactivity of additional members of this class with a variety of different electrophilic centers.

Experimental Section

Preparation and Purification of Materials. Phenyl benzenethiolsulfonate[19] (**3**) and phenyl α-disulfone[20] (**2**) were prepared and purified using previously described procedures. *p*-Anisyl *p*-methoxybenzenesulfinyl sulfone (**4a**) was also prepared by a previously described procedure,[6] and phenyl benzenesulfinyl sulfone[21] (**4b**) was prepared from benzenesulfinic acid using the same general procedure, condensation of 2 mol of the sulfinic acid in the presence of 1 mol of dicyclohexylcarbodiimide,[22] employed to synthesize **4a**. Upon crystallization from methylene chloride-hexane it melted at 76–78 °C. Reagent grade 5% sodium hypochlorite solution (Baker) was standardized iodimetrically using the procedure described by Kolthoff and Sandell.[23] The standardized solution was stored in the refrigerator and its titer checked periodically to ensure that it remained unchanged. Dioxane was purified by the procedure described by Wiberg,[24] and after final fractional distillation was stored frozen in the freezer until used. Monobasic (KH_2PO_4) and dibasic (K_2HPO_4) potassium phosphate were analytical reagent grade and were used without further purification. *p*-Methoxybenzenesulfinic acid was prepared as described in an earlier paper.[6] Benzenesulfinic acid was obtained by acidification of commercial sodium benzenesulfinate (Aldrich Chemical) and purified by being recrystallized several times from water, mp 83–85 °C.

The Arenesulfinate–Hypochlorite Reaction. Products and Stoichiometry. A weighed sample of benzenesulfinic acid was carefully neutralized to sodium benzenesulfinate using dilute sodium hydroxide and a pH meter, and the resulting solution was treated with a measured amount of excess standard 5% sodium hypochlorite solution. The solution was allowed to stand for 1–2 min, and the amount of excess hypochlorite was then determined iodimetrically using the procedure of Kolthoff and Sandell.[23] Duplicate experiments confirmed that 1 mol of hypochlorite was consumed per mol of sulfinate taken.

In a separate experiment a sample of sodium benzenesulfinate in water, prepared as described above, was treated with exactly 1 mol of sodium hypochlorite per mol of sulfinate. After the solution had stood for a few minutes the water was removed under reduced pressure and the residue was dried for several hours under an oil pump vacuum at 50 °C. The infrared spectrum of the residue (KBr pellet) was identical with that of a known sample of sodium benzenesulfonate.

Kinetic Studies. The kinetics of the reaction of the arenesulfinates with hypochlorite ion were followed at 275 nm (sodium benzenesulfinate) or 280 nm (sodium *p*-methoxybenzenesulfinate) using stopped-flow spectrophotometry. The reactions were carried out in water in K_2HPO_4-KH_2PO_4 buffers. A solution of the sulfinate was prepared by dissolving a known amount of the sulfinic acid in the phosphate buffer, and this solution was placed in one of the reservoir syringes of the stopped-flow spectrophotometer. A solution containing a known amount of standard sodium hypochlorite solution dissolved in the same phosphate buffer was placed in the other reservoir syringe, and the decrease in absorbance upon mixing the two solutions was monitored using an oscilloscope in the usual way. The pH of each actual run was measured separately by mixing exactly equal volumes of the two reaction solutions in a small beaker and then determining the pH of the resulting solution using a Radiometer PHM62 pH meter. The solutions always contained initially 0.08 M of the major phosphate buffer component, with the amount of the other phosphate component being varied as required to give a reaction solution of the desired pH.

Table III. Reactivity of the α-Effect Nucleophiles Hypochlorite and Hydrogen Peroxide Anion in Substitutions at Different Sulfur Centers[a]

Substrate and reaction	Electrophilic center	(k_{OCl}/k_{OH})	(k_{HO_2}/k_{OH})
2 (eq 13)	>SO_2	10.4	72
4a (eq 14)	>S=O	4.5	9.8
3 (eq 15)	>S	0.03	4.1

[a] Data for k_{HO_2}/k_{OH} are from ref 6 and 17. Those for k_{OCl}/k_{OH} are from present work.

Reaction of Hypochlorite with Oxidized Derivatives of Aryl Disulfides. Kinetic Studies. In all cases the rates of the reactions were followed by stopped-flow spectrophotometry. For both phenyl benzenethiolsulfonate (**3**) and phenyl α-disulfone (**2**) the general procedure was the same. A solution of the sulfur compound in 60% dioxane (v/v) was placed in one of the reservoir syringes of the stopped-flow spectrophotometer and a solution of standard sodium hypochlorite in 60% dioxane was placed in the other syringe. The decrease in the absorbance upon mixing the two solutions was then monitored on the oscilloscope. A wavelength of 235 nm was used for following the reaction involving OCl^- and **3** and one of 245 nm for the runs with the α-disulfone. In the case of the runs with *p*-anisyl *p*-methoxybenzenesulfinyl sulfone (**4a**), a solution of **4a** in anhydrous dioxane was placed in one syringe and a solution of hypochlorite in 20% dioxane in the other syringe. Upon rapid mixing of equal volumes this gives a 60% dioxane solution of the two reactants, and Kice and Mullan[6] have shown that the kinetics of the reaction of **4a** with nucleophiles can be reliably studied using this procedure. The progress of the reaction was monitored by following the decrease in optical density at 305 nm.

Stoichiometry and Products. Because of the lack of solubility of the sulfur substrates in water the stoichiometry and products of their reactions with hypochlorite had to be investigated in aqueous dioxane.

The stoichiometry of the reactions was studied by rapidly mixing a solution containing a weighed amount of the sulfur compound in anhydrous dioxane with an aqueous solution containing excess standard sodium hypochlorite. After 3 min an aliquot of the final solution was removed and analyzed iodometrically[23] for residual hypochlorite content. Removal of additional aliquots at time intervals from 6 to 60 min after mixing showed that the very rapid consumption of hypochlorite by reaction with the sulfur compound was followed by a much slower decrease in hypochlorite titer, which was unrelated to the sulfur compound–hypochlorite reaction, and which apparently resulted from the fact that during the initial reaction of hypochlorite with the sulfur substrate under these particular reaction conditions (no added base) sufficient acidity develops (see eq 5 and 6) for there to be a significant amount of HOCl present at the end of the sulfur compound–hypochlorite reaction. Solutions containing hypochlorous acid in aqueous dioxane are not stable, although those containing only hypochlorite are. As a result the final solutions slowly lose hypochlorite titer on standing. However, this process is enough slower than the very rapid initial consumption of hypochlorite through reaction with the sulfur compound so that there was no difficulty in determining just how much hypochlorite was consumed in actual reaction with each sulfur compound. A series of experiments indicated this to be 3.2 ± 0.1 mol of OCl^- per mol of **3** in the reaction with the thiolsulfonate, 1.1 ± 0.1 mol of OCl^- per mol of **2** in the reaction with the α-disulfone, and 2.1 ± 0.2 mol of OCl^- per mol of **4a** in the reaction with the sulfinyl sulfone.

The products of the reaction of thiolsulfonate **3** with hypochlorite were explored in the following experiment. A solution containing 1.8 mmol of sodium hypochlorite in 6 mL of water was rapidly added to a solution of 0.60 mmol of **3** in 10 mL of dioxane. As soon as the addition was complete dilute sodium hydroxide was added by micropipet with good stirring until the solution stayed weakly alkaline. The solution was then allowed to stand for 5 min before being poured into 100 mL of water. The aqueous solution was then extracted with chloroform. Workup of the chloroform extracts yielded no products. The aqueous layer after the chloroform extraction was then evaporated to dryness under reduced pressure and dried for several hours under high vacuum at 50 °C. An infrared spectrum of the residue (KBr pellet) was identical with that of a known sample of sodium benzenesulfonate, showing that $PhSO_3Na$ was the only water-soluble organic material formed. The weight of the residue was 0.330 g. Assuming the stoichiometry shown in eq 6 one would predict that reaction of 0.60 mmol of **3** with hypochlorite would result in the formation of 0.216 g of $PhSO_3Na$ and 0.176 g of NaCl. The weight of the residue is therefore 85% of that predicted assuming no losses during workup, and, given that and the clean infrared spectrum, we conclude that the yield of $PhSO_3Na$ is at least 85% of the theoretical for eq 6.

The products of the reaction of α-disulfone **2** with hypochlorite were examined via a generally analogous experiment. A solution containing 0.37 mmol of sodium hypochlorite and 0.40 mmol of sodium hydroxide in 4 mL of water was added rapidly with good stirring to 30 mL of dioxane containing 0.37 mmol of **2.** As soon as the addition was complete additional dilute sodium hydroxide was added until the solution stayed weakly alkaline. The final solution was then poured into a large volume of water and the aqueous solution extracted with chloroform. Workup of the chloroform extracts and the aqueous layer proceeded as in the experiment with **3.** No organic products were found upon removal of the chloroform. The residue from the evaporation of the aqueous layer was shown by infrared examination (KBr pellet) to contain sodium benzenesulfonate as the only organic product. From the weight of the residue we estimated that it contained 0.61 mmol of $PhSO_3Na$, after allowance for the fact that from the stoichiometry of eq 5 there should be half that number of moles of NaCl also present. This corresponds to 82% of the theoretical yield of $PhSO_3Na$ expected from the stoichiometry of eq 5.

The reaction of phenyl benzenesulfinyl sulfone (**4b**) with less than the stoichiometric amount of hypochlorite required for complete conversion of **4b** to 2 mol of $PhSO_3Na$ was carried out as follows. A solution containing 1.78 mmol of sodium hypochlorite in 10 mL of water was added rapidly with good stirring to a solution of 0.470 g (1.77 mmol) of **4b** dissolved in 20 mL of anhydrous dioxane. As soon as the addition was complete the mixture was poured into 100 mL of water and the cloudy aqueous mixture was extracted twice with two 25-mL portions of chloroform. The chloroform extracts were washed with water and then dried over sodium sulfate. Removal of the chloroform at room temperature under reduced pressure left a residue which was kept under high vacuum at room temperature for several hours to remove residual dioxane. The infrared spectrum of the residue showed that it contained a large amount of phenyl α-disulfone. The amount of α-disulfone in the residue was estimated from the intensity of the characteristic strong SO_2 group absorption in the infrared at 1355 cm^{-1} to be 0.05 g (0.18 mmol). Recrystallization of the residue from a small amount of benzene allowed the isolation of 0.02 g (0.074 mmol) of pure α-disulfone, identical in all respects with a known sample.

The aqueous layer remaining after the chloroform extraction was evaporated to dryness under reduced pressure and the residue (0.480 g) was examined by infrared (KBr pellet). The infrared spectrum was consistent with the organic components of the residue being a mixture of sodium benzenesulfonate, $PhSO_3Na$, and benzenesulfinate, $PhSO_2Na$. The amount of sulfinate in the residue was determined by treating a weighed portion of the residue with excess sodium hypochlorite and determining the amount of hypochlorite consumed as described in an earlier section. This titration showed that the total residue contained 0.953 mmol of $PhSO_2Na$. To further demonstrate that $PhSO_2Na$ and $PhSO_3Na$ were the only organic components in the residue from the aqueous layer another portion of the residue was treated in aqueous solution with an amount of hypochlorite just sufficient to oxidize all the $PhSO_2Na$ present to $PhSO_3Na$. Evaporation of the solution from this reaction to dryness gave a residue with an infrared spectrum (KBr pellet) identical with that of a known sample of $PhSO_3Na$.

To estimate the amount of $PhSO_3Na$ present in the residue we assumed that besides the amount of $PhSO_2Na$ already determined there would be present the amount of sodium chloride (1.77 mmol) expected from the reaction of an equivalent amount of hypochlorite, and that the remainder of the residue was then $PhSO_3Na$. On this basis we estimated the residue to contain 0.22 g (1.22 mmol) of sodium benzenesulfonate.

Acknowledgment. This research was supported in its initial stages by National Science Foundation Grant MPS 75-19408, and during its later stages by the Robert A. Welch Foundation (Grant D-650).

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(13) If the mechanism of eq 10a were to involve nucleophilic attack of $ArSO_2^-$ on the oxygen of OCl^- it would also be very hard to understand why this process should have a rate constant 350 times greater than that for eq 9, since one would think that nucleophilic attack by the $ArSO_2^-$ anion on OCl^- anion would be more difficult for purely electrostatic reasons than attack on the oxygen in the uncharged HOCl molecule.

(14) One referee has suggested that our results do not require that **5** (eq 10b) and **6** (eq 11) be intermediates, for they could also be transition states (energy maxima). To explain the formation of both α-disulfone and cleavage products from the reaction of OCl^- with $PhS(O)SO_2Ph$ he suggests that one could have attack of OCl^- on **4b** to give *two* transition states, *both* resembling **6** in structure, but differing from each other in conformation. One of these would lead to cleavage products, the other to α-disulfone. While in principle conceivable, we feel that such an explanation is inherently much less straightforward and realistic than the one in eq 11 where **6** represents an actual intermediate, which can then decompose in either of two ways. Similarly, if one is to consider **5** in eq 10b as a transition state rather than an intermediate, then one must assume that partial cleavage of the O-Cl bond in OCl^- is synchronous with its nucleophilic attack on the sulfur of $ArSO_2^-$. While again in principle possible, such a formulation seems much more contrived and involved than the straightforward picture in eq 10b with **5** as an actual intermediate. Therefore, although we would agree that our results do not *absolutely* conclusively establish the presence of **5** and **6** as intermediates on the reaction coordinates of the respective reactions, we still feel that the mechanistic picture given in eq 10b and 11 where these structures are considered to be intermediates is far and away the simplest and most attractive interpretation of the results.

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