in the two chambers were brought to temperature and then mixed. The final solution was poured into spectrophotometer cell C, and the apparatus was placed in the thermostated cell compartment of a Cary Model 15 spectrophotometer. The decrease in optical density at 296 mμ with time was followed. Plots of log $(A - A_\infty)$ *vs.* time were nicely linear. For the runs with mercaptan the same procedure was used except that a standard solution of the mercaptan was used in place of that of the sulfinic acid.

The Relative Nucleophilicity of Some Common Nucleophiles toward Sulfinyl Sulfur. The Nucleophile-Catalyzed Hydrolysis of Aryl Sulfinyl Sulfones[1]

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Abstract: The relative reactivity of seven common nucleophiles in a displacement reaction at sulfinyl sulfur (eq 8) may be determined from kinetic data on their catalysis of the hydrolysis of an aryl sulfinyl sulfone (IIa) in aqueous dioxane. These data for sulfinyl sulfur (Table IV) are compared with analogous data for substitutions at sulfenyl sulfur (eq 11), peroxide oxygen (eq 9), sp^3 carbon (eq 10), and sulfonyl sulfur (eq 12). This comparison reveals the following interesting points. (1) The substitution at sulfonyl sulfur shows a completely different pattern of reactivity ($F^- > AcO^- \gg Cl^-$) than the one at sulfinyl sulfur ($Cl^- > AcO^- > F^-$). (2) In the substitutions at both sulfenyl sulfur and peroxide oxygen, nucleophiles such as iodide or thiocyanate show a considerably greater reactivity compared to chloride ion than they do in the one at sulfinyl sulfur. (3) The relative reactivities of the various nucleophiles in the substitutions at sulfinyl sulfur and sp^3 carbon are very similar. These facts are discussed with reference to the theory of hard and soft acids and bases (HSAB). The conclusions are (a) that sulfonyl sulfur is a much harder and sulfenyl sulfur a significantly softer electrophilic center than sulfinyl sulfur, and (b) that sulfinyl sulfur is a medium soft electrophilic center analogous to sp^3 carbon.

Equation 1 is a generalized representation of a nucleophilic substitution reaction. In a protic

$$Nu^- + SX \longrightarrow NuS + X^- \qquad (1)$$

solvent the relative reactivity of a series of nucleophiles in such a reaction depends greatly on the nature of the center in the substrate SX which is being attacked by the nucleophile.[2] Nucleophiles which are "hard" bases,[3] *i.e.*, of low polarizability and high proton basicity, show up to particular advantage in substitutions involving attack on such centers as carbonyl carbon[4] or tetracoordinate phosphorus.[5] On the other hand, nucleophiles which are "soft" bases,[3] *i.e.*, of high polarizability and low proton basicity, do particularly well in substitutions involving centers such as divalent oxygen[6] or Pt^{2+}.[7] Edwards and Pearson,[8] in what has become a classic paper, attempted to evaluate and explain the relative importance of basicity, polarizability, and other effects in determining the reactivity of a nucleophile toward these and other centers in protic solvents. Recently, Pearson and Songstad[9] have shown how the various data and conclusions can also be easily understood within the framework of the theory of hard and soft acids and bases (HSAB).

In their paper, Edwards and Pearson[8] made some predictions about the reactivity patterns that might be observed for nucleophiles reacting with different sulfur centers, but they pointed out that unfortunately no quantitative data were yet available for any of these centers. In fact for sulfinyl sulfur, -S(=O)-, there were not even any qualitative data. Since there has been much interest in recent years in reactions involving substitution at the sulfinyl sulfur of sulfoxides, sulfinate esters, and related compounds,[10-16] it would seem that having quantitative data for sulfinyl sulfur would be of considerable value. Furthermore, comparison of this data with suitable data for substitutions at other sulfur

(1) This research supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, Grant AF-AFOSR-106-65. Preliminary communication: J. L. Kice and G. Guaraldi, *Tetrahedron Letters*, 6135 (1966).

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(3) R. G. Pearson, *J. Am. Chem. Soc.*, **85**, 3533 (1963); *Science*, **151**, 172 (1966).

(4) W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 1778 (1960).

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(6) J. O. Edwards, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Division, John Wiley and Sons, Inc., New York, N. Y., 1962, pp 67-106.

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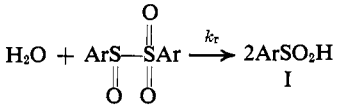
centers would then allow a test of some of the Edwards and Pearson[8] predictions.

In earlier work,[17] we have shown that the hydrolysis of aryl sulfinyl sulfones II (eq 2) in aqueous dioxane



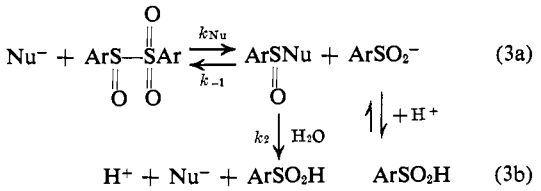
$$H_2O + ArS(O)_2SAr \xrightarrow{k_r} 2ArSO_2H \quad (2)$$

II

IIa, Ar = p-$CH_3OC_6H_4$
b, Ar = p-$CH_3C_6H_4$

can be markedly catalyzed by the addition of small amounts of various nucleophiles. The mechanism of this nucleophile-catalyzed hydrolysis of II is as shown in Chart I. From kinetic measurements of the catalytic

Chart I. Mechanism of Nucleophile-Catalyzed Hydrolysis of Aryl Sulfinyl Sulfones



$$Nu^- + ArS(O)_2SAr \underset{k_{-1}}{\overset{k_{Nu}}{\rightleftharpoons}} ArSNu + ArSO_2^- \quad (3a)$$

$$ArSNu \xrightarrow{k_2, H_2O} H^+ + Nu^- + ArSO_2H \quad (3b)$$

$ArSO_2H + H^+$

effect of a series of nucleophiles under appropriate conditions, one can extract for each nucleophile a value of k_{Nu}, the rate constant for nucleophilic attack of Nu^- on the sulfinyl sulfur of II. These k_{Nu} values provide the type of quantitative data on nucleophilic reactivity in a substitution at sulfinyl sulfur that is desired.

Results

Previous studies[17] using the three halide ions I^-, Br^-, and Cl^- as catalysts for the hydrolysis of IIa and IIb in 60% dioxane containing 0.01–0.80 M $HClO_4$ have shown that under these conditions the kinetics of the nucleophile-catalyzed hydrolysis are such that

$$k_r - k_r^0 = k_{Nu}(Nu^-) + k_{Nu}'(Nu^-)(H^+) \quad (4)$$

where k_r = experimental first-order rate constant for hydrolysis of II in the presence of Nu^- and k_r^0 = experimental first-order rate constant for hydrolysis of II in the absence of Nu^- under otherwise identical conditions. The relative magnitudes of k_{Nu} and k_{Nu}' in all cases were such that at $(H^+) < 0.10$ M the k_{Nu} term was the almost exclusive contributor to the nucleophile-catalyzed rate. All of the solutions used in this previous study[17] contained enough perchloric acid ($(H^+) > 0.01$ M) so that the $ArSO_2^-$ formed in eq 3a was immediately and completely converted to the sulfinic acid, $ArSO_2H$. Because of this the reaction $ArSO_2^- + ArS(O)Nu \rightarrow II + Nu^-$, *i.e.*, the reaction having the rate constant k_{-1}, played no role under these conditions. This was confirmed[17] by the fact that runs to which a significant amount of $ArSO_2^-$ was added initially showed the same rate as those without any added sulfinate.

This procedure of avoiding the potential complications introduced by the k_{-1} reaction *via* the expedient of operating in a medium of sufficient acidity to ensure complete protonation of all $ArSO_2^-$ produced in eq 3a is fine for hydrolyses catalyzed by nucleophiles such as I^-, Br^-, or Cl^-, which are such weak bases that they will not be protonated themselves by a medium of this acidity, but it is, of course, totally unsuited to any study of the catalysis by such nucleophiles as AcO^- or F^-, which are more basic than $ArSO_2^-$ itself. Furthermore, since preliminary experiments showed that the $ArSO_2^- + ArS(O)Nu$ reaction is indeed important under conditions where the pH of the medium is such that a significant fraction of the $ArSO_2^-$ remains unprotonated, one must take it into account when dealing with kinetic data obtained under these conditions.

For situations where the k_{-1} reaction is important $(k_r - k_r^0)$ will be given by[18]

$$k_r - k_r^0 = \frac{k_{Nu}(Nu^-)}{\left(1 + \frac{k_{-1}(ArSO_2^-)}{k_2}\right)} \quad (5a)$$

This can be written in a more useful form for our purposes as

$$\frac{1}{k_r - k_r^0} = \frac{1}{k_{Nu}(Nu^-)}\left[1 + \frac{k_{-1}(ArSO_2^-)}{k_2}\right] \quad (5b)$$

Examination of eq 5b suggests how one may obtain accurate values of k_{Nu} under conditions where the k_{-1} reaction is important. Specifically, one carries out a series of runs at constant (Nu^-) but with varying concentrations of initially added $ArSO_2^-$, the amount of $ArSO_2^-$ added being always considerably larger than the total amount of the same species that will be formed by the hydrolysis of II. These runs are carried out in a buffer whose pH is such that all $ArSO_2^-$ will remain unprotonated. One then plots $1/(k_r - k_r^0)$ for these runs *vs.* $(ArSO_2^-)$. The intercept of this plot will be $1/k_{Nu}(Nu^-)$. Since the slope of the plot is $k_{-1}/k_2 \cdot k_{Nu}(Nu^-)$, one can also obtain k_{-1}/k_2, which provides information about the behavior of the reactive sulfinyl intermediate ArS(O)Nu.

Catalysis of the Hydrolysis of IIa by Acetate Ion. The rate of hydrolysis of IIa was determined in three different acetate buffers in the presence of varying amounts of added sodium p-methoxybenzenesulfinate. The concentration of acetate ion in all three buffers was the same, but the buffer ratio of (HOAc)/(AcO^-) varied from 10 to 0.1. The results are summarized in Table I. Figure 1 shows a plot of the data for all three

Table I. Rate of Hydrolysis of IIa in 60% Dioxane in Acetate–Acetic Acid Buffers[a]

$(AcO^-) \times 10^3$, M	(HOAc)/(AcO^-)	$(ArSO_2^-) \times 10^3$, M	$k_r \times 10^3$, sec^{-1}	$[1/(k_r - k_r^0)] \times 10^{-2}$ [b]
1.03	10	2.00	5.6	2.8
		1.37	6.4	2.3
		0.72	7.6	1.8
		0.60	8.3	1.6
	1.0	2.20	5.3	3.0
		1.55	6.2	2.4
		0.71	8.1	1.6
		0.46	9.1	1.4
	0.1	1.47	6.4	2.3
		0.67	8.3	1.6
		0.42	9.5	1.3

[a] All runs at 21.4°; $(IIa)_0$, 5.0–7.0 $\times 10^{-5}$ M. [b] k_r^0 equals 2.0×10^{-3} sec^{-1}.[17]

(17) J. L. Kice and G. Guaraldi, *J. Am. Chem. Soc.*, 89, 4113 (1967).

(18) Since the k_{-1} reaction becomes important only at very low (H^+), where $k_{Nu}'(Nu^-)(H^+)$ (the acid- and nucleophile-catalyzed term in eq 4) is vanishingly small compared to $k_{Nu}(Nu^-)$, we can neglect any contribution to $(k_r - k_r^0)$ from the $k_{Nu}'(Nu^-)(H^+)$ term.

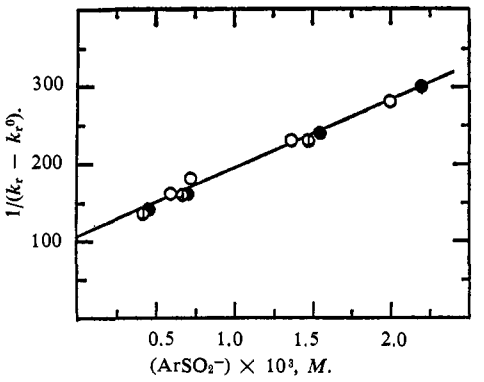
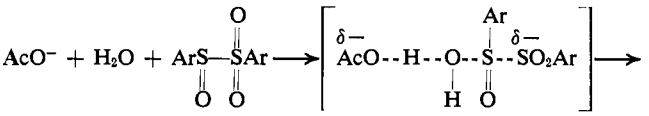


Figure 1. Hydrolysis of IIa in acetate buffers. Data of Table I plotted according to eq 5b: ○, (HOAc)/(AcO^-) = 10; ●, (HOAc)/(AcO^-) = 1.0; ⓘ, (HOAc)/(AcO^-) = 0.1.

buffers according to eq 5b. From Figure 1 one sees that the results for all three acetate buffers are nicely correlated by a single line. This proves that it is acetate ion, whose concentration is the same in all three buffers, and not hydroxide ion, whose concentration changes by 100-fold, which is responsible for the catalysis of the hydrolysis of IIa which is being observed.

The fact that added $ArSO_2^-$ depresses the rate of the acetate-catalyzed hydrolysis rules out the otherwise plausible possibility that AcO^- exerts its catalytic effect, not as shown in Chart I (Nu^- = OAc^-), but rather by acting as a general base (eq 6). Were the role of acetate



(6)

as shown in eq 6, one could not explain why added sulfinate ion retards the reaction. Such retardation is, however, readily understood in terms of the mechanism in Chart I.

From the intercept of Figure 1, k_{OAc} is calculated to be 9.0 M^{-1} sec^{-1}. From the slope one estimates k_{-1}/k_2 as 8.6×10^2.

Catalysis of the Hydrolysis of IIa by Fluoride Ion. If a second nucleophile capable of catalyzing the hydrolysis of II is added to an acetate buffer, k_r under such conditions will be given by

$$k_r = k_r^0 + \frac{k_{OAc}(AcO^-)}{\left[1 + \frac{k_{-1}(ArSO_2^-)}{k_2}\right]} + \frac{k_{Nu}(Nu^-)}{\left[1 + \frac{k_{-1}'(ArSO_2^-)}{k_2'}\right]} \quad (7a)$$

Let us define the rate of hydrolysis of IIa in the presence of acetate alone under these conditions as k_r'. This is equal to

$$k_r' = k_r^0 + \frac{k_{OAc}(AcO^-)}{\left[1 + \frac{k_{-1}(ArSO_2^-)}{k_2}\right]} \quad (7a')$$

and can be calculated from the data in Table I. Equation 7a can then be rewritten as

$$\frac{1}{k_r - k_r'} = \frac{1}{k_{Nu}(Nu^-)}\left[1 + \frac{k_{-1}'(ArSO_2^-)}{k_2'}\right] \quad (7b)$$

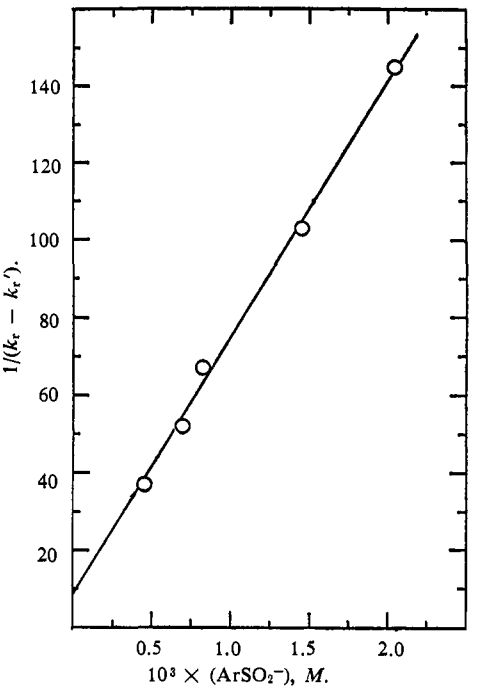


Figure 2. Hydrolysis of IIa in a 1:1 HOAc-AcO^- buffer in the presence of 9.7×10^{-3} M chloride ion. Data of Table II plotted according to eq 7b.

This indicates that k_{Nu} for the second nucleophile should be obtainable from the intercept of a plot of $1/(k_r - k_r')$ *vs.* $(ArSO_2^-)$ for a series of runs at a constant concentration of added Nu^- but varying sulfinate ion concentration.

To test the validity of this procedure a series of experiments was carried out with chloride ion as the added nucleophile, since k_{Nu} for chloride was already accurately known.[17] The data are shown in the first part of Table II and are plotted according to eq 7b in Figure 2. From the intercept of Figure 2 k_{Nu} for Cl^- is calculated to be 12 M^{-1} sec^{-1}, which is exactly the same value as that obtained from experiments under

Table II. Catalysis of the Hydrolysis of IIa by Nucleophiles in an Acetate Buffer in 60% Dioxane[a]

Nu^-, concn, M	$(ArSO_2^-) \times 10^3$, M	$k_r \times 10^3$, sec^{-1}	$k_r' \times 10^3$, sec^{-1} [b]	$(1/(k_r - k_r') \times 10^{-2}$
Cl^-, 0.97×10^{-2}	2.04	12.4	5.5	1.45
	1.45	16.0	6.3	1.03
	0.82	22.6	7.6	0.67
	0.69	27.1	8.0	0.52
	0.46	35.7	8.8	0.37
F^-, 1.07×10^{-2}	2.15	19.3	5.4	0.72
	1.52	23.5	6.1	0.58
	0.89	30.0	7.4	0.44
	0.76	34.0	7.8	0.38
	0.53	38.7	8.6	0.33
SCN^-, 0.11×10^{-2}	2.19	11.6	5.3	1.60
	1.58	14.1	6.0	1.23
	0.92	19.8	7.3	0.80
	0.84	24.2	7.6	0.60
	0.60	28.9	8.4	0.49

[a] All runs at 21.4° in a 1:1 acetate-acetic acid buffer containing 1.03×10^{-3} M acetate ion; $(IIa)_0$ equal to $4.0\text{–}7.0 \times 10^{-5}$ M. [b] k_r' calculated from eq 7a' using k_{OAc} and k_{-1}/k_2 as determined from Figure 1.

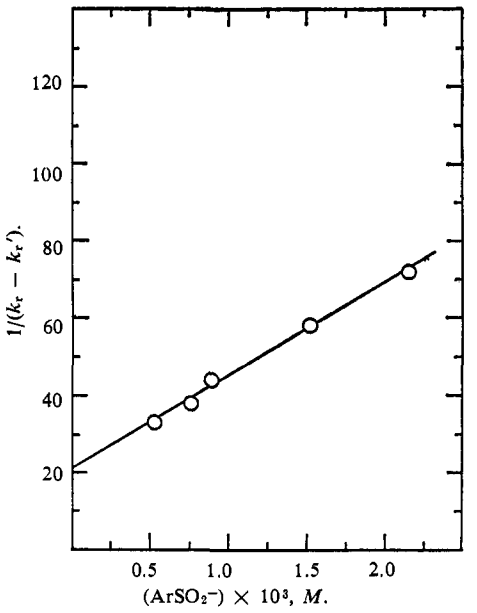


Figure 3. Hydrolysis of IIa in a 1:1 HOAc–AcO⁻ buffer in the presence of 1.07×10^{-2} M fluoride ion. Data of Table II plotted according to eq 7b.

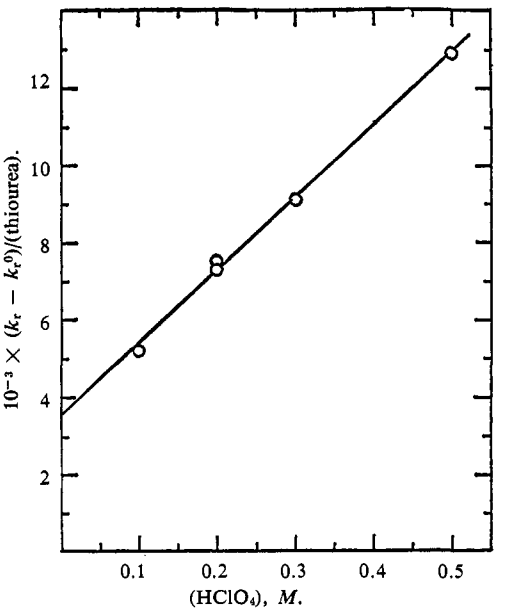


Figure 4. Hydrolysis of IIa in the presence of thiourea. Data of Table III plotted according to eq 4.

conditions where the k_{-1} reaction is not important. We conclude that accurate values of k_{Nu} can be obtained by the procedure just described.

A similar set of runs with fluoride ion as the added nucleophile is shown in the second part of Table II, and the data are plotted in Figure 3. From the plot k_{Nu} for F^- is calculated to be 4.4 M^{-1} sec^{-1} and k_{-1}'/k_2' is 1.1×10^3.

Catalysis of the Hydrolysis of IIa by Thiocyanate Ion. A set of runs was carried out in the 1:1 HOAc–AcO⁻ buffer using thiocyanate ion as the added nucleophile. These are shown in the last part of Table II. A plot of these data according to eq 7b gives an intercept from which k_{Nu} for SCN^- is estimated to be 1.5×10^2 M^{-1} sec^{-1} and a slope from which k_{-1}'/k_2' is calculated to be 1.2×10^4. Because in this instance the intercept of the plot is rather small compared to the slope, we felt that k_{Nu} could not be determined as accurately by this procedure as in the previous cases discussed.

There has been considerable uncertainty in the past regarding the pK_a of thiocyanic acid, HSCN. Recent work[19] suggested, however, that it was probably a strong enough acid so that SCN^- would not be significantly protonated at perchloric acid concentrations ($\sim$0.01 M) known[17] to be sufficient to suppress completely the k_{-1} reaction. Studies on the nucleophile- and acid-catalyzed racemization of optically active phenyl benzenethiolsulfinate reported in an accompanying paper[20] confirmed that this was so. Consequently several runs were made with SCN^- as catalyst for the hydrolysis of IIa under such conditions. These are shown in the first part of Table III. They indicate the correct value of k_{Nu} for SCN^- is 1.7×10^2 M^{-1} sec^{-1}, or slightly higher than the value estimated from the data in Table II.

(19) T. D. B. Morgan, G. Stedman, and P. A. E. Whincup, *J. Chem. Soc.*, 4813 (1965).
(20) J. L. Kice and G. B. Large, *J. Am. Chem. Soc.*, 90, 4069 (1968).

Table III. Catalysis of the Hydrolysis of IIa by Nucleophiles in Acidic 60% Dioxane[a]

Nucleophile	(Nu) × 10⁴, M	$(HClO_4)$, M	$k_r \times 10^2$, sec^{-1}	$(k_r - k_r^0)/(Nu)^b$
SCN^-	0.84	0.010	1.62	1.7×10^2
	1.21	0.013	2.2	1.7×10^2
	1.67	0.01	3.1	1.7×10^2
Thiourea	0.126	0.10	6.8	5.2×10^3
		0.20	9.4	7.3×10^3
	0.0252	0.20	2.1	7.5×10^3
		0.30	2.5	9.1×10^3
		0.50	3.4	12.9×10^3

[a] All runs a 21.4°. Initial concentration of IIa, 0.7–1.1 × 10^{-4} M. [b] k_r^0 equals rate of hydrolysis of IIa in the absence of the nucleophile under otherwise identical conditions. See ref 17 for values used.

Catalysis of the Hydrolysis of IIa by Thiourea. Catalysis of the hydrolysis of IIa by thiourea was studied under conditions ($(HClO_4)$ = 0.10–0.50 M) similar to those employed in our earlier study[17] of catalysis by iodide, bromide, or chloride. The results are shown in the second part of Table III. A plot of $(k_r - k_r^0)/(Nu)$ *vs.* $(HClO_4)$ is linear (Figure 4), as would be expected from eq 4. For thiourea k_{Nu} is 3.5×10^3 M^{-1} sec^{-1} and k_{Nu}', the rate constant for the acid- and thiourea-catalyzed hydrolysis, is 1.9×10^4 M^{-2} sec^{-1}.

Discussion

Relative Reactivity of Nucleophiles toward Sulfinyl Sulfur. Values of the rate constant k_{Nu} for reaction 8 in 60% dioxane for all nucleophiles studied are given

$$Nu^- + ArS(=O)_2SAr \xrightarrow{k_{Nu}} ArSNu + ArSO_2^- \qquad (8)$$

Ar = *p*-$CH_3OC_6H_4$

in Table IV. (The data for chloride, bromide, and iodide ion are taken from an earlier publication.[17]) Also of use in our further discussion are the values of

Table IV. Nucleophilic Reactivity toward the Sulfinyl Sulfur of IIa

Nucleophile	k_{Nu} (eq 8), M^{-1} sec^{-1} [a]	k_{Nu}/k_{Cl}
F^-	4.4	0.37
AcO^-	9.0	0.75
Cl^- [b]	12	(1.0)
Br^- [b]	65	5.4
SCN^-	1.7×10^2	14
I^- [b]	1.0×10^3	83
Thiourea	3.5×10^3	2.9×10^2

[a] All data are at 21.4° in 60% dioxane (v/v) as solvent. [b] Reference 17.

k_{Nu}/k_{Cl} shown in the last column of Table IV. These can be compared with analogous data for substitutions at other types of centers. Such data are shown in Table V for displacements at (1) peroxide oxygen[6] (eq 9), (2) sp^3 carbon[8,21] (eq 10), and (3) sulfenyl sulfur[20] (eq 11). This comparison reveals that k_{Nu}/k_{Cl} changes with nucleophile in much the same way for the substitutions at sulfinyl sulfur and sp^3 carbon. On the other hand, in the substitutions at sulfenyl sulfur or peroxide oxygen the nucleophiles iodide, thiocyanate, and thiourea are much more reactive relative to chloride than they are in eq 8 and 10. Work currently in progess in this laboratory[22] indicates that the substitution at sulfonyl sulfur in eq 12 shows yet a third type of behavior, in that nucleophiles such as Cl^- or Br^- are quite unreactive compared to such species as F^- or OAc^-.

Table V. Relative Nucleophilicity of Some Common Nucleophiles in Various Substitution Reactions

	k_{Nu}/k_{Cl}		
Nucleophile	Subst at peroxide oxygen (eq 9)[a]	Subst at sp^3 carbon (eq 10)[b]	Subst at sulfenyl sulfur (eq 11)[c]
F^-	...	0.10	...
AcO^-	*d*	0.48	...
Cl^-	(1.0)	(1.0)	(1.0)
Br^-	2.8×10^2	7.0	35
SCN^-	5.0×10^2	54	5.4×10^3
I^-	2.0×10^5	1.0×10^2	1.4×10^4
Thiourea	*e*	2.3×10^2	...

[a] Solvent, water; ref 6. [b] Solvent, water; ref 8 and 21. [c] Solvent, 60% dioxane (v/v); ref 20. [d] Too slow to measure. [e] Too fast to measure.

$$Nu^- + HOOH_2^+ \longrightarrow NuOH + H_2O \quad (9)$$

$$Nu^- + CH_3Br \longrightarrow CH_3Nu + Br^- \quad (10)$$

$$Nu^- + PhS\overset{+}{S}(OH)Ph \longrightarrow PhSNu + PhSOH \quad (11)$$

$$Nu^- + ArS(O_2)\text{—}S(O_2)Ar \longrightarrow ArS(O_2)\text{—}Nu + ArSO_2^- \quad (12)$$

Nucleophiles such as iodide, thiocyanate, and thiourea are considered by HSAB[3,9] to be much "softer" bases than chloride ion, while those such as fluoride or acetate are considered to be much "harder" bases. According to HSAB[9] soft nucleophiles react especially well with soft electrophilic centers and hard nucleophiles react especially readily with hard electrophilic centers. The fact that nucleophile reactivity in the substitution at sulfonyl sulfur (eq 12)[22] follows the pattern $F^- > AcO^- >> Cl^-$ while for the substitution at sulfinyl sulfur (eq 8) one finds $Cl^- > AcO^- > F^-$ means that sulfinyl sulfur is a much softer electrophilic center than sulfonyl sulfur. This is in accord with expectations since the sulfinyl group possesses an unshared pair of outer-shell electrons on sulfur whereas sulfonyl sulfur does not; sulfinyl sulfur also has a lower positive charge on sulfur. Both these factors should made it a softer electrophilic center.[9]

The different response of k_{Nu}/k_{Cl} to changes in Nu^- for substitution at sulfinyl (eq 8) and sulfenyl (eq 11) sulfur is discussed in detail in an accompanying paper.[20] There it is concluded that the results indicate that sulfenyl sulfur is a significantly softer electrophilic center than sulfinyl sulfur, and that sulfenyl sulfur is actually quite a soft electrophilic center. The series –SX, –S(O)X, and $-SO_2X$ would thus seem to span quite a range as far as hardness or softness of the sulfur atom as an electrophilic center is concerned, with sulfinyl sulfur occupying an intermediate position between the quite soft sulfenyl center and the quite hard sulfonyl center.

The reasonably close similarity in the k_{Nu}/k_{Cl} values for substitution at >S(O) (eq 8) and sp^3 carbon (eq 10) suggests that the two centers are about alike as far as softness is concerned. Since the carbon of a methyl group has been classed[9] as a "medium soft" electrophilic center, this would suggest that the same term should be applied to sulfinyl sulfur.

Two factors, however, prevent one from being completely dogmatic about this conclusion. The first is that the data for eq 10 were obtained in water as solvent, while those for eq 8 were obtained in 60% dioxane. Although we feel that both media are sufficiently aqueous solvents so that there should be no sizable solvent effect on k_{Nu}/k_{Cl} of the type encountered[23] when one compares data for a given substitution reaction in protic *vs.* aprotic solvents, there could be a small solvent effect, and, if there were, it would be such as to make the values of k_{Nu}/k_{Cl} for eq 8 in Table IV somewhat smaller than they would be in water for those nucleophiles softer than Cl^-, and somewhat larger than they would be in water for those nucleophiles harder than Cl^-. The net effect would be that a comparison of the data in Tables IV and V would make sp^3 carbon appear somewhat softer relative to >S(O) than is actually the case.

The second potential source of some uncertainty is that the leaving groups in the two reactions are not the same. Pearson and Songstad[9] have noted that having a soft base as the leaving group in a substitution can apparently enhance the reactivity of a given center toward soft nucleophiles, while having a hard base as the leaving group can make it more reactive toward hard nucleophiles. They call this a symbiotic effect. If Br^- is actually a significantly harder base than $ArSO_2^-$, the comparison of k_{Nu}/k_{Cl} for eq 8 and 10 could tend to make sp^3 carbon appear somewhat harder relative to sulfinyl sulfur than is actually the case.

(21) C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, 75, 141 (1953).
(22) G. J. Kasperek, unpublished results.
(23) A. J. Parker, *J. Chem. Soc.*, 1328, 4398 (1961).

One notes that any solvent effect and any symbiotic effect would tend to compensate each other. For this reason, plus the fact that we doubt that either is very large, we believe one can probably conclude with reasonable certainty that sulfinyl sulfur represents a medium soft electrophilic center analogous to sp^3 carbon.

An interesting aspect of the data for eq 8 in Table IV is that fluoride ion is not a great deal less reactive than chloride ion ($k_F/k_{Cl} = 0.37$). Mislow, *et al.*,[10] have reported that, whereas aryl alkyl sulfoxides racemize readily in aqueous dioxane containing 4 *M* HCl, they are unaffected by aqueous dioxane containing a similar concentration of HF. The present results suggest that the failure of HF to racemize sulfoxides is not due to any lack of reactivity of fluoride ion toward tricoordinate sulfur. Presumably it must therefore be due to the much lower acidity of the hydrofluoric acid solution.

Experimental Section

Preparation and Purification of Materials. The preparation or purification of most of the reagents has already been described.[17] Sodium fluoride, potassium thiocyanate, sodium acetate, and thiourea were all Analytical Reagent grade and were in general further purified by recrystallization before use.

Procedure for Kinetic Runs. The same procedure outlined in an earlier paper[17] was followed in all cases.

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General Acid Catalysis of Acetal Hydrolysis. The Hydrolysis of 2-Aryloxytetrahydropyrans

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Abstract: The rates of acid-catalyzed hydrolysis of a series of 2-alkoxy- and 2-aryloxytetrahydropyrans have been measured in 50% dioxane–H_2O. The value of ρ determined for hydrolysis of 2-(*para*-substituted phenoxy)tetrahydropyrans is −0.92. The D_2O solvent isotope effect (k_{D_2O}/k_{H_2O}) progressively decreases as electron withdrawal in the leaving group becomes greater: from 2.82 for 2-ethoxytetrahydropyran to 1.33 for 2-(*p*-nitrophenoxy)-tetrahydropyran. The value of ΔS^* likewise becomes considerably more negative: +7.9 eu in the case of the ethoxy derivative and −7.6 eu in the case of 2-(*p*-nitrophenoxy)tetrahydropyran Thus, it is likely that, as C–O bond breaking becomes easier and at the same time basicity of the acetal decreases, the solvent becomes more involved in the critical transition state with the most probable mechanism for the aryloxy derivatives involving partially rate-determining protonation by hydronium ion. General acid catalysis by formate buffers was also observed for hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran and 2-(*p*-chlorophenoxy)tetrahydropyran.

There is little doubt that the acid-catalyzed hydrolysis of acetals generally involves preequilibrium protonation of the acetal followed by a unimolecular rate-determining decomposition to an alcohol and a resonance-stabilized carbonium ion.[1] The recent findings, however, of possible participation by solvent,[2,3] buffer,[2] and neighboring functional groups[4–7] in the rate-determining step of hydrolysis reactions of certain types of acetals are of great importance in regard to the insight provided into the mechanistic possibilities which glycosidic enzymes could be employing. The structural features that will facilitate such mechanisms over the normal A1 mechanism have not as yet been clearly established.

Carboxyl group participation has been postulated to occur in the hydrolysis of *o*-carboxyphenyl β-D-glucoside[4] and 2-methoxymethoxybenzoic acid[5] although the mechanism of the participation is not definitely established. With aliphatic glycosides, 2-carboxyethyl and carboxymethyl β-D-glucopyranoside, however, carboxyl group participation was not observed,[8] nor was intramolecular carboxyl group participation detected in the hydrolysis of ketals of aliphatic alcohols.[9] Piszkiewicz and Bruice[7] did, however, find evidence for neighboring acetamido group participation with *o*- and *p*-nitrophenyl 2-acetamido-2-deoxyglucopyranosides. Thus, glycoside hydrolysis reactions in which neighboring functional groups have been found to participate involve substituted phenoxy derivatives in which the leaving group is quite good in comparison to glycosides of aliphatic alcohols, but with which protonation will be more difficult. However, a systematic study of the effect of the leaving group on the mechanism of acetal or glycoside hydrolysis has not been made. Therefore, the hydrolysis reactions of a series of 2-alkoxy- and 2-aryloxytetrahydropyrans have been studied. These tetrahydropyran derivatives offer several advantages for study over the corresponding glycosides including

(1) For the evidence which has led to this mechanism and the pertinent references, see E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1967).
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