Procedure for Kinetic Runs. A standard solution of the α-disulfone in dioxane was prepared and the proper volume of this solution was pipetted into the reaction flask of an apparatus of the same type as that used previously to follow the kinetics of the disproportionation of sulfinic acids,[29] or the thiolsulfinate-sulfinic acid reaction.[30] The proper volumes of standard aqueous solutions of perchloric acid and lithium perchlorate were then pipetted into the same reaction vessel, and the solutions were thoroughly mixed. The final solution was deaerated by bubbling nitrogen through it and the apparatus for 5 min. The reaction vessel was then immersed in a constant-temperature bath, and after 5 min, to allow the solution to reach bath temperature, an initial aliquot was removed and quickly cooled to room temperature by chilling it in ice-water. The absorbance of this aliquot was then measured at the wavelength corresponding to the λ_{max} of the α-disulfone in dioxane. (These wavelengths have already been listed for three of the α-disulfones used. For the remaining two, they were 244 mμ for Ar = C_6H_5 and 258 mμ for Ar = p-$CH_3C_6H_4$.) Other aliquots were removed at appropriate time intervals over 2–3 reaction half-lives and an infinity point was taken after 8–10 half-lives. The absorbances of these various samples were determined in the same way as for the initial point. The absorbance of the infinity point was close to zero for every α-disulfone except the p-MeO compound. In that case a solution having an initial optical density of 0.75 gave an optical density for the infinity point of 0.16. In all cases plots of log $(A - A_\infty)$ *vs.* time showed excellent linearity.

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(29) J. L. Kice and K. W. Bowers, *J. Am. Chem. Soc.*, **84,** 605 (1962).

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

The Relative Nucleophilicity of Some Common Nucleophiles toward Sulfonyl Sulfur. The Nucleophile-Catalyzed Hydrolysis and Other Nucleophilic Substitution Reactions of Aryl α-Disulfones[1a]

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Abstract: The relative reactivity of nine common nucleophiles in a displacement reaction at sulfonyl sulfur (eq 2) in 60% dioxane has been determined from either kinetic data on their catalysis of the hydrolysis of aryl α-disulfones (**2**) or, in the case of primary and secondary amines and azide ion, from direct measurement of their rate of reaction with **2**. These data for sulfonyl sulfur (Table VII) are compared in Table VIII with data for some of these same nucleophiles in an exactly analogous displacement at sulfinyl sulfur (eq 1). The substitution at sulfonyl sulfur shows an entirely different pattern of nucleophile reactivity ($F^- \gg AcO^- \gg Cl^- > Br^- > H_2O$) than the one at sulfinyl sulfur ($Br^- > Cl^- \cong AcO^- > F^- \gg H_2O$). Interpreted in terms of the theory of hard and soft acids and bases (HSAB) these results indicate that sulfonyl sulfur is a much harder electrophilic center than sulfinyl sulfur, exactly as HSAB would have predicted it should be. Comparison of the data for sulfonyl sulfur with analogous data on nucleophilic reactivity in a substitution at another hard electrophilic center, carbonyl carbon (Table IX), reveals that the order of reactivity of the various nucleophiles toward sulfonyl sulfur ($RNH_2 > N_3^- > F^- > NO_2^- > AcO^-$) is about the same as toward carbonyl carbon.

In protic solvents the relative reactivity of a group of nucleophiles in a substitution reaction can change quite markedly with a change in the nature of the electrophilic center at which the substitution takes place.[2] In general, nucleophiles which are of low polarizability and high electronegativity, so-called "hard" bases,[3] enjoy an advantage over other nucleophiles in substitutions at centers such as carbonyl carbon[4] or tetracoordinate phosphorus.[5] Nucleophiles which are of high polariazability and low electronegativity, so-called "soft" bases,[3] react particularly readily in substitutions involving centers such as Pt^{II} [6] or peroxide oxygen.[7] A thoughtful and thorough analysis of these effects was first given by Edwards and Pearson.[8] More recently, Pearson and Songstad[9] have shown that the data can also be nicely rationalized using the concepts of the theory of hard and soft acids and bases (HSAB).

In an earlier study[10] the relative reactivity of a series of common nucleophiles toward sulfinyl sulfur was determined by measurement of the rates of a series of nucleophilic substitutions involving aryl sulfinyl sulfones (eq 1). The present paper shows that similar data for nucleophilic substitution at sulfonyl sulfur can be obtained from measurement of the rates of analogous substitutions of aryl α-disulfones (eq 2). Since eq 1 and 2 involve the same leaving group ($ArSO_2$) and have been studied in the same solvent (60% dioxane), comparison of the results for the two systems allows one to evaluate in a completely unequivocal manner what effect a change in substitution site from sulfinyl to sulfonyl sulfur has on the relative reactivity of various nucleophiles.

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(1) (a) This research supported by the National Science Foundation, Grant GP-6952; (b) NDEA Fellow, 1966–1969; (c) NSF Summer Undergraduate Research Participant, 1968.

(2) J. O. Edwards, "Inorganic Reaction Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1965, pp 51–72.

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

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

(5) Reference 2, pp 59–63, 177–180.

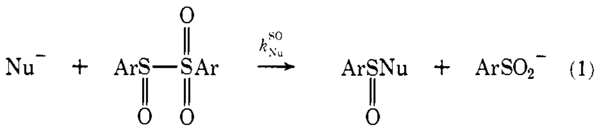
(6) R. G. Pearson, H. Sobel, and J. Songstad, *J. Am. Chem. Soc.*, **90,** 319 (1968).

(7) J. O. Edwards, "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, New York, N. Y., 1962, pp 67–106.

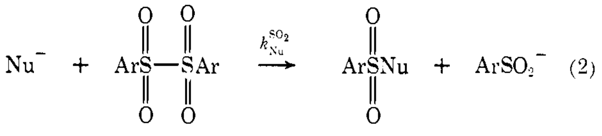
(8) J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84,** 16 (1962).

(9) R. G. Pearson and J. Songstad, *ibid.*, **89,** 1827 (1967).

(10) J. L. Kice and G. Guaraldi, *ibid.*, **90,** 4076 (1968).



$$\mathrm{Nu^-} + \mathrm{Ar}\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}-\overset{\mathrm{O}}{\overset{\|}{\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}}}\mathrm{Ar} \xrightarrow{k_{\mathrm{Nu}}^{\mathrm{SO}}} \mathrm{Ar}\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}\mathrm{Nu} + \mathrm{ArSO_2^-} \quad (1)$$



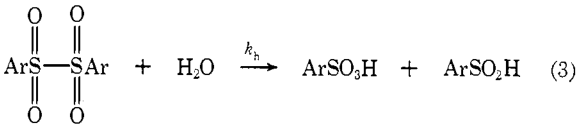
$$\mathrm{Nu^-} + \mathrm{Ar}\overset{\mathrm{O}}{\overset{\|}{\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}}}-\overset{\mathrm{O}}{\overset{\|}{\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}}}\mathrm{Ar} \xrightarrow{k_{\mathrm{Nu}}^{\mathrm{SO_2}}} \mathrm{Ar}\overset{\mathrm{O}}{\overset{\|}{\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}}}\mathrm{Nu} + \mathrm{ArSO_2^-} \quad (2)$$

2

HSAB theory[9] would predict that sulfonyl sulfur should be a significantly harder electrophilic center than sulfinyl sulfur. Expressed in terms of the concepts used by Edwards and Pearson[8] this means that the basicity and electronegativity, rather than the polarizability, of a series of nucleophiles should be paramount in determining their order of relative reactivity toward sulfonyl sulfur, in contrast to the situation with sulfinyl sulfur[10] where polarizability, electronegativity, and basicity are all three important. The objective of the present work was to investigate the extent to which this prediction was in fact borne out by experiment by (1) suitable comparison of the results for sulfinyl and sulfonyl sulfur from eq 1 and 2 and by (2) comparing the behavior of sulfonyl sulfur with that of other centers, like carbonyl carbon, where basicity and electronegativity are thought to be the principal factors determining relative reactivity of a series of nucleophiles in substitutions at that center.

Results

The procedure for obtaining data on the reactivity of nucleophiles in the reaction shown in eq 2 varied with the nucleophile involved. Thus, with some nucleophiles, such as primary or secondary amines or azide ion, the product $\mathrm{ArSO_2Nu}$ was not readily hydrolyzed further in 60% dioxane, and kinetic measurements on such systems gave the rate of conversion of the α-disulfone to $\mathrm{ArSO_2Nu}$. On the other hand, with other nucleophiles, such as acetate or fluoride ion, the product $\mathrm{ArSO_2Nu}$ underwent rapid hydrolysis to the sulfonic acid. In such systems what one can study kinetically is the catalysis of the hydrolysis of α-disulfones (eq 3) by the nucleophile.



$$\mathrm{Ar}\overset{\mathrm{O}}{\overset{\|}{\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}}}-\overset{\mathrm{O}}{\overset{\|}{\underset{\mathrm{O}}{\underset{\|}{\mathrm{S}}}}}\mathrm{Ar} + \mathrm{H_2O} \xrightarrow{k_{\mathrm{h}}} \mathrm{ArSO_3H} + \mathrm{ArSO_2H} \quad (3)$$

Catalysis of the Hydrolysis of α-Disulfones by Added Nucleophiles. The hydrolyses of the α-disulfones were followed spectrophotometrically using the same procedure described in an accompanying paper.[11] Plots of log $(A - A_\infty/A_0 - A_\infty)$ *vs.* time showed excellent linearity in every case.

Catalysis by Acetate Ion. The rate of hydrolysis of phenyl α-disulfone (**2a**, Ar = $\mathrm{C_6H_5}$) was measured in a variety of acetate buffers in 60% dioxane at four different temperatures. The results are summarized in Table I. The following points are worth noting. (1) A series of runs at 80.3° at different buffer ratios ranging from $(\mathrm{HOAc})/(\mathrm{AcO^-}) = 10$ to $(\mathrm{HOAc})/(\mathrm{AcO^-}) = 0.10$, but with a fixed $(\mathrm{AcO^-})$ concentration, show that there is no significant dependence of k_h on the buffer ratio. This demonstrates that it is acetate ion, not hydroxide ion, which is responsible for all the increase in rate of hydrolysis which is observed. (2) Plots of k_h *vs.* $(\mathrm{AcO^-})$ are linear in all cases, showing that the rate of the acetate-catalyzed reaction is proportional to the first power of acetate ion concentration. (3) The slopes of such plots are equal to k_OAc, the actual second-order rate constant for the acetate ion catalyzed hydrolysis. (4) The last two runs in the table show that k_OAc exhibits only a very small solvent isotope effect $(k_\mathrm{OAc}{}^{\mathrm{H_2O}}/k_\mathrm{OAc}{}^{\mathrm{D_2O}}) = 1.1$.

Table I. Catalysis of the Hydrolysis of Phenyl α-Disulfone by Acetate Ion in 60% Dioxane[a]

Temp, °C	$(\mathrm{AcO^-}) \times 10^3$, *M*	$(\mathrm{HOAc}) \times 10^3$, *M*	$k_\mathrm{h} \times 10^4$, sec^{-1}	k_OAc,[b] M^{-1} sec^{-1}
90.8	0.43	0.43	3.8	0.34
	0.72	0.72	4.6	
	1.08	1.08	5.7	
	1.44	1.44	7.1	
	1.80	1.80	8.0	
	2.17	2.17	9.0	
80.3	4.0	40.0	7.6	0.18
	4.0	4.0	7.7	
	4.0	0.40	8.2	
	1.0	1.0	2.9	
	1.0	10.0	3.1	
	2.0	2.0	4.2	
	3.0	3.0	5.5	
	5.0	5.0	9.2	
67.9	3.6	3.6	3.2	0.076
	7.2	7.2	6.0	
	10.8	10.8	8.4	
54.9	0.00	0.00	0.19	0.033
	3.6	3.6	1.6	
	5.8	5.8	2.4	
	7.2	7.2	2.7	
	9.4	9.4	3.4	
	13.0	13.0	4.6	
	14.4	14.4	5.1	
	18.0	18.0	6.1	
	100	100	33.5	
	100	100	30.8 ($\mathrm{D_2O}$)	$(k_\mathrm{OAc}{}^{\mathrm{H_2O}}/k_\mathrm{OAc}{}^{\mathrm{D_2O}}) = 1.1$

[a] Initial concentration of **2a**, 5×10^{-5} *M*. [b] Evaluated from slope of plot of k_h *vs.* $(\mathrm{AcO^-})$.

From a plot of log k_OAc *vs.* $1/T$ one calculates the following activation parameters for the acetate-catalyzed hydrolysis: $E_\mathrm{a} = 15.6$ kcal/mole; $\Delta S^{\ddagger} = -19.8$ eu.

Catalysis by Fluoride Ion. The rate of hydrolysis of **2a** was measured at four different temperatures spanning a 60° temperature range in 1:1 $\mathrm{HOAc{-}AcO^-}$ buffers containing varying amounts of added fluoride ion. The results are summarized in the first part of Table II. Figure 1 shows a plot of k_h *vs.* $(\mathrm{F^-})$ for the data at 80.3°. Equally good linear relationships between k_h and $(\mathrm{F^-})$ were obtained at the other three temperatures.

The values of k_F for **2a** calculated from these plots are given in the last column of the table. From a plot of log k_F *vs.* $1/T$ one estimates $E_\mathrm{a} = 14.4$ kcal/mole and $\Delta S^{\ddagger} = -15.9$ eu for the fluoride-catalyzed reaction of **2a**.

Effect of Aryl Group Structure on k_F. The variation of k_F with changes in the structure of the aryl group of the α-disulfone was investigated at 21.3° using **2a**, **2b** (Ar = p-$\mathrm{CH_3C_6H_4}$), **2c** (Ar = p-$\mathrm{ClC_6H_4}$), and **2d** (Ar = p-$\mathrm{CH_3OC_6H_4}$). The data for **2b–d** are shown in the last three sections of Table II. A plot of the log k_F values for **2a–d** *vs.* σ for the *para* substituent of the aryl group gives a good straight line with a slope, ρ, of +5.0. (One

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[11] J. L. Kice and G. J. Kasperek, *J. Am. Chem. Soc.*, 91, 5510 (1969).

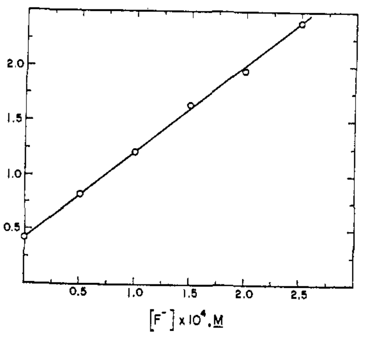


Figure 1. Fluoride ion catalyzed hydrolysis of **2a** in 60% dioxane at 80.3°. Plot of k_h *vs.* (F^-) for a series of runs in a 1:1 HOAc-AcO^- buffer 0.002 *M* in AcO^-.

will recall that the spontaneous hydrolysis of **2**[11] also shows a large positive ρ value, +3.5.)

Catalysis by Chloride and Bromide Ion. In contrast to the marked catalysis of the hydrolysis of **2a** by very small concentrations ($\sim 10^{-4} M$) of added fluoride ion, even quite large concentrations of chloride or bromide ion have only a small effect on the hydrolysis rate. This can be seen from Table III which summarizes the data obtained with these additives at 80.3°.

Table II. Catalysis of the Hydrolysis of Aryl α-Disulfones by Fluoride Ion in 60% Dioxane[a]

$ArSO_2SO_2Ar$, Ar =	Temp, °C	(AcO^-) in 1:1 HOAc-AcO^-, buffer, *M*	(F^-) $\times$ 10^4, *M*	$k_h \times 10^3$, sec^{-1}	k_F, M^{-1} sec^{-1} [b]
C_6H_5	80.3	0.002	0.50	0.82	
			1.0	1.21	7.8
			1.5	1.64	
			2.0	1.95	
			2.5	2.4	
	54.9	0.002	2.0	0.43	
			3.0	0.60	1.8
			4.0	0.79	
			5.0	0.99	
	36.0	0.020	4.0	0.27	
			12.0	0.65	
			20.0	0.94	0.39
			28.0	1.20	
			40.0	1.68	
	21.3	0.020	8.0	0.13	
			16.0	0.23	
			24.0	0.34	0.126
			32.0	0.43	
			40.0	0.54	
			50.0	0.66	
			50.0[c]	0.64	
p-ClC_6H_4	21.3	0.020	3.2	0.95	
			6.4	1.33	
			9.6	1.65	1.20
			12.8	2.16	
			16.0	2.45	
p-$CH_3C_6H_4$	21.3	0.020	20	0.053	
			40	0.092	
			60	0.13	0.018
			80	0.17	
			100	0.19	
p-$CH_3OC_6H_4$	21.3	0.020	16	0.0073	
			40	0.016	
			60	0.022	0.0034
			80	0.029	
			100	0.034	

[a] Initial concentration of **2**, 5×10^{-5} *M*. [b] Evaluated from slope of plot of k_h *vs.* (F^-); see Figure 1 for an example. [c] Benzenesulfinic acid, 0.001 *M*, added initially.

Table III. Hydrolysis of Phenyl α-Disulfone in the Presence of Added Chloride or Bromide in 60% Dioxane

Temp, °C	($HClO_4$), *M*	($LiClO_4$), *M*	(Cl^-), *M*	(Br^-), *M*	$k_h \times 10^4$, sec^{-1}	k_{Cl} or k_{Br}, M^{-1} sec^{-1} [a]
80.3	0.01	0.40	0.00		1.13	
		0.30	0.10		1.42	
		0.20	0.20		1.72	0.00030
		0.10	0.30		2.02	
		0.00	0.40		2.36	
80.3	0.01	0.20		0.20	1.47	
		0.10		0.30	1.63	0.00017
		0.00		0.40	1.80	

[a] Calculated from slope of a plot of k_h *vs.* (X^-).

From a plot of k_h *vs.* (Cl^-) one finds that k_{Cl} has a value of only 3×10^{-4} M^{-1} sec^{-1} at 80.3°, or only about 4/100,000 the rate constant for the fluoride ion catalyzed reaction at the same temperature.

A similar plot of the data for bromide ion yields a value for k_{Br} of 1.7×10^{-4} M^{-1} sec^{-1} for the same reaction conditions.

Catalysis by Nitrite Ion. This anion, which is intermediate between acetate and fluoride in its catalytic effectiveness, was studied in the same manner as for fluoride ion. The results are given in Table IV. From plots of k_h *vs.* (NO_2^-) the values of k_{NO_2} shown in the last column of the table were obtained. A plot of log k_{NO_2} *vs.* $1/T$ yields $E_a = 12.9$ kcal/mole and $\Delta S^{\ddagger} = -24.6$ eu for the activation parameters of the nitrite ion catalyzed hydrolysis of **2a**.

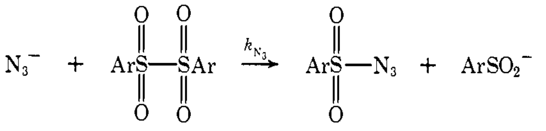
Table IV. Catalysis of the Hydrolysis of Aryl α-Disulfones by Nitrite Ion in 60% Dioxane[a]

$ArSO_2SO_2Ar$, Ar =	Temp, °C	(AcO^-) in 1:1 HOAc-AcO^- buffer, *M*	(NO_2^-) $\times$ 10^3 *M*	$k_h \times 10^4$ sec^{-1}	k_{NO_2}, M^{-1} sec^{-1} [b]
C_6H_5	80.3	0.002	0.50	8.7	
			1.0	12.3	0.79
			1.5	16.5	
	67.9	0.002	0.30	4.3	
			0.60	5.1	
			0.90	6.5	0.47
			1.2	8.4	
			1.5	9.2	
	54.9	0.002	0.60	2.3	
			0.90	2.9	0.20
			1.2	3.5	
			1.5	4.0	
	39.7	0.002	0.60	0.84	
			0.90	1.10	
			1.2	1.32	0.082
			1.5	1.55	
p-$CH_3C_6H_4$	80.3	0.002	0.00	1.24	
			0.50	2.28	0.20
			1.0	3.3	
			1.5	4.2	

[a] Initial concentration of **2**, 5×10^{-5} *M*. [b] Calculated from slope of plot of k_h *vs.* (NO_2^-) at each temperature.

A series of runs with **2b** at 80.3° (last part of Table IV) showed that k_{NO_2} for that compound was only $0.26k_{NO_2}$ for **2a** under the same conditions, thereby further demonstrating what we have already seen from the fluoride-catalyzed reactions, *i.e.*, that the rate constants are very sensitive to changes in the structure of the aryl group.

Reaction of α-Disulfones with Sodium Azide. Reaction of sodium azide ($0.0125M$) with **2b** ($0.005M$) in 60% dioxane gave a 90% yield of *p*-toluenesulfonyl azide (**3b**). The kinetics of this reaction can be followed spectrophotometrically by the same type of procedure used to follow the hydrolysis of **2b**, although a slightly smaller over-all change in optical density is involved. The results of such a kinetic study are given in Table V. A large excess of azide ion over **2b** was employed so that the disappearance of **2b** followed first-order kinetics. A plot of k_1, the experimental first-order rate constant, *vs.* (N_3^-) was linear. From its slope k_{N_3} for **2b** is found to be 0.115 M^{-1} sec^{-1} at 21.3°.



$$N_3^- + ArSO_2\text{—}SO_2Ar \xrightarrow{k_{N_3}} ArSO_2\text{—}N_3 + ArSO_2^- \quad (4)$$

3

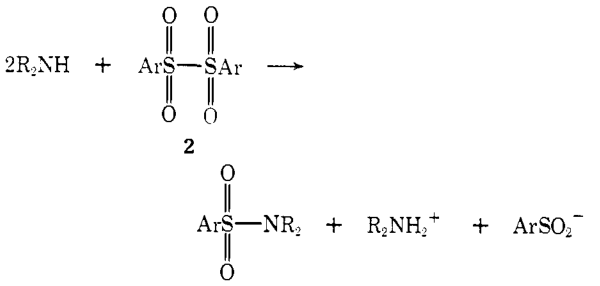
Table V. Reaction of Azide Ion with *p*-Tolyl α-Disulfone in 60% Dioxane at 21.3° [a]

$(\mathbf{2b})_0 \times 10^5$, M	$(N_3^-) \times 10^2$, M	$k_1 \times 10^3$, sec^{-1} [b]	k_{N_3}, M^{-1} sec^{-1} [c]
7.0	2.0	2.24	
	1.6	1.96	
	1.2	1.41	0.115
	0.80	0.97	
	0.40	0.47	

[a] Initial concentration of **2b**, 7×10^{-5} M. Ionic strength maintained at 0.04 in all runs by addition of lithium perchlorate. [b] Experimental first-order rate constant for disappearance of **2b**. [c] Evaluated from slope of a plot of log k_1 *vs.* (N_3^-).

Because of absorption by azide ion at the wavelength maximum for **2a** the kinetics of its reaction with azide could not be followed.

Reaction of Primary and Secondary Amines with α-Disulfones. Primary and secondary amines are known[12] to react with aryl α-disulfones to give sulfonamides (eq 5). In neutral or weakly alkaline 60% dioxane the sulfonamides do not themselves hydrolyze at an appreciable rate.



$$2R_2NH + ArSO_2\text{—}SO_2Ar \longrightarrow ArSO_2\text{—}NR_2 + R_2NH_2^+ + ArSO_2^- \quad (5)$$

2

Although one might think that hydroxide ion, formed from

$$R_2NH + H_2O \rightleftharpoons R_2NH_2^+ + OH^-$$

would be able to compete with the amine for the α-disulfone, it turns out that primary and secondary *n*-alkylamines are sufficiently reactive that in a 1 : 1 amine–alkylammonium salt buffer containing 0.01 M or more amine the reaction with the amine (eq 5) is the only process of importance.

The kinetics of eq 5 can be followed spectrophotometrically in the same general way as the hydrolysis of **2**. All of the α-disulfone–amine reactions were studied under conditions where the amine was present in at least 100-fold stoichiometric excess over **2**, so that the disappearance of the α-disulfone followed first-order kinetics. The results are summarized in Table VI. Plots of the experimental first-order rate constant for the disappearance of **2b**, k_1, *vs.* [amine] are linear in all cases. The slope of the plot of k_1 *vs.* [amine] is in each case equal to k_{Nu}, the second-order rate constant for eq 2 with Nu^- = amine. These rate constants are shown in the last column of Table VI.

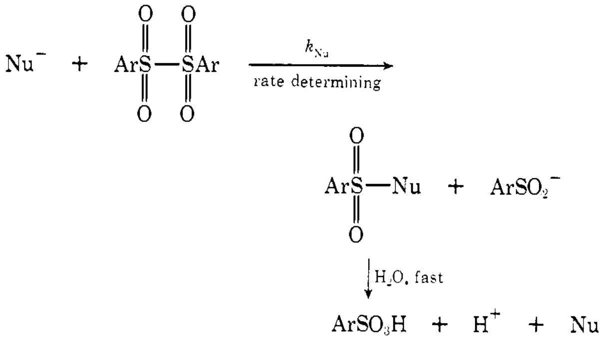
Table VI. Reaction of Primary and Secondary Amines with *p*-Tolyl α-Disulfone in 60% Dioxane at 21.3° [a]

Amine	$(\mathbf{2b})_0 \times 10^5$, M	(Amine) $\times 10^2$, M [b]	(Amine-H^+) $\times 10^2$, M	$k_1 \times 10^3$, sec^{-1} [c]	k_{amine}, M^{-1} sec^{-1} [d]
n-BuNH$_2$	5.0	2.4	2.4	79	
		2.0	2.0	67	
		1.6	1.6	48	3.3
		1.2	1.2	37	
		0.80	0.80	26	
Et$_2$NH	5.0	4.0	4.0	10.2	
		3.6	3.6	8.6	
		2.8	2.8	6.9	0.24
		2.0	2.0	5.1	
		0.80	0.80	2.2	
i-BuNH$_2$	5.0	3.2	3.2	51	
		2.8	2.8	45	1.6
		2.0	2.0	33	
		0.8	0.8	13.2	

[a] Ionic strength maintained at 0.04 in all runs by addition of lithium perchlorate. [b] Solutions prepared by adding calculated amount of HCl to solution of the amine. [c] Experimental first-order rate constant for disappearance of **2b**. [d] Evaluated from slope of plot of k_1 *vs.* (amine).

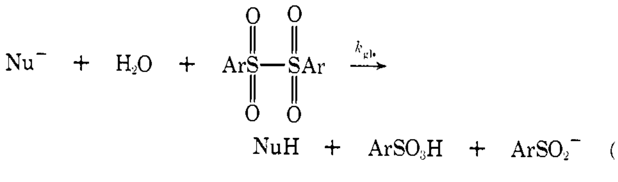
Discussion

Mechanism of the Nucleophile-Catalyzed Hydrolysis of α-Disulfones. In principle catalysis of the hydrolysis of **2** by added nucleophiles could be due either to nucleophilic catalysis (eq 6) or to general base catalysis by the nucleophile of the attack of water on **2** (eq 7). Measurement of the solvent isotope effect associated



$$Nu^- + ArSO_2\text{—}SO_2Ar \xrightarrow[\text{rate determining}]{k_{Nu}} ArSO_2\text{—}Nu + ArSO_2^- \quad (6)$$

$$ArSO_2\text{—}Nu \xrightarrow{H_2O,\ \text{fast}} ArSO_3H + H^+ + Nu^-$$



$$Nu^- + H_2O + ArSO_2\text{—}SO_2Ar \xrightarrow{k_{gb}} NuH + ArSO_3H + ArSO_2^- \quad (7)$$

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(12) H. J. Backer, *Rec. Trav. Chim.*, **70**, 254 (1951).

with the acetate ion catalyzed hydrolysis revealed that $(k_{\mathrm{H_2O}}^{\mathrm{OAc}}/k_{\mathrm{D_2O}}^{\mathrm{OAc}})$ was only 1.1. This is entirely consistent with the nucleophilic catalysis mechanism in eq 6 and totally inconsistent with eq 7, since all previous examples where acetate functions as a general base catalyst in the manner shown in eq 7 have been associated with much larger solvent isotope effects, ranging from 1.7 to 2.7.[13]

Since, even though they are both weaker bases than acetate ion, fluoride and nitrite are both much better catalysts for the hydrolysis of **2**, it seems mandatory that if acetate is acting as a nucleophilic catalyst they must also be functioning in that capacity. Chloride and bromide ion have never been observed to act as general base catalysts for hydrolysis reactions, and so their weak catalytic effect on the present reaction must also be due to nucleophilic catalysis.

We thus conclude that in every case the catalysis of the hydrolysis of **2** by the various nucleophiles studied in the present work involves nucleophilic catalysis according to the mechanism shown in eq 6. Furthermore, since initial addition of $\mathrm{ArSO_2^-}$ in large excess over that which is formed by hydrolysis of **2** (see runs with **2a** at 21.3° in Table II for an example) does not lead to any decrease in the rate, the attack of the nucleophiles on **2** must be the rate-determining step of the nucleophile-catalyzed hydrolyses. As a result the second-order rate constants (k_{OAc}, k_{F}, etc,) for the different nucleophile-catalyzed hydrolyses are in each instance the rate constant ($k_{\mathrm{Nu}}^{\mathrm{SO_2}}$ of eq 2) for the attack of the nucleophile on the sulfonyl group of **2**.

For those nucleophiles, like azide ion or the primary and secondary amines, which form stable products $\mathrm{ArSO_2Nu}$ on reaction with **2**, the second-order rate constants ($k_{\mathrm{N_3}}$, k_{amine}) for their reactions with the α-disulfone are obviously also equal to $k_{\mathrm{Nu}}^{\mathrm{SO_2}}$ for those nucleophiles.

Relative Reactivity of Nucleophiles toward Sulfonyl Sulfur. Values of $k_{\mathrm{Nu}}^{\mathrm{SO_2}}$ for reaction 2 ($\mathrm{Ar} = \mathrm{C_6H_5}$) in 60% dioxane at 21.3° for all nucleophiles studied are given in Table VII. (The values for the primary and secondary amines are calculated from the rate constants for the reactions of these nucleophiles with **2b** ($\mathrm{Ar} = p\text{-}\mathrm{CH_3C_6H_4}$) assuming that $k_{\mathrm{Nu}}^{\mathrm{SO_2}}$ shows the same dependence on Ar as does the spontaneous hydrolysis of **2**,[11] another reaction involving attack of an uncharged nucleophile on **2**. In the case of azide ion we assumed that $k_{\mathrm{N_3}}$ for **2a** would be greater than that measured for **2b** by the same factor by which k_{F} for these two α-disulfones differs.) One sees that the spread in reactivity between the most reactive nucleophile studied, *n*-butylamine, and the least reactive, bromide ion, is about 10^7. Also noteworthy is the fact that fluoride ion is over 10^4 more reactive toward sulfonyl sulfur than either chloride or bromide ions. Azide ion is even more reactive than fluoride ion by a factor of 6.

Table VII. Reactivity of Nucleophiles toward Phenyl α-Disulfone

Nucleophile	$k_{\mathrm{Nu}}^{\mathrm{SO_2}}$ (eq 2), M^{-1} sec$^{-1\,a}$	$(k_{\mathrm{Nu}}^{\mathrm{SO_2}}/k_{\mathrm{OAc}}^{\mathrm{SO_2}})$
n-$\mathrm{BuNH_2}$	13	5.9×10^3
i-$\mathrm{BuNH_2}$	6.4	2.9×10^3
$\mathrm{Et_2NH}$	0.96	4.4×10^2
$\mathrm{N_3^-}$	0.72	3.3×10^2
$\mathrm{F^-}$	0.13	59
$\mathrm{NO_2^-}$	0.022	10
$\mathrm{AcO^-}$	0.0022	(1.0)
$\mathrm{Cl^-}$	$3.5 \times 10^{-6\,b}$	0.0016^c
$\mathrm{Br^-}$	$2.0 \times 10^{-6\,b}$	0.0009^c

[a] All data are at 21.3° in 60% dioxane as solvent. [b] Calculated from data at 80.3° assuming $k_{\mathrm{Cl}}^{\mathrm{SO_2}}$ and $k_{\mathrm{Br}}^{\mathrm{SO_2}}$ show the same dependence on temperature as $k_{\mathrm{OAc}}^{\mathrm{SO_2}}$. [c] Measured at 80.3°.

For comparison with data on the relative reactivity of various nucleophiles toward other centers, it is advantageous to express the data for sulfonyl sulfur in terms of the relative reactivity of each nucleophile compared to that of acetate ion as the standard. These values of $(k_{\mathrm{Nu}}^{\mathrm{SO_2}}/k_{\mathrm{OAc}}^{\mathrm{SO_2}})$ are given in the last column of Table VII.

Comparison of the Reactivity of Nucleophiles toward Sulfonyl and Sulfinyl Sulfur. The reactivity ($k_{\mathrm{Nu}}^{\mathrm{SO}}$) of a series of nucleophiles in a nucleophilic substitution at the sulfinyl group of *p*-anisyl *p*-methoxybenzenesulfinyl sulfone (eq 1, $\mathrm{Ar} = p\text{-}\mathrm{CH_3OC_6H_4}$) was measured in an earlier study.[10] Since eq 1 and 2 have been studied in the same solvent (60% dioxane) and both involve an arenesulfinate ion ($\mathrm{ArSO_2^-}$) as the leaving group, comparison of $(k_{\mathrm{Nu}}^{\mathrm{SO}}/k_{\mathrm{OAc}}^{\mathrm{SO}})$ for eq 1 with $(k_{\mathrm{Nu}}^{\mathrm{SO_2}}/k_{\mathrm{OAc}}^{\mathrm{SO_2}})$ for the same nucleophiles in eq 2 provides an unambiguous indicator of the change in relative reactivity of the various nucleophiles caused by a change in substitution site from sulfinyl to sulfonyl sulfur. The relevant data for those nucleophiles for which data are available for both eq 1 and eq 2 are shown in Table VIII. Inspection of this table reveals that *the change in substitution site from sulfinyl to sulfonyl sulfur leads to an almost complete reversal in the reactivity order of the various nucleophiles.* Toward sulfinyl sulfur the relative reactivity of the nucleophiles is in the order $\mathrm{Br^-} > \mathrm{Cl^-} \cong \mathrm{AcO^-} > \mathrm{F^-} >>> \mathrm{H_2O}$, an order both qualitatively and quantitatively similar to that found for SN2 substitutions at sp^3 carbon.[14] On the other hand, toward sulfonyl sulfur the relative reactivity of the same nucleophiles is in the order $\mathrm{F^-} \gg \mathrm{OAc^-} \gg \mathrm{Cl^-} > \mathrm{Br^-} > \mathrm{H_2O}$, fluoride and acetate being now both much more reactive than chloride or bromide. Note, however, that with the two oxygen nucleophiles, acetate and water, $(k_{\mathrm{H_2O}}^{\mathrm{SO}}/k_{\mathrm{OAc}}^{\mathrm{SO}})$ is about the same as $(k_{\mathrm{H_2O}}^{\mathrm{SO_2}}/k_{\mathrm{OAc}}^{\mathrm{SO_2}})$, even though in both instances acetate is much more reactive than water.

Table VIII. Relative Nucleophilicity toward Sulfinyl *vs.* Sulfonyl Sulfur[a]

Nucleophile	Sulfinyl sulfur $(k_{\mathrm{Nu}}^{\mathrm{SO}}/k_{\mathrm{OAc}}^{\mathrm{SO}})$ in eq 1	Sulfonyl sulfur $(k_{\mathrm{Nu}}^{\mathrm{SO_2}}/k_{\mathrm{OAc}}^{\mathrm{SO_2}})$ in eq 2
$\mathrm{Br^-}$	7.2	0.0009
$\mathrm{Cl^-}$	1.3	0.0016
$\mathrm{OAc^-}$	(1.0)	(1.0)
$\mathrm{F^-}$	0.49	59
$\mathrm{H_2O}$	$1.1 \times 10^{-5\,b}$	$3.0 \times 10^{-5\,b}$

[a] All data are for 60% dioxane as solvent. For eq 1 $\mathrm{Ar} = p\text{-}\mathrm{MeOC_6H_4}$: for eq 2, $\mathrm{Ar} = \mathrm{C_6H_5}$. [b] $k_{\mathrm{H_2O}}^{\mathrm{SO}}$ and $k_{\mathrm{H_2O}}^{\mathrm{SO_2}}$ are the rates of spontaneous hydrolysis of **1** (ref 10) and **2** (ref 11), respectively.

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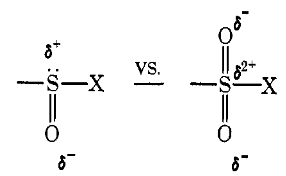
(13) For a compilation, see S. L. Johnson, "Advances in Physical Organic Chemistry," Vol. 5, V. Gold, Ed., Academic Press, New York, N. Y., 1967, p 281.

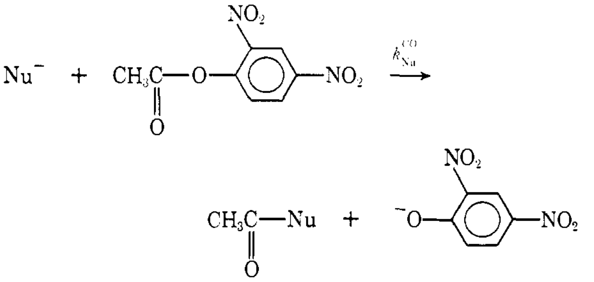
(14) See ref 10 for a full discussion of this point.

In the terminology of HSAB[3] nucleophiles like fluoride ion, acetate ion, or water are considerably harder bases than chloride or bromide ions. The application of HSAB to nucleophilic substitution reactions[9] leads to the conclusion that hard nucleophiles should react particularly readily with hard electrophilic centers and soft nucleophiles with soft electrophilic centers. *The HSAB interpretation of the results in Table VIII would accordingly be that sulfonyl sulfur represents a much harder electrophilic center than sulfinyl sulfur.*

Is this in accord with what HSAB theory would have predicted in advance about these two centers? According to HSAB, two of the principal factors which tend to make an electrophilic center hard are (1) the absence of unshared pairs of easily excited outer shell electrons on the atom being attacked and (2) a high positive charge on that atom.[15] Sulfinyl sulfur has an unshared pair of outer shell electrons on sulfur; sulfonyl sulfur does not. Because of the dipolar character of an $>S^{\delta+}{=}O^{\delta-}$ bond sulfonyl sulfur also has a significantly higher positive charge on sulfur than does sulfinyl sulfur. HSAB would have predicted that the combination of these two effects should make sulfonyl sulfur a much harder electrophilic center than sulfinyl sulfur, and this is just what we have found experimentally.



Comparison of the Reactivity of Nucleophiles toward Sulfonyl Sulfur and Carbonyl Carbon. Thanks to the work of Jencks and Gilchrist,[16] data are available on the reactivity of a wide range of nucleophiles toward both 2,4-dinitrophenyl acetate (eq 8) and 1-acetoxy-4-methoxypyridinium perchlorate, 4 (eq 9). With all nucleophiles studied the rate-determining step in eq 9 is without doubt the attack of the nucleophile on the carbonyl carbon of 4, *not* the breakdown of the tetrahedral intermediate 5. The same is probably true for most nucleophiles in eq 8. Jencks and Gilchrist's[16] data therefore provide an accurate measure of the relative reactivity of the various nucleophiles toward carbonyl carbon, another hard electrophilic center.



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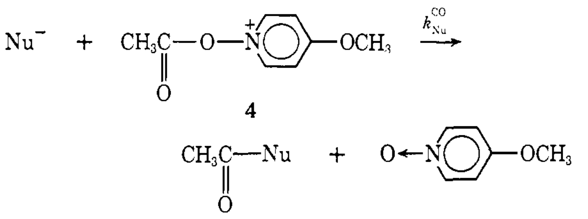

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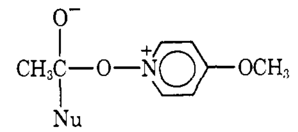

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Values of $(k_{Nu}^{CO}/k_{OAc}^{CO})$ for both eq 8 and 9 are shown in Table IX for all those nucleophiles studied by Jencks and Gilchrist[16] for which $(k_{Nu}^{SO_2}/k_{OAc}^{SO_2})$ is also available for eq 2. One sees that the pattern of relative reactivities is roughly the same for sulfonyl sulfur and carbonyl carbon. Thus for sulfonyl sulfur the relative reactivity of the various nucleophiles is in the order $n\text{-BuNH}_2 \gg N_3^- > F^- > NO_2^- > AcO^- \gg H_2O$, while for carbonyl carbon in eq 8 or 9 it is $n\text{-BuNH}_2 \gg N_3^- \gg NO_2^- > F^- > AcO^- \gg H_2O$. The only difference is the reversal in the order of relative reactivities of fluoride and nitrite, the former being more reactive toward sulfonyl sulfur but less reactive toward carbonyl carbon. Since it is likely that fluoride ion is a harder base than nitrite or acetate ion, this difference *perhaps* suggests that sulfonyl sulfur is a somewhat harder electrophilic center than carbonyl carbon. Because of the difference in the nature of the leaving group in eq 2 as compared to eq 8 and 9 and the fact that the latter two reactions were studied in water rather than 60 %dioxane, this conclusion must be considered to be strictly tentative, however.

Table IX. Relative Nucleophilicity toward Sulfonyl Sulfur *vs.* Carbonyl Carbon

Nucleophile	Sulfonyl sulfur[a]	Carbonyl carbon[b]	
	$(k_{Nu}^{SO_2}/k_{OAc}^{SO_2})$ in eq 2	$(k_{Nu}^{CO}/k_{OAc}^{CO})$ in eq 8	$(k_{Nu}^{CO}/k_{OAc}^{CO})$ in eq 9
n-BuNH$_2$	5.9×10^3	2.1×10^{5c}	3.1×10^{3c}
N_3^-	3.3×10^2	1.7×10^3	3.5×10^2
F^-	59	5.6	3.3
NO_2^-	10	15	7.7
AcO^-	(1.0)	(1.0)	(1.0)
H_2O	3×10^{-5d}	3.5×10^{-4}	2×10^{-4}

[a] Solvent, 60% dioxane; temperature, 21.3°; Ar = C_6H_5. [b] Solvent, water; temperature, 25°. [c] Data are for n-PrNH$_2$ rather than for n-BuNH$_2$ [d] $k_{H_2O}^{SO_2}$ is the spontaneous rate of hydrolysis of 2 (ref 11)

One other aspect of the results deserves comment. Azide ion is usually classified by HSAB as a base of hardness comparable to chloride ion. As such its high reactivity toward hard electrophilic centers like sulfonyl sulfur and carbonyl carbon is surprising. Perhaps a partial answer to this dilemma is provided if we remember that azide ion is a much stronger base than chloride ion, and in terms of the oxibase scale equation

$$\log (k/k_0) = \alpha E + \beta H$$

which Davis[17] has proposed to correlate nucleophilic reactivity in various substitutions, the βH term (H = pK_a of NuH + 1.74) should be very important in deter-

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[15] The other principal factor, the size of the atom, is not important here because for both sulfinyl and sulfonyl sulfur we are dealing with attack at sulfur.

[16] W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **90**, 2622 (1968).

[17] R. E. Davis, "Organosulfur Chemistry," M. J. Janssen, Ed., Interscience Publishers, New York, N. Y., 1967, pp 311-328; R. E. Davis, "Survey of Progress in Chemistry," Vol. 2, A. F. Scott, Ed., Academic Press, New York, N. Y., 1964, pp 189-238.

mining the rates of substitutions at hard electrophilic centers. Since H for N_3^- is 6.46 while that for Cl^- is about -3 one can see how azide ion could be much more reactive in substitutions at this type of center than chloride ion.

Experimental Section

Preparation and Purification of Materials. The preparation and purification of the various α-disulfones have been described in an accompanying paper,[11] as was the purification of the dioxane used as solvent. Lithium bromide, sodium bromide, and sodium fluoride were all reagent grade and were recrystallized from distilled water and dried before using. Sodium acetate, sodium nitrite, acetic acid, and sodium azide were all reagent grade and were used without further purification. The various amines were of the highest purity obtainable from Matheson Coleman and Bell and were further purified by distillation from barium oxide before use.

Reaction of 2b with Sodium Azide. *p*-Tolyl α-disulfone (**2b**), 0.62 g (2.00 mmoles), and sodium azide, 0.33 g (5.0 mmoles), were dissolved in 400 ml of 60% dioxane (v/v) and the solution was heated for 5 hr at 60°. The solution was then evaporated to dryness under reduced pressure. The residue was treated with a mixture of water and ether. The ether layer was washed first with dilute sulfuric acid, then with dilute sodium hydroxide, and finally with water. The ether layer was then dried over anhydrous magnesium sulfate and the ether was evaporated under reduced pressure. The residue crystallized upon being cooled and scratched with a stirring rod: yield, 0.35 g (90%) of *p*-toluenesulfonyl azide; mp 22° (lit.[18] mp 22°); infrared spectrum identical with that of a known sample prepared by the method of Curtius.[18]

Procedure for Kinetic Runs on the Catalysis of the Hydrolysis of 2 by Added Nucleophiles. The exact procedure depended on the temperature at which the run was to be carried out. For those runs carried out at temperatures *higher* than 21.3° the procedure was as follows. A standard solution of the α-disulfone was prepared in dioxane and the proper volume of this solution was pipetted into the reaction flask of the same apparatus used in an accompanying paper[11] to study the uncatalyzed hydrolysis of **2**. The proper volumes of standard aqueous solutions of the other reagents required were then pipetted into the same reaction vessel, and the solutions were thoroughly mixed. From this point on, the procedure was the same as that used for following the uncatalyzed hydrolysis.[11]

For the runs at 21.3° the apparatus employed was that used by Kice and Guaraldi[19] in studying the hydrolysis of **1** in 60% dioxane. To make a run, 3 ml of a standard solution of the α-disulfone in freshly distilled dioxane was placed in chamber A of this apparatus, and 2 ml of an aqueous solution containing all the remaining reagents was placed in chamber B. The apparatus was then immersed in the constant-temperature bath. After 5 min the two solutions were rapidly mixed, and the resulting solution was transferred to chamber C of the apparatus, a 1-cm spectrophotometer cell. The apparatus was then immediately placed in a thermostated cell holder inside a Cary Model 15 spectrophotometer, and the progress of the hydrolysis of **2** was monitored spectrophotometrically at the same wavelengths used[11] for the uncatalyzed hydrolysis.

Procedure for Kinetic Studies of the Reaction of Azide with 2b. The general procedure was the same as for the runs at 21.3° with the catalyzed hydrolysis. However, because of the absorption of sodium azide in the 240-mμ range, the kinetics of the disappearance of **2b** were followed at 275 mμ, rather than at 258 mμ. At 275 mμ **2b** still has an appreciable absorption but azide does not.

Procedure for Kinetic Studies of the Reaction of Amines with 2b. The general procedure was exactly the same as that used for studying the other reactions of **2b** at 21.3°. The disappearance of the α-disulfone was followed spectrophotometrically at 270 mμ. The 1:1 RNH_2-RNH_3^+ buffer solutions were prepared by adding the calculated amount of standard hydrochloric acid solution to a standard solution of the amine in water.

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(18) T. Curtius and G. Kraemer, *J. Prakt. Chem.*, **125**, 323 (1930).

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

Pyrolysis of Azabullvalenes and 7-Azabicyclo[4.2.2]deca-2,4,7,9-tetraenes. Unsaturated Heterocyclic Systems. LXII[1,2]

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Contribution from the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210. *Received April 1, 1969*

Abstract: 8-Methoxy-7-azabicyclo[4.2.2]deca-2,4,7,9-tetraene (**1a**) and methoxyazabullvalene (**2a**) heated at 600° in the gas phase give an identical mixture containing quinoline (75%), 2-methoxyquinoline (10%), 1-methoxyisoquinoline (7%), and 3-methoxyisoquinoline (1%), in addition to several very minor products. Under the same conditions, the 2- and 9-methyl derivatives of **1a** and the methyl homolog of **2a** yield chiefly methylquinolines (> 95%). Most notably, methyl-**2a** affords all seven possible methylquinolines, with 2-methylquinoline predominating (32%). In contrast, the 2- and 9-methyl derivatives of **1a** give only six methylquinolines, the 2 isomer being totally absent. The thermal aromatization of **1a** and **2a** is one which most likely passes through a common intermediate; this intermediate, however, must become nonidentical when a single methyl group is placed on the two structures, despite the fact that considerable methyl scrambling occurs. A mechanistic scheme is proposed to account for these interesting and unprecedented observations.

Mechanistically intriguing thermal rearrangements of polyunsaturated hydrocarbons have recently gained the attention of numerous researchers.[3,4] Current interest in such interconversions has been heightened by the awareness that orbital symmetry factors[5] may

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[1] For the previous paper in this series, see L. A. Paquette, J. R. Malpass, G. R. Krow, and T. J. Barton, *J. Am. Chem. Soc.*, **91**, 5296 (1969).

[2] The authors are grateful to the National Institutes of Health, the Alfred P. Sloan Foundation, and the Lilly Research Laboratories for grants which contributed to the financial support of this research.

[3] (a) G. Schröder, *Chem. Ber.*, **97**, 3140 (1964); (b) E. E. van